



# Effective Health Care Program

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Comparative Effectiveness Review  
Number 65

## **Interventions for Adolescents and Young Adults With Autism Spectrum Disorders**



Agency for Healthcare Research and Quality  
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# *Comparative Effectiveness Review*

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Number 65

## **Interventions for Adolescents and Young Adults With Autism Spectrum Disorders**

**Prepared for:**

Agency for Healthcare Research and Quality  
U.S. Department of Health and Human Services  
540 Gaither Road  
Rockville, MD 20850  
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## Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices and health care services to meet the needs of Medicare, Medicaid, and the Children's Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting comparative effectiveness reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see [www.effectivehealthcare.ahrq.gov/reference/purpose.cfm](http://www.effectivehealthcare.ahrq.gov/reference/purpose.cfm)

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input from are essential to the Effective Health Care Program. Please visit the Web site ([www.effectivehealthcare.ahrq.gov](http://www.effectivehealthcare.ahrq.gov)) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

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

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# Interventions for Adolescents and Young Adults With Autism Spectrum Disorders

## Structured Abstract

**Objectives.** We systematically reviewed evidence on therapies for adolescents and young adults (ages 13 to 30) with autism spectrum disorders (ASD). We focused on the outcomes, including harms and adverse effects, of interventions addressing the core symptoms of ASD; common medical and mental health comorbidities occurring with ASD; the attainment of goals toward functional/adult independence; educational and occupational/vocational attainment; quality of life; access to health and other services; and the transitioning process (i.e., process of transitioning to greater independent functioning). We also addressed the effects of interventions on family outcomes including parent distress and satisfaction with interventions.

**Data sources.** We searched MEDLINE® via PubMed, PsycINFO®, the Educational Resources Information Clearinghouse, and the Cumulative Index of Nursing and Allied Health Literature databases as well as the reference lists of included studies.

**Review Methods.** We included studies published in English from January 1980 to December 2011. We excluded intervention studies with fewer than 20 adolescents or young adults with ASD or fewer than 20 parents or family members of such individuals and studies lacking relevance to ASD treatment.

**Results.** We identified 32 unique studies, most of which were poor quality. Five studies, mostly of medical interventions, were fair quality, and none were good. In the behavioral literature, studies of group- and computer-based interventions reported short-term gains in social skills. Two poor-quality studies of educational interventions reported some gains in vocabulary and reading. Four small studies investigated disparate interventions addressing highly specific adaptive/life skills with some positive results in studies typically of short duration. Studies of vocational interventions, all of poor quality, reported that on-the-job supports may promote employment in the community. Little evidence supports the use of medical interventions in adolescents and young adults with ASD; however, antipsychotic medications and serotonin reuptake inhibitors were associated with improvements in specific challenging behaviors. Similarly, little evidence supports the use of allied health interventions including facilitated communication.

**Conclusions.** Few studies have been conducted to assess treatment approaches for adolescents and young adults with ASD, and as such there is very little evidence available for specific treatment approaches in this population; this is especially the case for evidence-based approaches to support the transition of youth with autism to adulthood. Of the small number of studies available, most were of poor quality, which may reflect the relative recency of the field. Five studies, primarily of medical interventions, had fair quality. Behavioral, educational, and adaptive/life skills studies were typically small and short term and suggested some potential improvements in social skills and functional behavior. Small studies suggested that vocational programs may increase employment success for some individuals. Few data are available to support the use of medical or allied health interventions in the adolescent and young adult

population. The medical studies that have been conducted focused on the use of medications to address specific challenging behaviors, including irritability and aggression, for which effectiveness in this age group is largely unknown and inferred from studies including mostly younger children.



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# Executive Summary

## Background

Autism Spectrum Disorders (ASD) are among the most common neurodevelopmental disorders, with an estimated prevalence of 1 in 110 children in the United States having an ASD.<sup>1</sup> ASDs are typically diagnosed in early childhood, often at or before preschool age. The diagnosis is fundamentally behaviorally based (i.e., there is no specific genetic test or clinical/laboratory procedure for diagnosis) and rests on documented core impairments related to social interaction, communication, as well as restricted and repetitive behavior.

Diagnoses made by clinical providers, often pediatricians, behavioral providers, child neurologists, child psychiatrists, or child psychologists, are based on documented symptom patterns in these domains. Numerous screening and diagnostic tools are available to help document and measure symptoms of autism, with research investigations increasingly utilizing such measures in combination with clinical diagnoses in order to more accurately describe, measure, and analyze the heterogeneity in presentation associated with ASD. In addition to impairments in core symptom areas, many individuals with ASD also have impaired cognitive skills, atypical sensory behaviors, or other complex medical and psychiatric symptoms and conditions, such as seizure disorders, motor impairments, hyperactivity, anxiety, and self-injury/aggression.

More than 55,000 individuals between the ages of 15 and 17 in the United States likely have an ASD.<sup>2</sup> For some individuals, core symptoms of ASD (impairments in communication and social interaction and restricted/repetitive behaviors and interests) may improve with intervention and over time<sup>3-5</sup>; however, some degree of impairment typically remains throughout the lifespan.<sup>6</sup> As children transition to adolescence and young adulthood, developmentally appropriate interventions to ameliorate core deficits may continue, but the focus of treatment often shifts toward promoting adaptive behaviors that can facilitate and enhance independent functioning.<sup>6</sup> Treatments for some must take into account new emergent symptoms as well as engagement with new developmental challenges (e.g., independent living, vocational engagement, postsecondary education).

There is also evidence to suggest that improvements in symptoms and improvements in problem behaviors may slow down or stop after youth with ASD leave high school.<sup>7</sup> This change in improvement is likely due, at least in part, to the termination of services received through the secondary school system upon high school exit, as well as the lack of adult services and long waiting lists for many services.<sup>7,8</sup> This issue of the lack of services available to help young adults with ASD transition to greater independence has been noted by researchers for a number of years and is increasingly a topic in the lay media.<sup>9</sup>

## Interventions Used To Treat ASD

Individuals with ASD have significant impairments in social interaction, communication, and repetitive behavior. As noted, some people with ASD also have impaired cognitive skills, atypical sensory behaviors, or other complex medical and psychiatric symptoms and conditions. The expression and severity of ASD symptoms differ widely across individuals and over time. Treatments may include a range of behavioral, psychosocial, educational, medical, and

complementary approaches focused on the transitional process and improving outcomes for parents/families of individuals with ASD during adolescence and adulthood.

## **ASD in Adolescence and Young Adulthood**

Current data suggest that attainment of independent living or employment in adulthood for individuals with an ASD is variable, with factors that predict the ability to live and work independently not well elucidated.<sup>6</sup> Research conducted to date has suggested that most individuals with ASD will require some sort of intervention, often at very intensive levels, throughout adolescence and adulthood, and the estimated costs of medical and nonmedical care (e.g., special education, daycare) are high. One study estimates that the total yearly societal per capita cost of caring for and treating a person with autism in the United States at \$3.2 million and at about \$35 billion for an entire birth cohort of individuals with autism.<sup>10</sup> A study of health care utilization in a large group health plan revealed increased medication costs in older children with an ASD compared with younger children, as well as similarly aged adolescents without an ASD; other care costs were also higher in this population, including a significantly increased rate of hospitalizations.<sup>11</sup>

Costs of transitional and employment programs are also high for young adults with ASD. In a recent analysis of U.S. Federal- and State-funded vocational rehabilitation programs, enrolled individuals with ASD were among the most costly of nine disability groups, with costs even higher among those with ASD and another concomitant disability. However, those with ASD had a higher rate of employment (40.8%) at the time of case closure compared with those with other disabilities, though with fewer work hours and lower wages than some other disability groups.<sup>12</sup>

There is no cure for ASD and no global consensus regarding which intervention strategies are most effective. Chronic management, often using multiple treatment approaches, may be required to maximize ultimate functional independence and quality of life by minimizing core ASD features, facilitating development and learning, promoting socialization, reducing maladaptive behaviors, and educating and supporting families. Investigators have noted that less data on therapies for adolescents or young adults exist than for younger children,<sup>13</sup> and such research is increasingly important as the prevalence of ASD continues to grow and as children with ASD diagnoses reach adolescence.

## **Objectives**

The goal of this review is to examine the effects of available interventions on adolescents and young adults with ASD, focusing on the following outcomes: core symptoms of ASD (impairments in social interaction, communication, and repetitive behavior); medical and mental health comorbidities; functional behaviors and independence; the transition to adulthood; and family outcomes.

## **Population**

We focused this review on therapies for adolescents and young adults (ages 13 to 30) with ASD as well as interventions aimed at family members.

## **Interventions**

Studies assessed interventions falling into the broad categories of behavioral, educational, adaptive/life skills, vocational, medical, and allied health approaches.

## Comparators

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

## Outcomes

Intermediate outcomes included changes in core ASD symptoms and in common medical and mental health comorbidities as well as effects on functional behavior, the transition process, and family outcomes. Long-term outcomes included changes in adaptive/functional independence, academic and occupational attainment or engagement, psychological well-being, and psychosocial adaptation. We also assessed the harms of interventions, defined by the Agency for Healthcare Research and Quality (AHRQ) Effective Health Care program as all possible adverse consequences of an intervention, including adverse events (Figure A).<sup>14</sup>

## Key Questions

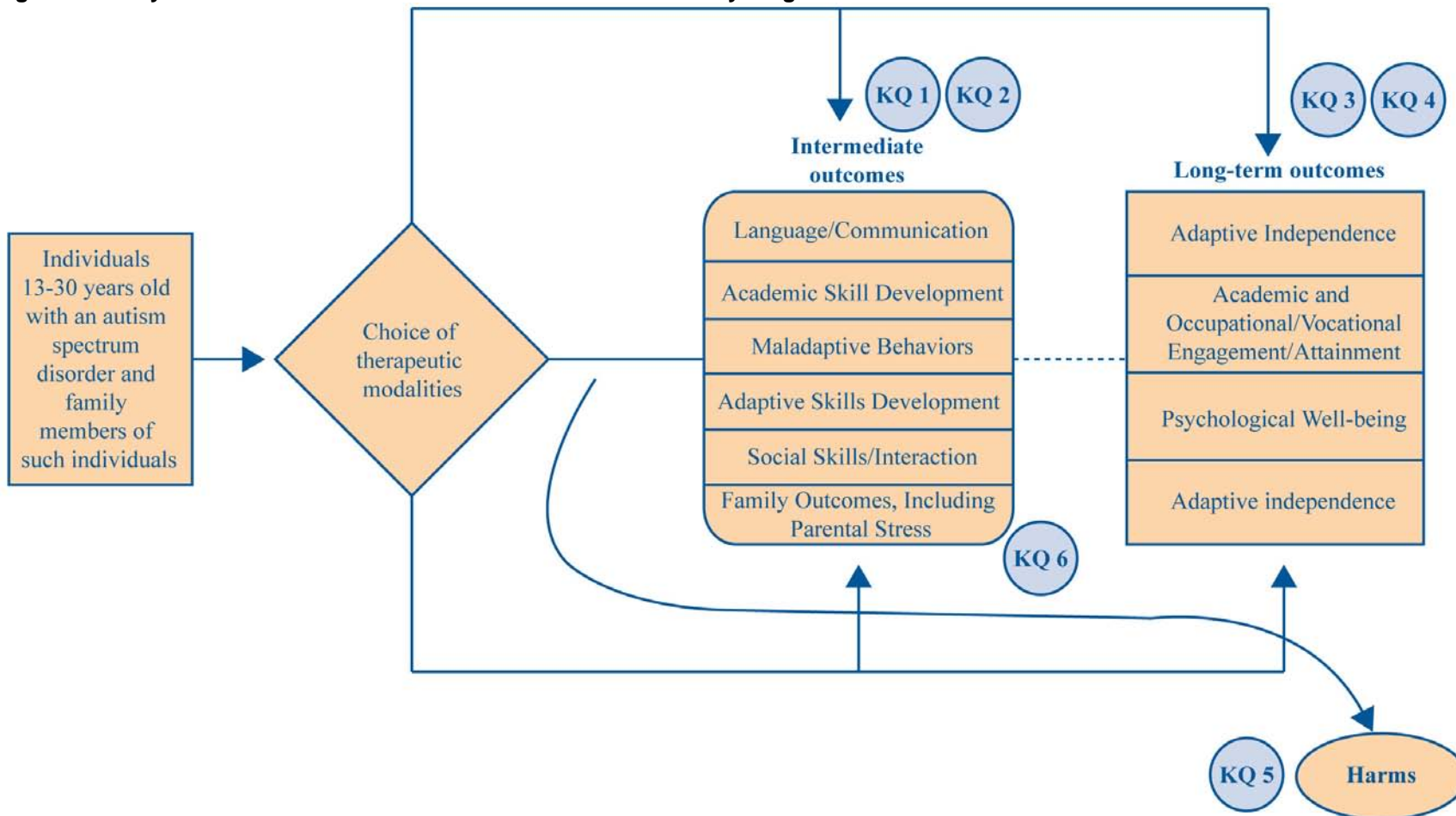
We have synthesized evidence in the published literature to address these Key Questions:

- **Key Question 1:** Among adolescents and young adults with ASD, what are the effects of available interventions on the core symptoms of ASD?
- **Key Question 2:** Among adolescents and young adults with ASD, what are the effects of available interventions on common medical and mental health comorbidities (e.g., epilepsy, sleep disorders, motor impairments, obesity, depression, anxiety, acute and episodic aggression, attention deficit hyperactivity disorder, etc.)?
- **Key Question 3:** Among adolescents and young adults with ASD, what are the effects of available interventions on functional behavior, attainment of goals toward independence, educational attainment, occupational/vocational attainment, life satisfaction, access to health and other services, legal outcomes, and social outcomes?
- **Key Question 4:** Among adolescents and young adults with ASD, what is the effectiveness of interventions designed to support the transitioning process, specifically to affect attainment of goals toward independence, educational attainment, occupational/vocational attainment, life satisfaction, access to health and other services, legal outcomes, and social outcomes?
- **Key Question 5:** Among adolescents and young adults with ASD, what harms are associated with available interventions?
- **Key Question 6:** What are the effects of interventions on family outcomes?

## Analytic Framework

The analytic framework summarizes the process by which individuals with ASD and their families/caregivers make and modify treatment choices (Figure A). Treatment choices may target intermediate outcomes including changes in communication skills, academic skill development, or social skills. Interventions lead to long-term outcomes such as adaptive independence and changes in psychosocial well-being. Family outcomes such as parent distress may also be targeted by interventions and may lead in turn to long-term outcomes. Finally, interventions may be associated with harms/adverse effects. Numbers in circles within the diagram indicate the placement of Key Questions in relation to the treatment process.

Figure A. Analytic framework for interventions for adolescents and young adults with ASD



KQ = Key Question

## Methods

### Input From Stakeholders

The topic was nominated in a public process. With key informant input, we drafted initial Key Questions, which were reviewed by AHRQ and posted to a public Web site for public comment. Using public input, we drafted final Key Questions, which were reviewed 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 available for public comment.

### Data Sources and Selection

#### Data Sources

We searched four databases: MEDLINE® via the PubMed interface, PsycINFO® (psychology and psychiatry literature), the Educational Resources Information Clearinghouse, and the Cumulative Index of Nursing and Allied Health Literature database. We used a combination of controlled vocabulary terms appropriate for each database (e.g., MEDLINE vocabulary term autistic disorder) and keywords related to ASD (e.g., Asperger syndrome). Appendix A of the full report details each search strategy. We hand searched reference lists of included articles and recent reviews for additional studies.

#### Inclusion and Exclusion Criteria

We included all study designs except single case reports provided that studies reported on an intervention aimed at individuals with ASD between the ages of 13 and 30 or family members of such individuals. We excluded studies that:

- Were not original research
- Did not report information pertinent to the Key Questions
- Did not address treatment modalities aimed at core symptoms of ASD, common comorbidities, functional/life skills outcomes, family-related outcomes, or assisting with the transition to adulthood
- Did not include aggregate data (i.e., included only individual data for each participant) or data presented only in graphics/figures
- Were single case reports
- Were not published in English
- Were published before 1980 and the publication of autism diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition.

We also excluded studies that included fewer than 20 total participants in the target age range with ASD or family members of such individuals. Our goal was to identify and review the best evidence for assessing the efficacy and effectiveness of therapies for adolescents and young adults with ASD, with an eye toward utility in the treatment setting.

Interventions to address ASDs are frequently behavioral in nature and highly intensive. They are also frequently adapted to be targeted to specific study participants given the significant heterogeneity of individuals with ASD. In part because this makes behavioral research complex and intensive, study sizes tend to be very small. A cutoff sample size of 20 provides a balance,



allowing us to review and comment on adequate literature for the review but with studies large enough to suggest effects of the interventions.

## Screening of Studies

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 tables. After initial data extraction, a second team member edited entries for accuracy, completeness, and consistency. In addition to outcomes for treatment effectiveness and family outcomes, 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) using a quality assessment methodology adapted from that used in a prior AHRQ review of therapies for children with ASD.<sup>15</sup> We resolved differences 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, and Table A describes the quality ratings.

**Table A. Description of study quality levels**

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

## Data Synthesis and Analysis

### Evidence Synthesis

We used summary tables to synthesize studies and summarized the results qualitatively.

### Strength of the Evidence

The degree of confidence that the observed effect of an intervention is unlikely to change is presented as strength of evidence. Strength of evidence can be regarded as insufficient, low,

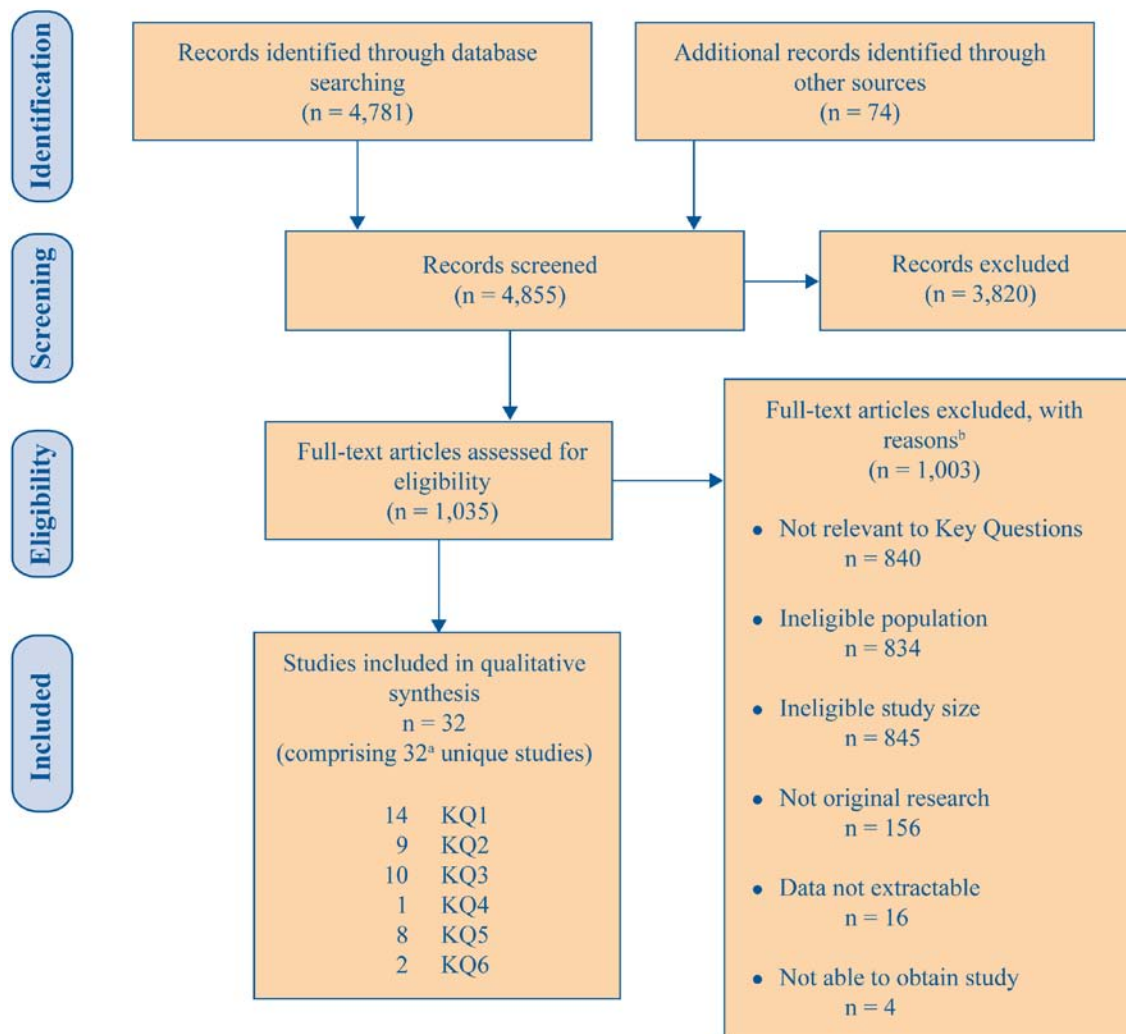
moderate, or high. It describes the adequacy of the current research, in quantity and quality, and the degree to which the entire body of current research provides a consistent and precise estimate of effect. We established methods for assessing the strength of evidence based on the AHRQ Effective Health Care program's Methods Guide for Effectiveness and Comparative Effectiveness Reviews.<sup>16</sup>

## Results

### Article Selection

Of the entire group of 4,855 citations, 1,035 articles required full-text review (Figure B). Of the 1,035 full-text articles reviewed, we retained 32 papers (comprising 32 unique studies) and excluded 1,003 papers.

**Figure B. Disposition of studies identified for this review**



KQ = Key Question; n = number

<sup>a</sup>One paper<sup>17</sup> reports two unique studies

<sup>b</sup>Numbers do not tally, as studies could be excluded for multiple reasons

## Organization of Results

As noted, we classified studies by broad category of intervention (behavioral, educational, vocational, adaptive/life skills, medical, and allied health). With the exceptions of studies of behavioral, medical, and vocational interventions, which included at least two studies addressing the same intervention, the other categories of interventions largely comprised single studies of unique interventions. Most studies (n=14) also targeted core symptoms of ASD (Key Question (1) or functional behavior/independent living skills (n=10) (Key Question (3). Nine studies, eight of which addressed medical interventions, examined comorbidities commonly occurring with ASD, which we defined broadly to encompass associated symptoms such as irritability (Key Question (2). Only studies of medical interventions addressed harms (Key Question 5).

One study addressed interventions targeting the transition process (Key Question 4), and two studies assessed effects of an intervention on family outcomes (Key Question 6). Because questions were addressed by a number of small, single studies of a given intervention, we discuss all studies together in the following sections instead of divided by Key Question. This approach allows us to present the findings of this disparate literature more clearly.

Across all categories of interventions, most studies (n=27) were of poor quality, and none was good quality. Five RCTs were fair quality: four that investigated pharmacologic agents<sup>18-21</sup> and one allied health study that assessed a leisure/recreation program.<sup>22</sup> Although positive results may be reported in individual studies, the poor quality of the studies and the lack of replication of the intervention studies mean that the strength of evidence for the body of evidence around any specific intervention is currently insufficient.

More research is needed to determine a measure of effect associated with any of the interventions described in this body of literature. Therefore, although we describe the results of individual studies in the report, the overall strength of evidence that any given intervention has a specific effect on outcomes is insufficient.

## Studies of Behavioral Interventions

We identified eight studies<sup>17, 23-28</sup> of behavioral interventions. One paper<sup>17</sup> reports two unique studies. Studies were conducted in the United States, Europe, and Canada and included a total of 302 participants. Seven studies (with two unique studies reported in one paper<sup>17</sup>) examined individual/group- or computer-based social skills interventions<sup>17, 23-25, 27, 28</sup> and an additional study assessed an intensive behavioral treatment provided at a semi-residential facility.<sup>26</sup> All studies were of poor quality. Individual studies assessing heterogeneous social skills approaches reported some benefits in emotion recognition, social functioning, and participation in social activity over the short term.<sup>17, 23-25, 27, 28</sup> The study of an intensive approach reported modest improvements in adaptive behavior over a 2-year period.<sup>26</sup> This study also assessed parental satisfaction with treatment, noting high levels of satisfaction overall.

## Studies of Educational Interventions

Two studies, both poor quality, examined educational interventions.<sup>29, 30</sup> Studies were conducted in the United States and Canada and included fewer than 50 total individuals with ASD. In one study, individuals with ASD and mean mental age scores of 3.3 years received language instruction using two teaching methods, with no significant difference observed between methods.<sup>29</sup> In a randomized study assessing strategies to promote reading comprehension,<sup>30</sup> scores generally improved overall in the short term.

## **Studies of Adaptive/Life Skills Interventions**

We identified four studies, all of poor quality, of various interventions focused on adaptive behavior.<sup>31-34</sup> Treatment duration varied tremendously from a daylong experiment to a study examining outcomes across a 2-year interval in a residential facility. Overall these studies included a total of 155 individuals with ASD. All studies were conducted in the United States, and at least two explicitly included participants with intellectual disability.<sup>31, 33</sup> Across studies, participants made very specific short-term gains in learning or successfully executing an adaptive or life skills-focused task, including lacing shoes or using a personal digital assistant to help with remembering activities. In one study of a residential facility employing a Treatment and Education of Autistic and related Communication Handicapped Children (TEACCH)-based model, exploratory analyses showed variable results with few significant changes in skills or negative behaviors over time across individuals in the TEACCH program or in institutions, family homes, or group homes.<sup>31</sup> Parents were significantly more satisfied with the TEACCH program overall.

A final poor-quality case series addressed the transitioning process by assessing effects related to implementing a classroom process—changing rooms throughout the school day—that individuals would likely encounter as they move to high school or college; the study reported no increase in disruptive behavior after the implementation of classroom rotation.<sup>34</sup>

## **Studies of Vocational Interventions**

We identified six papers from five unique study populations that addressed the impact of supported employment/vocational interventions.<sup>8, 35-39</sup> Studies were conducted in the United States and Europe and included more than 1,900 individuals with ASD; roughly 1,700 of these were included in an administrative database study assessing use of vocational rehabilitation services. All studies were considered poor quality. Interventions all involved finding and implementing on-the-job supports (broadly defined as services to promote job placement and job retention) for young adults with ASD. Studies comparing supported employment in the community with sheltered workshops reported that participants in supported employment groups experienced reductions in autism symptoms and improvements in quality of life in one study assessing those outcomes,<sup>37, 38</sup> and improvements in measures of cognition in another study.<sup>35</sup>

In long-term studies of a job-finding program in the United Kingdom,<sup>8, 39</sup> young adults in a supported employment group were significantly more likely to find paid employment than those in the control group (63.3% vs. 25%), with the majority of those employed showing job satisfaction. One final study identified individuals with ASD in a U.S. vocational rehabilitation dataset. These data illustrated that the presence of on-the-job supports was associated with a higher likelihood of employment in the community (competitive or supported).<sup>36</sup>

## **Studies of Medical Interventions**

Eight studies of pharmacologic agents, four of fair<sup>18-21</sup> and four of poor quality,<sup>40-43</sup> met our review criteria. The studies included a total of 272 individuals with ASD, and all were conducted in the United States, Canada, or Europe in academic clinics. All studies were funded using institutional and grant sources. Three randomized controlled trials (RCTs), one fair quality<sup>21</sup> and two poor,<sup>20, 40</sup> addressed the efficacy of antipsychotic medications including risperidone and haloperidol. One fair-quality RCT investigated the opiate antagonist naltrexone.<sup>19</sup> Of five studies

examining serotonin reuptake inhibitors (SRIs),<sup>18, 20, 41-43</sup> two RCTs were fair quality,<sup>18, 20</sup> and three case series were poor.<sup>41-43</sup>

All studies of medical interventions addressed outcomes related to comorbid conditions such as irritability or harms of treatments. Studies of antipsychotic medications reported some reductions in repetitive behavior, aggression, hyperactivity, and irritability in treatment groups over time periods of 7 to 24 weeks. Brief treatment with naltrexone (4 weeks) was associated with increases in stereotypy (repetitive or ritualistic behavior or movement) in the treated group. Studies of SRIs reported some improvements in treated participants in measures of irritability, repetitive behavior, and aggression over treatment durations of 7 to 12 weeks. One longer term case series reported improvements in general symptom severity and compulsive behavior in individuals receiving fluoxetine for a mean of 6 months.<sup>43</sup>

All medical studies reported harms of treatment. Harms or adverse effects reported in studies of antipsychotic medications included sedation, gastrointestinal complaints, weight gain, increased appetite, fatigue, dystonia, and depression.<sup>21, 40, 44</sup> Adverse effects described in the study of naltrexone included nausea, fatigue, sedation, and an increase in self-injurious behavior and stereotypy.<sup>19</sup> Harms noted in studies of SRIs included fatigue, tremor, tachycardia, agitation, gastrointestinal complaints, sedation, anxiety, agitation, and insomnia.<sup>18, 20, 41-43</sup>

## Studies of Allied Health Interventions

We identified five studies of disparate allied health interventions<sup>22, 45-48</sup> including one fair-quality RCT investigating a leisure/recreation program,<sup>22</sup> two poor-quality case series addressing music therapy,<sup>47, 48</sup> and two poor case series addressing facilitated communication.<sup>45, 46</sup> Studies included a total of 174 individuals with ASD, and the duration of treatment ranged from 20 hours to 12 months in 4 studies,<sup>22, 45, 46, 48</sup> one study of music therapy reviewed data from participants who had participated in varying hours of therapy.<sup>47</sup> Studies of music therapy reported some improvements in social skills using unvalidated measures.<sup>47, 48</sup> Studies assessing facilitated communication noted little communication improvement associated with facilitation and some evidence of facilitator influence on participants' responses.<sup>45, 46</sup> The study examining a recreation program reported improvements in stress-related scores for individuals in the intervention group compared with those in the control group ( $p < 0.001$ ). Overall quality of life scores similarly improved for intervention participants compared with the control group.<sup>22</sup>

## Discussion

### Key Findings

Despite a growing population of adolescents and young adults who have diagnoses of an ASD and the need for effective intervention across the lifespan, very little research is available to help understand the impact of specific intervention approaches for adolescents and young adults with ASD. The available research is lacking in scientific rigor. We identified a total of 32 studies (one paper reported two separate studies), of which 10 were randomized controlled trials. Although RCTs are often considered the gold standard for assessing intervention effectiveness, particularly in a complex behavioral field with emerging research such as this, observational designs can be rich sources of information. Nonetheless, most studies were of poor quality; only five were fair quality and none were good quality. The strength of the evidence (degree of confidence that the observed effect of an intervention is unlikely to change) across all

interventions and outcomes was insufficient as studies were typically of poor quality, addressed disparate interventions and outcomes, and lack replication (Table B).

**Table B. Summary of strength of evidence and key outcomes of studies**

Intervention	Strength of Evidence	Summary/Conclusions/Comments
<b><i>Behavioral</i></b>		
Individual or group-based social skills training <sup>23, 24, 27, 28</sup>	Insufficient	<ul style="list-style-type: none"> <li>• 4 poor-quality studies, 2 reporting on manualized (i.e., has a published treatment manual) intervention.</li> <li>• Some gains in social skills on largely parent-reported measures in short-term studies.</li> <li>• 2 studies lacked comparison groups; diagnostic approach, participant characteristics, treatment fidelity not clearly reported.</li> </ul>
Computer-based social skills training <sup>17, 25</sup>	Insufficient	<ul style="list-style-type: none"> <li>• 3 poor-quality, short-term studies (one paper<sup>17</sup> reported 2 separate studies).</li> <li>• Some improvements in emotion recognition in treated participants; no differences in measures of generalization.</li> <li>• Systematic diagnostic approach not reported within studies; concomitant interventions and treatment fidelity not reported.</li> </ul>
Intensive behavioral treatment <sup>26</sup>	Insufficient	<ul style="list-style-type: none"> <li>• 1 poor-quality case series with diverse participants.</li> <li>• Some gains in adaptive behavior reported.</li> <li>• Intervention not clearly described; treatment fidelity and concomitant interventions not reported; assessors not masked.</li> </ul>
<b><i>Educational</i></b>		
Vocabulary teaching <sup>29</sup>	Insufficient	<ul style="list-style-type: none"> <li>• 1 poor-quality nonrandomized trial.</li> <li>• Neither teaching method significantly more effective in increasing nouns.</li> <li>• Inclusion/exclusion criteria not clearly stated; attrition and differences in concomitant interventions not reported; assessors not masked.</li> </ul>
Reading comprehension <sup>30</sup>	Insufficient	<ul style="list-style-type: none"> <li>• 1 poor quality RCT; two facilitation methods increased comprehension compared with baseline scores.</li> <li>• Randomization method not clearly reported; assessors not masked and differences in concomitant interventions not reported.</li> </ul>
<b><i>Adaptive/Life Skills</i></b>		
Specific life/transitional skills <sup>32-34</sup>	Insufficient	<ul style="list-style-type: none"> <li>• 3 poor-quality, short-term studies assessing highly specific skills and unique interventions (shoe lacing, digital device use, rotating classroom schedule).</li> <li>• Some gains seen in individual studies but most lacked comparison groups.</li> <li>• Systematic diagnostic approach not reported within studies; participants often not clearly characterized; differences in concomitant interventions and treatment fidelity often not reported.</li> </ul>
TEACCH <sup>31</sup>	Insufficient	<ul style="list-style-type: none"> <li>• 1 poor-quality cohort study; desirability of living situation and use of programming rated more highly for TEACCH than other conditions; group homes rated more desirable than institutions.</li> <li>• Nonrandom assignment to groups; systematic diagnostic approach not reported within study; inclusion/exclusion criteria not clearly stated; interventions not fully described; assessors not masked.</li> </ul>
<b><i>Vocational</i></b>		
On-the-job supports/supported employment <sup>8, 35-39</sup>	Insufficient	<ul style="list-style-type: none"> <li>• 5 poor-quality studies.</li> <li>• Individual studies of different on-the-job supports (broadly defined as services to promote job placement and job retention) reported increased rates of employment in the community relative to those without on-the-job supports. Because the individual studies have not been replicated and are of poor quality, the strength of evidence for the effect seen is insufficient, as more research is needed to quantify the degree to which these interventions are likely to have an effect.</li> <li>• Nonrandom assignment to groups in 3 studies, no comparison group in 2 case series; attrition not always reported and interventions not always fully described; treatment fidelity and differences in concomitant interventions frequently not reported; assessors not masked.</li> </ul>

**Table B. Summary of strength of evidence and key outcomes of studies (continued)**

Intervention	Strength of Evidence	Summary/Conclusions/Comments
<b>Medical</b>		
Antipsychotics <sup>20, 21, 40</sup>	Insufficient	2 fair-quality RCTs and 1 poor quality crossover study. Improvements in aggression, irritability/agitation, repetitive behavior, sensory motor behaviors, and overall behavioral symptoms in participants receiving risperidone. Treatment adherence not reported in 2 studies; assessors not masked and participants not clearly characterized in 1 study.
Opioid receptor antagonists <sup>19</sup>	Insufficient	1 poor-quality crossover study. Significant increase in stereotypy in treated participants. Participants not clearly characterized; adherence and differences in concomitant interventions not reported.
Serotonin reuptake inhibitors <sup>18, 20, 41-43</sup>	Insufficient	2 fair-quality RCTs, 3 poor quality case series. Studies had inconsistent results: RCT of fluvoxamine reported decreases in repetitive behavior, aggression, autistic symptoms, and language usage. Case series addressing sertraline, fluoxetine, and clomipramine reported some benefits, while a crossover study of clomipramine vs. placebo reported no significant differences in autistic symptoms between groups. Lack of comparison groups in 3 studies; treatment adherence not reported; assessors not masked in some studies.
<b>Allied Health</b>		
Facilitated communication <sup>45, 46</sup>	Insufficient	2 poor-quality case series. Facilitated communication did not increase participants' communication or literacy abilities over their independent abilities. No comparison groups; differences in concomitant interventions not reported; assessors not masked.
Music therapy <sup>47, 48</sup>	Insufficient	2 poor-quality case series. Some gains in social skills reported using unvalidated and largely subjective measures. No comparison groups or measures of treatment fidelity; participants not clearly characterized; assessors not masked; differences in concomitant interventions not reported.
Leisure/recreation program <sup>22</sup>	Insufficient	1 fair-quality RCT. Positive effects on stress and quality of life in leisure group participants compared with controls. Attrition and treatment fidelity not reported; randomization method not clearly described; differences in concomitant interventions not reported.

RCT = randomized controlled trial; TEACCH = Treatment and Education of Autistic and Communication related Handicapped Children

In the behavioral literature research, social skills interventions utilizing individual/group<sup>23, 24, 27, 28</sup> and computer-based interventions<sup>17, 25</sup> suggested improvements across a variety of caregiver-reported social skills and emotion recognition capacities respectively. However, each study employed a different approach and paradigm, making comparison across interventions impossible. Likewise, such social skills interventions have yet to demonstrate consistent generalization of skills across settings and often limit interventions to individuals with average to above average verbal and/or cognitive abilities.

Only a single poor-quality case series examined the effects of a more intensive, comprehensive intervention approach. This study suggested improvement in adaptive skills and high levels of family satisfaction with services for 34 adolescents receiving treatment in a residential treatment setting over the course of 2 years. Given the lack of adequate comparison

group in this setting, there is very little information surrounding the impact of comprehensive behavioral intervention approaches for this population.

Research into educational approaches for adolescents and young adults with ASD is very limited, with only two small crossover studies identified in this population. These studies<sup>29, 30</sup> focused on the impact of highly specified educational strategies and outcomes (e.g., vocabulary development) and ultimately provide little evidence to support selection of either specific or various broad-based educational strategies.

Studies of adaptive/life skills-focused interventions meeting our criteria were of poor quality, addressed disparate interventions, and typically included few participants. Individual studies documented specified short-term gains in learning or successfully executing an adaptive or life skills-focused tasks, but the applicability and generalization of these findings is limited by the highly specified approaches utilized.<sup>31-34</sup> Additionally, studies were typically uncontrolled and of short duration.

Among five studies of supported employment/vocational interventions,<sup>8, 35-39</sup> all focused on on-the-job supports as the employment/vocational intervention. No other vocational interventions were reported in the literature meeting our study criteria. Our ability to know the ultimate benefit of supported employment programs is limited given the existing research. No study utilized random assignment, making it difficult to draw conclusions about the effectiveness of the programs, and all studies were poor quality. Three small studies focused on employment as an outcome of interest reported that supported employment interventions increased rates of employment for young adults with ASD.<sup>8, 36, 39</sup> Additional studies reported that supported employment was associated with improvements in quality of life and core symptoms<sup>37, 38</sup> and cognitive functioning<sup>35</sup> in supported employment participants relative to young adults with ASD in sheltered work settings.

Supported employment interventions remain understudied. For example, only one study examined rates of employment for programs that lasted 3 years or longer.<sup>8</sup> Further, this longer term study did not include a control group, making it impossible to determine the rates of employment over time for young adults with ASD who were not participating in the supported employment intervention. Finally, none of the studies examined whether increased employment rates or improvements in other outcomes were sustained after the termination of the supported employment intervention.

The use of medical interventions in adolescents and young adults with ASD is common.<sup>49</sup> However, there is little evidence that supports the use of medical interventions specifically in this population. Overall, most studies focused on the use of medications to address specific challenging behaviors (i.e., aggression or irritability). Four studies were fair quality,<sup>18-21</sup> and four were poor.<sup>40-43</sup> The most consistent findings were identified for antipsychotic medications. A fair quality RCT studying risperidone found improvements in aggression, repetitive behavior, sensory motor behaviors, and overall behavioral symptoms.<sup>21</sup> A crossover study of risperidone also showed a significant reduction of irritability/agitation ratings with risperidone treatment, but the control was indirect.<sup>40</sup> A placebo-controlled crossover study found that haloperidol significantly improved hyperactivity/defiance ratings, but no significant difference was found for irritability/agitation or other symptoms.<sup>20</sup> While limited literature supports the use of risperidone in adolescents or young adults with ASD, the efficacy of risperidone in studies including mostly children has moderate strength of evidence<sup>50</sup> that is consistent with the results of the one fair RCT and one poor crossover study in adults with ASD. There is therefore no evidence to suggest



that the effects of risperidone for irritability/agitation in ASD are specific to a particular age range.

A number of studies of SRIs were identified but with limited consistency across studies as a whole. An RCT of fluvoxamine showed decreases in repetitive behavior, aggression, autistic symptoms, and language usage.<sup>18</sup> In contrast, no significant differences were observed in a crossover study of clomipramine versus placebo.<sup>20</sup> Three case series of SRIs were also identified, including sertraline, fluoxetine, and clomipramine, with each study reporting some benefit to treatment.<sup>41-43</sup> A recent study not meeting criteria for this review contributes to the limited data on SRIs: the placebo-controlled RCT<sup>51</sup> of fluoxetine included 37 individuals with ASD with a mean age of 34.31 and reported improvements in repetitive behavior and ASD symptoms in the treatment group and mild harms. This study used a different medication than the one fair quality study in our age range, so it would be unlikely to influence the strength of evidence for a specific medication. It is possible, however, that a systematic review of SRIs in the broader age range of adults with ASD could provide data that might increase our confidence in the effect.

A crossover study of the opioid receptor antagonist naltrexone found no significant improvements in problem behavior and showed worsening of stereotyped behavior with naltrexone treatment compared with placebo.<sup>19</sup>

Based upon the published studies in adolescents and adults with ASD, the strength of evidence is insufficient for harms associated with medications tested in this population. As in the case of efficacy, the data on adverse effects associated with risperidone, including sedation and weight gain, are consistent with the high strength of evidence for these adverse effects in children with ASD.<sup>50</sup> The available evidence therefore appears consistent in supporting our understanding of the risk of these adverse events in ASD without being limited to a specific age range. Of course, this does not mean that other medications tested in ASD are free of adverse effects. It is reasonable to expect that, in contrast to efficacy, which is more likely to be specific to disorder and symptom, adverse effects are more likely to extend across diverse groups of subjects studied. Clinicians evaluating the evidence and sharing information with families routinely take this perspective, as does the Food and Drug Administration in mandating that all adverse events be listed for a drug, rather than just those for a particular indication.

Few studies of allied health interventions met our criteria.<sup>45-47</sup> One fair quality RCT assessed a 12-month recreation program<sup>22</sup> and reported improved quality of life and lower stress scores in individuals participating in the leisure/recreation program compared with those on a waiting list. Two studies of facilitated communication used approaches designed to assess the effects of facilitation both with and without facilitators' awareness of the word being prompted. Both studies demonstrated some facilitator influence without specific effects on participants' independent ability to communicate. One retrospective study of a music therapy program reported some positive effects on participants' social skills using largely subjective outcome measures.<sup>47</sup> One poor-quality case series<sup>48</sup> included 22 young adults engaged in a music therapy intervention. Nearly all participants reported making friends during the program and were generally satisfied with the program. Both studies assessed outcomes shortly after treatment, so longer term effects of the interventions are not known.

## **Applicability of the Evidence**

Study populations across interventions were highly variable. A number of studies included individuals with ASD and significant intellectual disability or language impairment, while studies assessing vocational and social skills-related behavioral interventions typically included

higher functioning individuals. Studies of medical interventions were all conducted in academic clinic settings, which may limit applicability to the general population. Thus there was substantial variability and limited information on developmental, cognitive, and behavioral characteristics of study populations.

## **Future Research**

The period of development representing the transition from adolescence to early adulthood presents numerous challenges for individuals with and without neurodevelopmental challenges. These challenges are compounded for individuals with ASD as they are presented with additional complexities requiring efforts to maximize the possibility of a positive transition and achievement of individual goals for independence. Despite increasing numbers of adolescents facing the transition from adolescence to adulthood, intervention research lags behind. To date, there is not sufficient strength of evidence for documenting the effects of any interventions in this age group on specific outcomes.

Overall, there is a dearth of evidence in all areas of care for adolescents and young adults with autism spectrum disorders and it is urgent that more rigorous studies be developed and conducted. It is unlikely that large scale implementation of interventions will be considered until a stronger evidence base is developed, despite growing numbers of individuals with need, and some small studies demonstrating initial promise. A fruitful area for consideration may be identifying programs/interventions that are appropriate candidates for developing treatment manuals to encourage standardized replication of promising approaches.

Basic understanding of the effects of aging on health, cognitive skills, and other domains of functioning is absent, and evaluations of interventions are rare. The lack of randomized, controlled trials is notable in all categories of intervention, but especially so in medical interventions, where substantial adverse events may be associated with medication use in adolescence. Only three studies<sup>8, 31, 37, 38</sup> (one reported in two publications) reported more than 12 months of followup; longer term data are needed in all areas of therapy. Furthermore, although early intervention for individuals with ASD is often delivered in the home or at specialized agencies, behavioral and educational interventions for adolescents and adults with ASD are likely to take place in existing community-based settings such as schools and businesses, with nonspecialists having a key role in implementation. Thus, another critical issue is to design interventions for implementation in such settings.

The behavioral literature generally focuses on a subset of individuals with ASD, often those who are higher functioning, and may not be representative of the range of individuals with ASDs. In particular, more attention is warranted to understand the impact of behavioral interventions in the lives of individuals and how these interventions generalize to real-world impact and outcome.

Few studies addressing educational interventions in the adolescent and young adult population have been conducted, and studies focusing on life skills or adaptive behaviors have included few individuals, typically in short-term studies focused on highly specific short-term intermediate outcomes. More research in both areas and over broader timeframes with more clearly defined populations is critical for helping individuals with ASD transition to greater independence.

In vocational research, studies are needed that illuminate which aspects of multifaceted supported employment programs have the greatest impact. Studies that do show evidence of effectiveness in this area should collect longer term data to describe the degree to which findings,

including the duration of employment, continue after the intervention itself is removed. These studies should also broaden the outcomes measured, to include other functional outcomes such as quality of life, educational attainment, residential outcomes, and social outcomes. Similarly, allied health studies are needed to understand best approaches to fostering independent living skills and ways in which improvements in motor skills may affect communication and other domains.

Medical studies conducted in adolescents and young adults have focused largely on problem behaviors, and additional data are needed on medical comorbidities in adolescents with ASD. Clear evidence from earlier studies of antipsychotics, which included mostly younger children, supports the use of risperidone and aripiprazole in children with ASD.<sup>50</sup> The only fair-quality study of risperidone in adults is consistent with the findings in children, but the strength of evidence based upon the adult literature alone is insufficient to draw firm conclusions. Population studies may be helpful to empirically group ASD patients by age in a way that fosters more effective studies of treatments. Understanding the age-appropriateness of potential medical treatments as based on social, physiological, pharmacological, and functional characteristics of the population would help to prioritize future research, including the ways in which medical comorbidities arise or increase as children with ASD move into adolescence and adulthood. Increased use of such standardized age groupings would facilitate comparisons of effectiveness within medical intervention categories as well as with nonmedical therapies. One way to support accomplishing this is by developing treatment networks with adequate numbers of patients of varying ages to participate in research.

Thus far, medication research in adolescents and young adults with ASD has been limited to compounds that are already approved for other indications. As targeted treatments for ASD emerge, initial studies will need to study adult populations to establish safety before moving into studies of adolescents and finally children. Study of compounds not yet on the market could be facilitated with partnerships between the academic and pharmaceutical communities. It will be critical to consider the appropriate outcome measures and settings in which to study medication response in adults. The heterogeneity in settings for adults with ASD is a significant impediment to assessing symptom response. Ideally, medications would be combined with an educational or psychosocial intervention that would mirror the school and therapeutic settings in which children with ASD show improvements in social, communication, or behavioral function. Without some level of educational or social challenge, it may be quite difficult to assess medication response.

Across all intervention types, research is needed on which outcomes to use in future studies. The Aberrant Behavior Checklist is the best outcome measure for behavioral symptoms in ASD in terms of both validity and reliability, but it does not directly index anxiety, mood, social, or communication function, nor does it capture broader outcomes such as quality of life. More outcome measures are needed to allow assessment of a broader range of symptoms, particularly in individuals who may be higher functioning. No studies provide adequate information on longer term outcomes, and particularly on outcomes related to achieving goals for independence and quality of life. To some degree, this reflects a lack of understanding and consensus about optimal outcomes and how to measure them.

We know little about which outcome measures are most appropriate and valid for this population specifically; nor do we have good, empirical evidence about which outcomes are valued by individuals and their families. Furthermore, it is unclear which outcomes are most likely to change as a result of the very different types of interventions assessed in this population.

Substantial, foundational research should be done to identify and validate outcome measures in the adolescent and young adult population with ASD.

Research is also necessary to understand how individuals' expression of ASD symptoms and the severity of symptoms may affect treatment over the lifespan. Foundational research is necessary to understand the goals of individuals with autism and their families as future research studies are planned. Similarly, little research addressing the effects of family and caregiver interactions and characteristics on the responses of individuals' with ASD to interventions exists.

Finally, for all research in this area, we encourage greater transparency in reporting, particularly as it relates to reporting of randomization approaches, characterization of study participants, description of the intervention and measures of fidelity and adherence. These are all necessary to correctly understand the potential impact of the interventions being reported.

#### Conclusions

Given the number of individuals affected by ASD, there is a dramatic lack of evidence on best approaches to therapies for adolescents and young adults with these conditions. In particular, families have little in the way of evidence-based approaches to support interventions capable of optimizing the transition of teens with autism into adulthood. Most of the studies identified were of poor quality; while the five fair-quality studies were primarily of medical interventions. Behavioral, educational, and adaptive/life skills studies were typically small and short term and suggested some improvements in social skills and functional behavior.

Individual studies also suggested that vocational programs may increase employment success, but the studies were small. By the same token, few data address the effectiveness and harms of medical or allied health interventions in the adolescent and young adult population. Although the studies that have been conducted focused on the use of medications to address specific challenging behaviors, the effectiveness in managing irritability and aggression in this age group remains largely unknown and can at best be inferred from studies including mostly younger children.

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# Introduction

## Need for Evidence Regarding Treatment of Autism Spectrum Disorders in Adolescents and Young Adults

Autism Spectrum Disorders (ASD) are among the most common neurodevelopmental disorders, with an estimated prevalence of one in 110 children in the United States having an ASD.<sup>1</sup> They are typically diagnosed in early childhood, often at or before preschool age. The diagnosis is fundamentally behaviorally based (i.e., there is no specific genetic test or clinical/laboratory procedure for diagnosis) and rests on documented core impairments related to social interaction, communication, as well as restricted and repetitive behavior. Diagnoses made by clinical providers, often pediatricians or behavioral providers, are based on documented symptom patterns in these domains.

Numerous screening and diagnostic tools are available to help document and measure symptoms of autism, with research investigations increasingly utilizing such measures in combination with clinical diagnoses in order to more accurately describe, measure, and analyze the heterogeneity in presentation associated with ASD. In addition to impairments in core symptom areas, many individuals with ASD also have impaired cognitive skills, atypical sensory behaviors, or other complex medical and psychiatric symptoms and conditions, such as seizure disorders, motor impairments, hyperactivity, anxiety, and self-injury/aggression.

More than 55,000 individuals between the ages of 15 and 17 in the United States likely have an ASD.<sup>2</sup> For some individuals, core symptoms of ASD (impairments in communication and social interaction and restricted/repetitive behaviors and interests) may improve with intervention and over time,<sup>3-5</sup> however, deficits typically remain throughout the lifespan although developmental expression may vary.<sup>6</sup> As children transition to adolescence and young adulthood, developmentally appropriate interventions to ameliorate core deficits may continue, but the focus of treatment often shifts toward promoting adaptive behaviors that can facilitate and enhance independent functioning.<sup>6</sup> Treatments for some must take into account that new symptoms may emerge with adolescence as well as engagement with new developmental challenges (e.g., independent living, vocational engagement, postsecondary education). In particular, families and caregivers have to make choices regarding care that cross a broad spectrum of clinical, behavioral and educational areas.

Current data suggest that attainment of independent living or employment in adulthood for individuals with an ASD is variable, with factors that predict the ability to live and work independently not well elucidated.<sup>6</sup> Furthermore, the limited extant research on outcomes for adolescents and young adults with ASD documents difficulties in achieving markers of functional independence, including employment, for the vast majority of these individuals.<sup>7</sup> Specifically, most adults with ASD live dependent lives that require considerable supports; fewer than a third have regular employment; most live with their parents or in supported living; and those who are employed are often in jobs that pay below a living wage.<sup>8-12</sup> In part because of these high levels of dependence, most individuals with ASD will require some sort of supports or intervention, often at intensive levels, throughout adolescence and adulthood.

The estimated costs of medical and non-medical care (e.g., special education, daycare) are prodigiously high. One study estimates that the total yearly societal per capita cost of caring for and treating a person with autism in the United States at \$3.2 million and at about \$35 billion for



an entire birth cohort of individuals with autism.<sup>13</sup> A study of health care utilization in a large group health plan revealed increased medication costs in older children with an ASD when compared with younger children, as well as similarly aged adolescents without an ASD; other care costs were also higher in this population, including a significantly increased rate of hospitalizations.<sup>14</sup>

Costs of transitional and employment programs are also high for young adults with ASD. A recent analysis of U.S. federal- and state-funded vocational rehabilitation programs showed that enrolled individuals with ASD were among the most costly of nine disability groups examined, with costs even higher among those with ASD and another comorbid disability. These data also showed, however, that those with ASD had a higher rate of employment (40.8%) at the time of case closure when compared with those with other disabilities, though with fewer work hours and lower wages than some other disability groups.<sup>15</sup>

Although few studies have examined this stage of the lifespan specifically, one study suggests that improvements in symptoms and problem behaviors observed while youth with ASD were in high school slowed down or stopped after they left high school.<sup>16</sup> Many individuals lose access to school- and age-linked services, and many of the services available to adults require waiting lists.<sup>16, 17</sup> The lack of services available to help young adults with ASD transition to greater independence has been noted by researchers for a number of years,<sup>18</sup> and is increasingly a topic in the lay media.<sup>19</sup> To date, the specific programs and interventions that underlie more positive functional, adaptive, social, and employment outcomes for individuals with ASD during the transition to adulthood and beyond are poorly understood. Further, it is unclear how such outcomes are best assessed in the face of the inherent heterogeneity and wide scope of impairments associated with ASD.<sup>6, 20</sup> This lack of information potentially limits the ability of individuals, families, practitioners and service systems to provide the appropriate care to optimize quality of life and minimize the costs associated with ASD over the lifespan.

This review examines the effects of available interventions in adolescents and young adults with ASD, focusing on the following outcomes: core symptoms of ASD; medical and mental health comorbidities; functional behaviors and independence; the transition to adulthood, and family outcomes.

## **Interventions Used To Treat ASD**

The expression and severity of symptoms of ASD differs widely across individuals and over time. Treatments may include a range of behavioral, psychosocial, educational, medical, and complementary approaches as well as those focused on transitional process and improving outcomes for parents/families of individuals with ASD.

The following sections briefly describe interventions discussed in the literature meeting our criteria for this review. Additional interventions for adolescents and young adults with ASD that did not meet criteria for our review are described in recent systematic and narrative reviews.<sup>21-27</sup>

### **Behavioral Interventions**

Studies of behavioral interventions available for this review are presented in the broad subcategories of social skills interventions and intensive behavioral interventions.

### **Social Skills Interventions**

Difficulty with reciprocal social interaction is considered one of the core impairments of ASD. The social impairment seen in ASD takes many forms and can vary greatly from one

individual to the next. For adolescents and young adults, social skills interventions often focus on enhancing individuals' interactions with peers and other adults by teaching skills necessary for fluid interaction including instruction perspective-taking, social problem-solving, and understanding social and emotional rules. Skill-based approaches have tried to address social vulnerability through direct group instruction as well as interactive computer based instruction.

## **Intensive Behavioral Interventions**

Comprehensive intensive behavioral interventions that focus simultaneously on multiple target areas are quite common for preschool children with ASD (e.g., University of California, Los Angeles/Lovaas model and early intensive behavioral intervention variants, Early Start Denver model, parent training paradigms). Studies that use behavioral approaches in an intensive and comprehensive fashion are uncommon during adolescence and young adulthood, although some programs for older individuals with ASD (not included in this review) may use elements of comprehensive approaches.

## **Educational Interventions**

Most children and adolescents with ASD receive a substantial amount of their treatment in an educational or center-based setting, often beginning early in life (e.g., preschool age). Educational interventions often aim at enhancing specific areas of academic functioning (e.g., reading skills), but also quite frequently attempt to address social, cognitive, and behavioral challenges within an educational setting. In addition to these targets, psychoeducational interventions are also often provided in an attempt to prevent or ameliorate specific areas of behavioral concern (i.e., sleep issues, puberty/sexuality related concerns) and provide family support.

## **Vocational Interventions**

Given the core and associated impairments related to ASD, many young adults exhibit challenges finding and sustaining involvement in appropriate and meaningful vocational activities. A number of interventions related to vocational attainment have focused on developing supportive mechanisms to secure employment. Such approaches often involve an interventionist, such as a job coach, and explicit instruction in the skills necessary to accomplish specific occupational functions. In addition, some approaches have attempted to incorporate instruction in the social and other skills necessary to identify and realize potential employment opportunities (e.g., interviewing).

## **Adaptive/Life Skills Interventions**

While comprehensive behavioral interventions for adolescents and young adults are uncommon, many interventions use applied behavior analysis-based intervention to target and improve important areas of daily functional impairment. These skills, often called adaptive or life skills, vary by specific targets (e.g., feeding, dressing) or more complex tasks (e.g., teaching a sequence of behavior). These interventions may also target reducing challenging behaviors (e.g., self-injury, self-stimulatory behavior, aggression) that interfere with day to day skills and functioning.

## Medical and Related Interventions

Medical interventions for symptoms of ASD include pharmacological agents, therapeutic diets, hormonal supplements, hyperbaric oxygen, chelating agents, and many other therapies. Risperidone (age 5 to 16 years) and aripiprazole (age 6 to 17 years), both atypical antipsychotic medications, are the only medical interventions that have U.S. Food and Drug Administration approval for patients with autistic disorder. Other core and related symptoms are treated with medications that are used in an “off-label” fashion. Antipsychotic medications act on the dopamine system and other neurotransmitter systems, such as serotonin.<sup>28-31</sup> Antipsychotic medications are generally divided into typical antipsychotics, which are older and primarily have affinity for dopamine D<sub>2</sub> receptors, and atypical antipsychotics which are newer and show a more diverse receptor profile. Typical antipsychotics studied in ASD include medications like haloperidol. Atypical antipsychotic medications include risperidone and aripiprazole, which are approved to treat irritability in children with autism, and have moderate and high evidence of efficacy based upon an earlier systematic review in children with ASD.<sup>32</sup>

Serotonin reuptake inhibitors (SRIs) are effective in treating anxiety, depression, and obsessive-compulsive disorder. There is overlap between the repetitive behaviors of ASD and obsessive compulsive disorder.<sup>33, 34</sup> Additionally, high blood levels of serotonin are a biomarker seen in 25 to 30 percent of children with autism, pointing to the serotonin system as a potential target for treatment.<sup>35, 36</sup> Randomized controlled trials and open-label trials with serotonin reuptake inhibitors in children with ASD have shown some promise but considerable variability in treating repetitive behaviors, anxiety, and aggression.<sup>32, 37</sup> SRIs include tricyclic antidepressants and more selective inhibitors. The newer class of SRIs, selective serotonin reuptake inhibitors, includes fluvoxamine, sertraline, and fluoxetine.

Opioid antagonists have been used in patients with ASD based upon the hypothesis that the opioid system may be involved in maintaining or reinforcing self-injurious behaviors.<sup>38</sup> Naltrexone is one opiate antagonist that has been investigated for treatment of self-injury, hyperactivity, or stereotyped movements in children with autism; although without evidence from randomized controlled trials favoring its use.<sup>39-41</sup>

## Allied Health Interventions

Several allied health interventions address core symptoms of ASD as well as associated difficulties and deficits. Social communication vulnerabilities are considered core features of ASD. As such, language difficulties and nonverbal communication challenges are often important targets of treatment. Historically, one communication intervention, facilitated communication, focused on helping individuals with communication and language challenges communicate via an interventionist or facilitator. More recently, interventions have utilized technology and augmentative communication therapies/devices in improving communication skills in individuals with ASD.

Other approaches have focused on teaching specific aspects of speech and language development (i.e., production, pragmatic language interventions). A number of additional interventions include occupational therapy techniques, movement and music therapies, as well as approaches aimed at sensory integration or addressing challenging sensory behaviors.

## Importance of this Review

Current data suggest that attainment of independent living or employment in adulthood for individuals with an ASD is variable, with factors that predict the ability to live and work independently not well elucidated.<sup>6</sup> Available data suggest that individuals with ASD will require some sort of intervention throughout adolescence and adulthood, and the estimated costs of medical and non-medical (e.g., special education, daycare) care are prodigiously high.<sup>27</sup> One study estimates that the total yearly societal per capita cost of caring for and treating a person with autism in the United States at \$3.2 million and at about \$35 billion for an entire birth cohort of individuals with autism.<sup>13</sup> A study of healthcare utilization in a large group health plan revealed increased medication costs in older children with ASD as compared with younger children as well as similarly-aged adolescents without ASD; other care costs were also higher in this population, and the rate of hospitalizations was significantly increased.<sup>14</sup>

Costs of transitional and employment programs are also high for young adults with ASD. A recent analysis of U.S. federal and state-funded vocational rehabilitation programs showed that the prevalence of ASD among those in training programs increased from 0.2 percent to 0.6 percent from 2002 to 2006; those with ASD were among the most costly of nine disability groups examined, with costs even higher among those with ASD and another comorbid disability. These data also showed, however, that those with ASD had a higher rate of employment (40.8%) at the time of case closure as compared with those with other disabilities, though with fewer work hours and lower wages than some other disability groups.<sup>15</sup>

There is no cure for ASD and no global consensus regarding which intervention strategies are most effective. Chronic management, often using multiple treatment approaches, may be required to maximize ultimate 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. Investigators in the area have noted that less research on therapies for adolescents or young adults exists than for younger children,<sup>42</sup> and such research is increasingly critical as the prevalence of ASD continues to grow and as children with ASD diagnoses reach adolescence.

## Scope and Key Questions

### Scope of This Report

We focused this review on interventions for adolescents and young adults between the ages of 13 and 30 with ASD (Autistic Disorder, Asperger syndrome, pervasive developmental disorder-not otherwise specified) and addressed questions related to the effectiveness of therapies targeting core symptoms of ASD (impairments in communication, social interaction, and behavior); aimed at common medical or mental health comorbidities, which include associated symptoms such as irritability; addressing the process of transitioning to adulthood; and addressing family outcomes.

### Key Questions

We have synthesized evidence in the published literature to address these Key Questions:

**Key Question 1:** Among adolescents and young adults with ASD, what are the effects of available interventions on the core symptoms of ASD?

**Key Question 2:** Among adolescents and young adults with ASD, what are the effects of available interventions on common medical and mental health comorbidities (e.g., epilepsy, sleep disorders, motor impairments, obesity, depression, anxiety, acute and episodic aggression, attention deficit hyperactivity disorder, etc.)?

**Key Question 3:** Among adolescents and young adults with ASD, what are the effects of available interventions on functional behavior, attainment of goals toward independence, educational attainment, occupational/vocational attainment, life satisfaction, access to health and other services, legal outcomes, and social outcomes?

**Key Question 4:** Among adolescents and young adults with ASD, what is the effectiveness of interventions *designed to support the transitioning process*, specifically to affect attainment of goals toward independence, educational attainment, occupational/vocational attainment, life satisfaction, access to health and other services, legal outcomes, and social outcomes?

**Key Question 5:** Among adolescents and young adults with ASD, what harms are associated with available interventions? Harms are defined by the Effective Health Care Program as all possible adverse consequences of an intervention, including adverse events.

**Key Question 6:** What are the effects of interventions on family outcomes?

## Organization of This Evidence Report

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

The Results section presents the findings of the evidence report, synthesizing them by category of intervention, Key Question, and outcomes reported. We report the number and type of studies identified, and we differentiate between total numbers of publications and unique studies. The final section of the report discusses key findings and expands on methodologic considerations relevant to each Key Question. We also outline the current state of the literature and challenges for future research in ASD in the target age range.

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. Exact Search Strings and Results
- Appendix B. Categorization of Study Designs
- Appendix C. Sample Data Extraction Forms
- Appendix D. Evidence Tables
- Appendix E. Quality Assessment Form
- Appendix F. Excluded Studies
- Appendix G. Quality of the Literature

We also include a list of abbreviations and acronyms at the end of the report.

## Uses of This Report

This evidence report addresses the Key Questions outlined previously using methods described in the report to conduct a systematic review of published literature. We anticipate that the report will be of value to clinicians who treat individuals with ASD, including pediatricians, psychologists, psychiatrists, allied health professionals, and other clinicians who provide care for ASD. The report itself is not a guideline. It is a review of evidence that other groups and

individuals can use in developing guidelines or treatment decisions, but we assume that those decisions would be made with other considerations as well, including an individual's diagnosis, severity of ASD symptoms, concomitant conditions, and ability to transition to more independent functioning.

In addition, this review will be of use to the National Institutes of Health, Centers for Medicare & Medicaid Services, and the Health Resources and Services Administration—all of which have offices or bureaus devoted to developmental issues. This report can bring practitioners up to date about the current state of evidence, 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 individuals affected by ASD and their families because of the high prevalence of ASD, significant personal costs associated with it, and the recurring need for individuals with ASD, their families, and their health care providers to make the best possible decisions among numerous options.

Researchers can obtain a concise analysis of the current state of knowledge in this field. They will be poised to pursue further investigations that are needed to understand best approaches to therapies for adolescents and young adults with ASD.

# Methods

## Topic Development and Refinement

The topic for this 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 adolescents and young adults with autism spectrum disorders (ASD). After review from the Agency for Healthcare Research and Quality (AHRQ), the questions and framework were posted to a public Web site. The public was invited to comment on these questions.

After reviewing the public commentary, we drafted final Key Questions and submitted them to AHRQ for review. We identified technical experts on the topic of ASD in adolescents and young adults to provide assistance during the project. Technical Expert Panel (TEP) members represented the clinical and research communities from a range of perspectives. They were invited to participate based on our commitment to engaging a range of experts who could help solidify the decisional dilemmas facing individuals and families with ASD. They included both researchers and clinicians with expertise in behavioral, medical, social, psychological and educational issues. The TEP contributed to AHRQ's broader goals of (1) creating and maintaining science partnerships as well as public-private partnerships and (2) meeting the needs of an array of potential customers and users of its products. Thus, the TEP was both an additional resource and a sounding board during the project. The TEP included six members serving as technical or clinical experts. 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 e-mail to:

- Refine the analytic framework and Key Questions at the beginning of the project;
- Discuss the preliminary assessment of the literature, including inclusion/exclusion criteria;
- Provide input on assessing the quality of the literature.

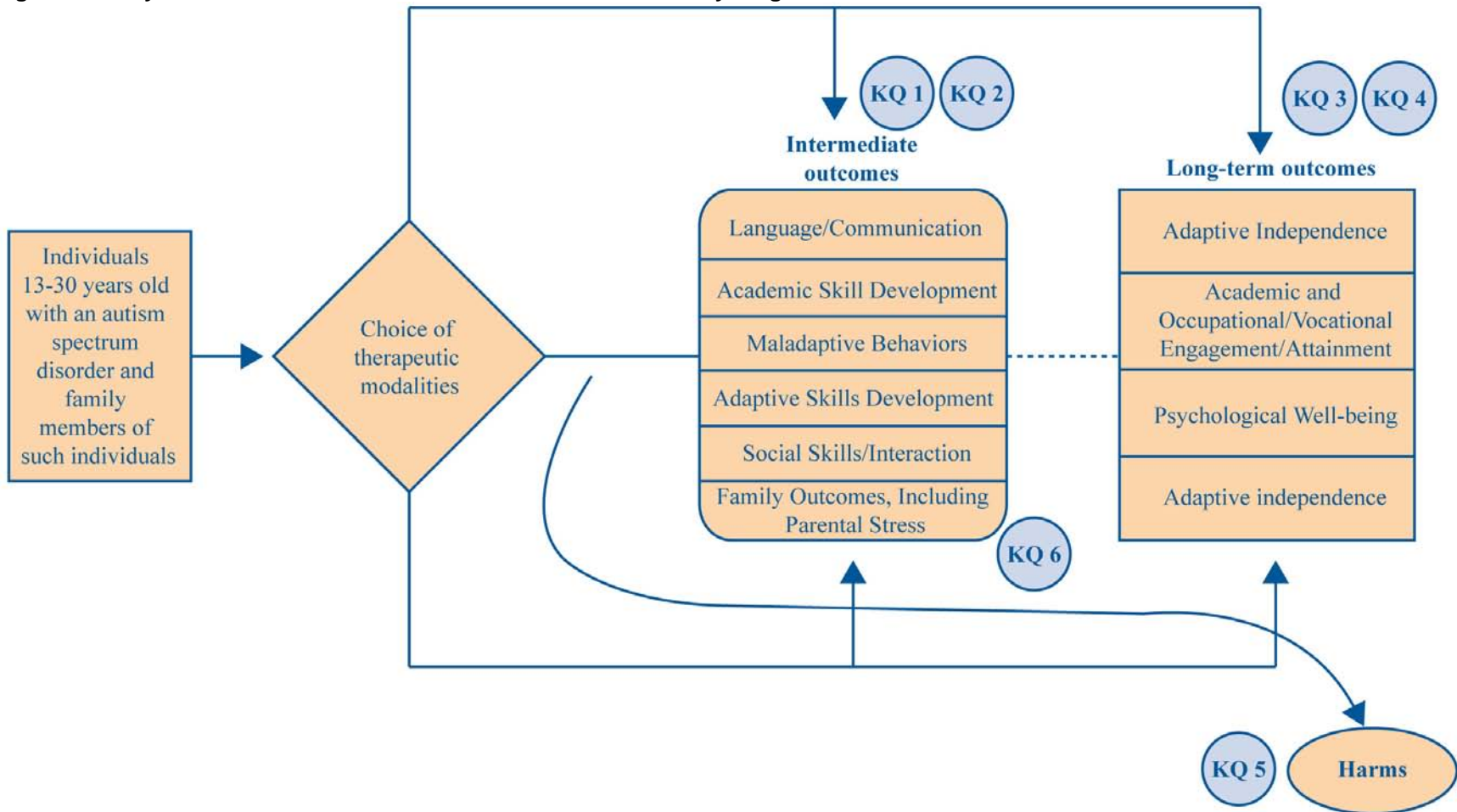
## Role of the AHRQ Task Order Officer

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

The analytic framework (Figure 1) summarizes the process by which individuals with ASD and their families/caregivers make and modify treatment choices. Treatment choices include surgical or nonsurgical approaches and may lead to intermediate outcomes including changes in communication skills, academic skill development, or social skills. Interventions may also lead to long-term outcomes such as adaptive independence and changes in psychosocial well-being. Interventions may also lead to changes in family outcomes such as parent distress and may be associated with harms/adverse effects. Numbers in circles within the diagram indicate the placement of Key Questions in relation to the treatment process.

Figure 1. Analytic framework for interventions for adolescents and young adults with ASD



KQ = Key Question



# Literature Search Strategy

## Databases

A librarian employed search strategies provided in Appendix A to retrieve research on therapies for adolescents and young adults with ASD. Our primary literature search employed 4 databases: MEDLINE® via the PubMed interface, PsycINFO® (psychology and psychiatry literature), the Educational Resources Information Clearinghouse, and the Cumulative Index of Nursing and Allied Health Literature database. 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 1980 and the publication of standardized diagnostic criteria for ASD (i.e., Diagnostic and Statistical Manual of Mental Disorders III).

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.

## Regulatory Information

The AHRQ Scientific Resource Center also searched for information on the following specific medications and interventions used to treat ASD. We requested regulatory information on these drugs and devices as they are either approved by the U.S. Food and Drug Administration to treat irritability in ASD or are beginning to be used in the ASD population and have not yet been well-reported in the published literature (i.e., hyperbaric oxygen):

- Risperidone
- Aripiprazole
- Hyperbaric oxygen chambers.

The Scientific Resource Center sought information in resources including the websites of the Food and Drug Administration and Health Canada and clinical trials registries such as ClinicalTrials.gov. We also gave manufacturers of these medications and devices an opportunity to provide additional information, though none did so.

## 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 and from 1980 to the present. Our searches were executed between September 2010 and December 2011. Appendix A provides our search terms and the yield from each database. We imported all citations into an electronic database.

## Process for Study Selection

### Inclusion and Exclusion Criteria

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

**Table 1. Inclusion and exclusion criteria**

Category	Criteria
Study population	Adolescents or young adults (ages 13-30) with ASD (autistic disorder, Asperger syndrome, PDD-NOS) or families/caregivers of individuals with ASD between the ages of 13-30
Interventions	Interventions aimed at ameliorating core symptoms of ASD, affecting independent functioning, adaptive behavior, or the transition process, or targeting family outcomes
Comparators	Placebo Other intervention
Outcomes	Social skills/interaction, language and communication, repetitive and other maladaptive behaviors, motor outcomes, psychological distress, adaptive skills development, academic skills development, and family outcomes including family distress and family satisfaction
Time period	Studies published from 1980–present with no limits on timing of outcomes
Setting	Any setting including educational, residential, and clinic
Publication languages	English only
Admissible evidence (study design and other criteria)	<p><u>Admissible designs</u></p> <ul style="list-style-type: none"> <li>Controlled trials, observational studies including prospective and retrospective cohort studies, prospective and retrospective case series</li> </ul> <p><u>Study size</u></p> <ul style="list-style-type: none"> <li>N ≥ 20 total individuals between 13-30 years of age with ASD or family members of such individuals</li> </ul> <p><u>Other criteria</u></p> <ul style="list-style-type: none"> <li>Original research studies that provide sufficient detail regarding methods and results to enable use and adjustment of the data and results</li> <li>Patient populations must include adolescents or young adults (13-30 years of age) with ASD or families/caregivers of individuals with ASD between the ages of 13-30</li> <li>Studies must address one or more of the following: <ul style="list-style-type: none"> <li>Treatment modality aimed at modifying ASD core symptoms, common comorbidities, family-related outcomes, or assisting with transitional issues</li> <li>Outcomes (including harms) related to interventions for ASD</li> </ul> </li> <li>Studies must include extractable data on relevant outcomes, including data presented in text or tables (vs. solely in figures)</li> <li>Studies must present aggregate data (vs. only data for each individual participant)</li> </ul>

ASD = autism spectrum disorders; N = number; PDD-NOS = pervasive developmental disorder-not otherwise specified

### Study Population

Studies needed to provide adequate information to ensure that participants fell within the target age range of age 13 to 30. We selected the lower bound of 13 as a previous AHRQ comparative effectiveness review of therapies for children with ASD included studies with individuals ≤ age 12.<sup>43</sup> As this review is focused in part on individuals in the period of transitioning to more independent functioning, we used the upper bound of 30 as individuals

with ASD can remain in the secondary school system until age 21. Thus some individuals may not experience the transition to more independent functioning in their twenties as would be expected for typically developing individuals. The upper age of 30 accounted for potential developmental delays in individuals with ASD.

For studies with populations including individuals with ASD either under the age of 13 or over age 30, we retained the study if we could infer that at least 50 percent of the study participants were in the 13 to 30 age range or if the mean age of participants was in the 13 to 30 age range. Similarly, for studies including individuals with ASD and those with other developmental disabilities we retained the study if we could isolate data on those participants with ASD.

We note that if a research study used a comparison group that did not contribute to an estimate of the contrast of interest in our review, we included the one arm of the study that was relevant. For example, an intervention study in which the intervention group is individuals with ASD and the comparison group is a group of individuals with Down Syndrome would not provide an estimate of the effect of the intervention for children with ASD. Rather than exclude this study, we include the group of individuals with ASD as a case series.

## **Sample Size**

We excluded studies that included fewer than 20 total participants in the target age range with ASD or family members of such individuals. Our goal was to identify and review the best evidence for assessing the efficacy and effectiveness of therapies for adolescents and young adults with ASD, with an eye toward utility in the treatment setting. Interventions to address ASDs are frequently behavioral in nature and highly intensive. They are also frequently adapted to be targeted to specific study participants given the significant heterogeneity of individuals with ASD. In part because this makes behavioral research quite complex and intensive, study sizes tend to be very small. A cutoff sample size of 20 provides a balance, allowing us to review and comment on adequate literature for the review but with studies large enough to suggest effects of the interventions.

With the assistance of our technical experts, we selected a minimum sample size of 20 in order to maximize our ability to describe the state of the current literature, while balancing the need to identify studies that could be used to assess treatment effectiveness.

## **Study Design**

We accepted any study designs except individual case reports. Our approach to categorizing study designs is presented in Appendix B.

## **Outcomes**

We assessed outcomes in the broad areas of social skills/interaction, language and communication, repetitive and other maladaptive behaviors, motor outcomes, psychological distress, adaptive skills development, academic skills development, and family outcomes including family distress and family satisfaction related to interventions. We considered intermediate outcomes as those that occur directly as a result of the intervention and that may also have longer term implications for the ultimate, functional outcomes that are the long-term goal of therapies. We also considered changes in long-term functional outcome areas, including adaptive independence/self care, academic/occupational/vocational engagement and attainment, psychological well-being, psychosocial adaptation, residential outcomes, legal outcomes,

social/relationship-focused outcomes (interpersonal relationships, community involvement/societal participation, self-actualization and acceptance, etc.), access to health services (conservatorship, access to day care, access to health care, access to social, financial, and other support systems), and use of public programs.

We also assessed the harms of interventions, defined by the AHRQ Effective Health Care program as the totality of adverse consequences of an intervention.<sup>44</sup> Harms may include—

- Adverse behavioral or psychosocial reactions to behavioral or other therapies (e.g., increased aggression or anxiety)
- Regression of language, skills, or behaviors
- Increases in or worsening of comorbid symptoms
- Adverse reactions to drug therapies (e.g., somnolence, weight gain)
- Reduction in and negative influences on quality of life.

## Language

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

## Screening of Studies

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

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

## Categorization of Interventions

Interventions to treat ASD overlap substantially<sup>21</sup> and cleanly identifying the category into which an intervention should be placed is difficult. We adapted the categorization approach we used in our previous review of therapies for children with ASD,<sup>43</sup> and studies fell into the following categories:

- **Behavioral interventions.** We defined behavioral interventions to include intensive behavioral and developmental interventions and social skills interventions employing either peer group- or computer-based approaches.
- **Educational interventions.** Educational interventions are those focusing on improving educational and cognitive skills and intended primarily to be administered in educational settings, or studies for which the educational arm was most clearly categorized.
- **Adaptive/life skills-focused interventions.** We considered those interventions focused on developing skills to assist with independent functioning and independent execution of activities of daily living as falling within this category. Interventions described in this

review include interventions targeting transitioning to a new school routine, self-care, and cognitive aids.

- **Vocational interventions.** We classified interventions targeting job skills, employment supports, or placing individuals into work as vocational interventions. Such interventions included in the literature meeting our criteria for this review comprise sheltered workshops, supported employment, and vocational rehabilitation.
- **Medical and related interventions.** We broadly defined medical and related interventions as those that included the administration of external substances to the body in order to treat symptoms of ASD; medical interventions represented in the literature included in this review comprised prescription medications.
- **Allied health interventions.** Allied health interventions included therapies that may be provided by occupational and physical therapists, including recreational therapies and promoting engagement in physical activity. We also considered therapies such as facilitated communication and music therapy as allied health interventions.

## Data Extraction and Data Management

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

The team abstracted several articles into the evidence table and then reconvened as a group to discuss the utility of the table design. We repeated this process through several iterations until we decided that the table included the appropriate categories for gathering the information contained in the articles. All team members shared the task of initially entering information into the evidence table. Another member of the team also independently reviewed the articles and edited all initial table entries for accuracy, completeness, and consistency. The full research team met regularly during the article extraction period and discussed issues related to data extraction (e.g., optimal level of detail in the description of the intervention, what constituted assessment of treatment fidelity). In addition to outcomes related to treatment effectiveness and family outcomes, we extracted all data available on harms. Harms encompass the full range of specific negative effects, including the narrower definition of adverse events.

The final evidence tables are presented in their entirety in Appendix D. Studies are presented in the evidence tables alphabetically by the last name of the first author within each year. When possible to identify, analyses resulting from the same study were grouped into a single evidence table.

## Individual Study Quality Assessment

We used a components approach to assessing the quality of individual studies, following methods outlined in the AHRQ Effective Health Care program's Methods Guide for Effectiveness and Comparative Effectiveness Reviews.<sup>45</sup> Decision rules regarding application of the tools were developed a priori by the research team. In some instances, it was appropriate to apply specific questions only to one body of literature (e.g., treatment fidelity to behavioral studies and medication adherence to medical studies) and we note those cases where appropriate. We assessed each domain individually and combined them for an overall quality level as

described below. Three levels were possible: good, fair, and poor (Table 2). Appendix E includes the questions we used to assess each domain.

**Table 2. Description of study quality levels**

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

## Determining Quality Levels

We assessed each domain described above individually and considered the individual ratings to determine an overall quality assessment of good, fair, or poor. We required that studies receive positive scores on all questions to receive a rating of good quality. We required that studies receive positive ratings on the following questions for a fair rating:

- Did the study employ a group design?
- Was there an appropriate comparison group?
- Was a systematic diagnostic approach used within the study?
- Were inclusion and exclusion criteria clearly stated?
- Was the intervention fully described?
- Did outcome measures demonstrate adequate reliability and validity?
- Were outcome data collected from sources appropriate to the target outcome?
- Was an appropriate statistical analysis used?

We rated studies without positive scores on these questions as poor quality and retained poor quality studies as part of the evidence base.

## Data Synthesis

There was significant heterogeneity among studies reporting therapeutic results of interventions for adolescents and young adults with ASD, including heterogeneity of population characteristics, heterogeneity of interventions, and heterogeneity of outcome measures. Therefore, it was not appropriate to perform any meta-analysis.

## Grading the Body of Evidence for Each Key Question

The assessment of the literature is done by considering both the observed effectiveness of interventions and the confidence that we have in the stability of those effects in the face of future research. The degree of confidence that the observed effect of an intervention is unlikely to change is presented as strength of evidence, and it can be regarded as insufficient, low, moderate, or high. Strength of evidence describes the adequacy of the current research, both in terms of quantity and quality, as well as the degree to which the entire body of current research provides a consistent and precise estimate of effect. Interventions that have demonstrated benefit in a small

number of studies but have not yet been replicated using the most rigorous study designs will therefore have insufficient or low strength of evidence to describe the body of research. Future research may find that the intervention is either effective or ineffective.

Methods for applying strength of evidence assessments are established in the AHRQ Effective Health Care Program’s Methods Guide for Effectiveness and Comparative Effectiveness Reviews<sup>46</sup> 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 (Table 3). Strength of evidence is assessed separately for major intervention-outcome pairs.

**Table 3. Domains used to assess strength of evidence<sup>a</sup>**

Domain	Explanation
Risk of bias	Degree to which the included studies for a given outcome or comparison have a high likelihood of adequate protection against bias (i.e., good internal validity), assessed through two main elements: <ul style="list-style-type: none"> <li>• Study design (e.g., RCTs or observational studies)</li> <li>• Aggregate quality of the studies under consideration.</li> </ul> Information for this determination comes from the rating of quality (good/fair/poor) done for individual studies
Consistency	Degree to which reported effect sizes from included studies appear to have the same direction of effect. This can be assessed through two main elements: <ul style="list-style-type: none"> <li>• Effect sizes have the same sign (that is, are on the same side of “no effect”)</li> <li>• The range of effect sizes is narrow</li> </ul>
Directness	Relates to whether the evidence links the interventions directly to health outcomes. For a comparison of two treatments, directness implies that head-to-head trials measure the most important health or ultimate outcomes. Evidence is indirect if: <ul style="list-style-type: none"> <li>• It uses intermediate or surrogate outcomes instead of ultimate health outcomes. In this case, one body of evidence links the intervention to intermediate outcomes and another body of evidence links the intermediate to most important (health or ultimate) outcomes</li> <li>• It uses two or more bodies of evidence to compare interventions A and B, e.g., studies of A vs. placebo and B vs. placebo, or studies of A vs. C and B vs. C but not A vs. B.</li> </ul> Indirectness always implies that more than one body of evidence is required to link interventions to the most important health outcomes. Directness may be contingent on the outcomes of interest.
Precision	Precision is the degree of certainty surrounding an effect estimate with respect to a given outcome (i.e., for each outcome separately). If a meta-analysis was performed, this will be the confidence interval around the summary effect size.

<sup>a</sup>Excerpted from Owens et al., 2010<sup>46</sup>

Based on the approach used in the prior AHRQ review of therapies for children with ASD,<sup>43</sup> we required at least three fair quality studies to be available to assign a low strength of evidence rather than considering it to be insufficient. 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 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 had established the maximum strength of evidence possible based upon these criteria, we assessed the number of studies and range of study designs for a given intervention-outcome pair, and downgraded the rating when the cumulative evidence was not sufficient to justify the higher rating. The possible grades were—

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

## **Applicability**

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

## **Peer Review and Public Commentary**

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

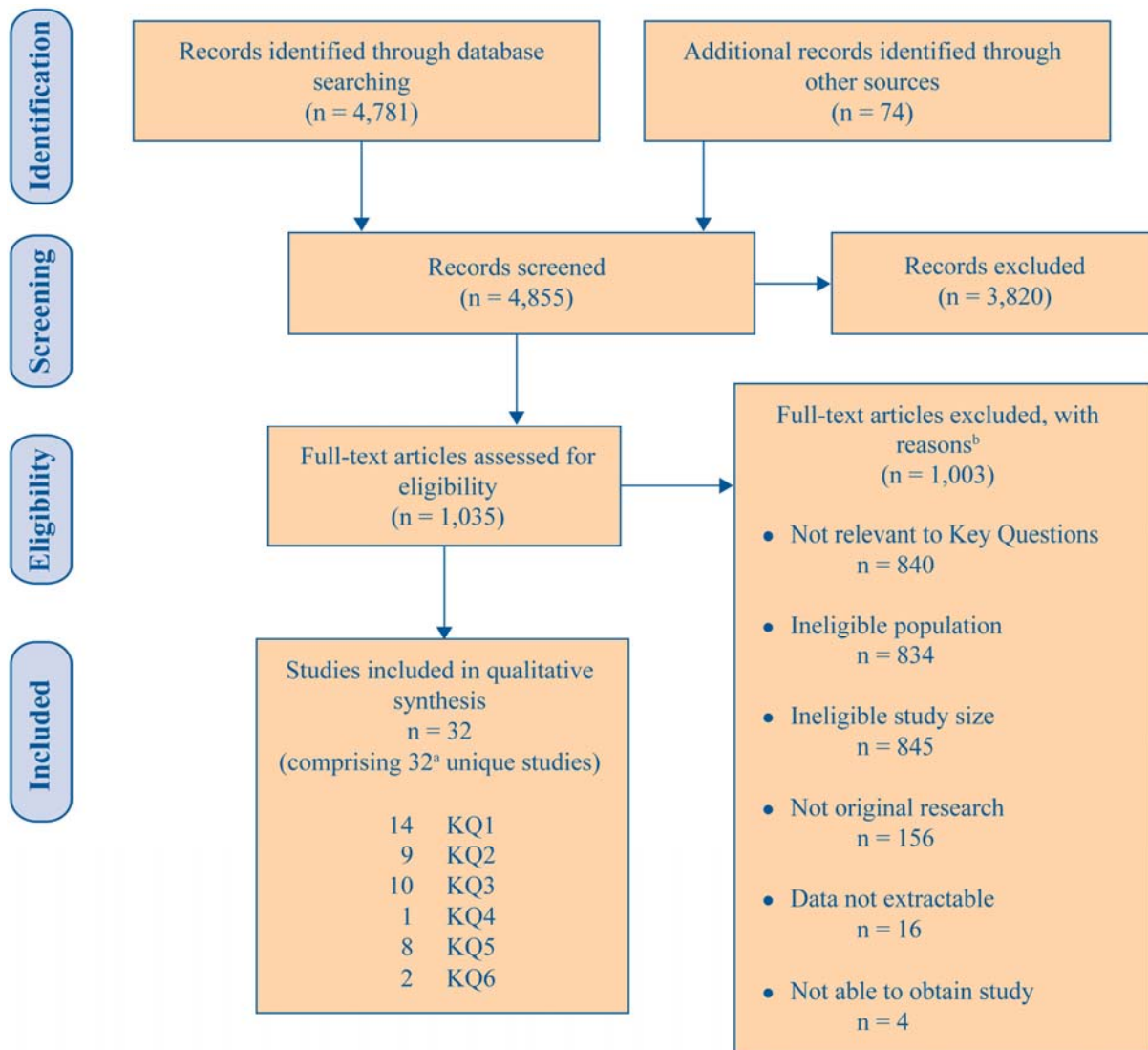


# Results

## Article Selection

We identified few studies addressing interventions for adolescents and young adults with autism spectrum disorders (ASD). Of the entire group of 4,855 citations identified, 1,035 required full text review (Figure 2). Of these 1,035 full-text articles reviewed, we retained 32 papers (comprising 32 unique studies) and excluded 1,003 papers. Reasons for article exclusion are listed in Appendix F.

**Figure 2. Disposition of studies identified for this review**



KQ = Key Question; n = number

<sup>a</sup>One paper<sup>47</sup> reports two unique studies.

<sup>b</sup>Numbers do not tally as studies could be excluded for multiple reasons.

## Organization of Results

As noted, we classified studies by broad category of intervention (behavioral, educational, vocational, adaptive/life skills, medical, and allied health). With the exceptions of studies of behavioral, medical, and vocational interventions, which included at least two studies addressing the same intervention, the other categories of interventions comprise single studies of unique interventions. Most studies (n=14) also targeted core symptoms of ASD (Key Question 1) or functional behavior/independent living skills (n=10) (Key Question 3). Nine studies, eight of which addressed medical interventions, examined comorbidities commonly occurring with ASD, which we defined broadly to encompass associated symptoms such as irritability (Key Question 2). Only studies of medical interventions addressed harms (Key Question 5).

One study addressed interventions targeting the transition process (Key Question 4), and two assessed effects of an intervention on family outcomes (Key Question 6). Because questions were addressed by a number of small, single studies of any given intervention, we discuss all studies together in the following sections instead of divided by Key Question. This approach allows us to present the findings of this disparate literature more clearly. We use headings to indicate the outcomes (e.g., core symptoms, functional behavior, harms, etc.) targeted in each study. It is nonetheless important to note that the studies in these categories typically assessed different interventions, and therefore could not be combined for an assessment of strength of evidence beyond insufficient for any specific intervention at this time.

We present findings beginning with an overview of the content of the literature as a whole, including the range of study designs used, approaches assessed and participants included. The detailed analysis of the literature provides further discussion and analysis of studies presented by broad category of intervention. Studies also are described in more detailed summary tables in the relevant section of text. For information on studies not included in the summary tables, please see the evidence tables in Appendix D; for information on quality scores for each study, see Appendix G.

## Overview of the Literature

The 32 unique studies described in this review included 10 randomized controlled trials (RCTs). Table 4 provides an overview of the characteristics of the literature overall.

**Table 4. Overview of the literature addressing interventions for adolescents and young adults with ASD**

Characteristic	RCTs	Nonrandomized Trials	Prospective Cohort Studies	Prospective Case Series	Retrospective Case Series	Cross-sectional Studies	Total Literature
Total n:	10	3	5	9	4	1	32
<b>Intervention Category</b>							
Behavioral	2	1	2	3	0	0	8
Educational	1	1	0	0	0	0	2
Adaptive/Life Skills	1	0	1	1	1	0	4
Vocational	0	2	1	0	1	1	5
Medical	5	0	0	2	1	0	8
Allied Health	1	0	0	3	1	0	5
<b>Treatment Duration</b>							
<1 month	3	0	0	2	0	0	5
>1 to ≤3 months	5	1	2	4	0	0	12
>3 to ≤6 months	0	1	0	0	1	0	2
>6 to ≤12 months	2	0	1	2	0	0	5
>12 months	0	1	2	1	2	0	6
Not specified	0	0	0	0	1	1	2
<b>Study Population</b>							
United States	5	1	2	5	3	1	17
Europe	3	2	3	2	1	0	11
Asia	2	0	0	2	0	0	4
Total N participants with ASD	341	114	200	296	233	1707 <sup>a</sup>	2891

ASD = autism spectrum disorders; n = number; RCT = randomized controlled trial

<sup>a</sup>1,707 individuals with ASD included in one study reporting data from an administrative database<sup>48</sup>

We did not rate any study as good quality. Five studies were fair quality,<sup>49-53</sup> and most studies were poor quality.<sup>17, 47, 48, 54-77</sup> Eighteen studies included comparison groups, and ten of these studies were randomized. Most studies were conducted in the United States or Europe, and participant ages across all studies ranged from 2 years to over 45 years. Only studies of medical interventions reported harms data.

## Studies of Behavioral Interventions

### Key Points

- Eight behavioral studies examined different social skills and intensive behavioral interventions and included individuals with ASD both with and without concomitant intellectual disability or language deficiencies. All studies were of poor quality.

- Most studies reported short-term gains in social skills as reported by parents or within study measures, but the diversity of the interventions precludes drawing a conclusion about effectiveness across the studies for behavioral interventions as a whole.
- Few studies reported evidence of generalization of skills beyond the treatment context.

## Overview of the Literature

We identified eight studies<sup>47, 61-64, 76, 77</sup> of behavioral interventions in seven unique populations (Table 5). Studies included two RCTs conducted in the United States<sup>61</sup> and United Kingdom,<sup>63</sup> one nonrandomized controlled trial conducted in the United States,<sup>76</sup> and three case series conducted in Canada,<sup>62</sup> the Netherlands,<sup>77</sup> and Italy.<sup>64</sup> One paper presented data from two separate studies conducted in the United Kingdom and involving two unique groups of participants.<sup>47</sup> Individuals in both studies received the same computer-based social skills software intervention, but comparators differed, and participants were randomized to intervention or control groups in only one study.<sup>47</sup> Five studies examined either individual or group<sup>61, 62, 76</sup> or computer-based intervention approaches<sup>47, 63</sup> focused on social skill development, including recognizing emotions, for individuals with ASD. One study conducted in Italy examined the impact of intensive behavioral treatment from a semi-residential rehabilitation center on adaptive behavior<sup>64</sup> while another examined social and adaptive outcomes from an individualized treatment program in the Netherlands.<sup>77</sup>

Participants ranged in age from 13 to 43 in the studies. One study<sup>64</sup> did not provide precise age data but notes that 34 participants were categorized as adolescents. Treatment duration ranged from 2 weeks to 2 years. We rated all studies as poor quality. Appendix G provides the quality ratings for each study.

## Detailed Analysis

### Behavioral Studies Addressing Core Symptoms of ASD

#### Individual or Group Social Skills Interventions

Most studies of behavioral interventions addressing effects on the core symptoms of ASD were short term and included a small number of individuals (Table 5). Among studies examining group-based social skills programs, one RCT examined the short-term outcome of a trial of a manualized (i.e., has a published treatment manual) outpatient social skills program, the Program for the Education and Enrichment of Relational Skills (PEERS).<sup>61</sup> The study included 33 adolescents (mean age 14.6 years) with average cognitive abilities (mean intelligence quotient [IQ] = 96.0 in treatment group and 88.3 in control group) randomized either to a 12-week program of group social skills intervention or to a delayed treatment control group. A later 14-week, nonrandomized trial of the PEERS program involved a separate group of 28 adolescents (mean age 14.6) diagnosed with high-functioning autism.<sup>76</sup> In both studies, participants in the treatment groups improved on parent-rated measures of social skills compared with control group participants, but limited teacher-rated measures indicated no differences between groups. The latter study assessed 12 of 14 treated participants 14 weeks after the end of intervention;<sup>76</sup> gains were maintained on most measures.

One prospective case series examined improvements in 28 hospitalized high-functioning adolescents (mean verbal IQ = 102.98 ± 13.33, mean age = 17.68 ± 3.14) receiving individualized treatment plans focused on psychoeducation.<sup>77</sup> At followup after 12 months of

treatment, social and daily behavioral functioning improved on parent- and tutor-reported measures as did ASD symptoms on self-reported measures. Participants did not report a change in problems related to daily behavioral functioning. Another prospective case series examined the impact of a 12-week social skills group for adolescents (mean age 14.6 years) with ASD. Adolescents recruited from community clinics with verbal skills sufficient to participate in a group intervention demonstrated parent-reported improvements related to problem behaviors and autism specific social concerns.<sup>62</sup>

### **Computer-Based Social Skills Interventions**

Among studies examining computer-based approaches, one RCT of a computer-based social skills training for adolescents with ASD randomized 22 children (age 12 to 18) to either training through 10 half-hour sessions with a computer program designed to train emotion recognition or to a control group.<sup>63</sup> The intervention group demonstrated fewer errors in recognizing the emotion depicted within the program from pre- to post-training, and relative to controls demonstrated improvement regarding emotion recognition via tasks presented within cartoons and stories.

An additional publication reported on two separate studies, one nonrandomized trial and one cohort study, with unique groups of participants. Both studies assessed emotion recognition abilities following completion of the Mind Reading computer-based training program.<sup>47</sup> In both studies, adults with ASD completing the program demonstrated improvements in recognizing faces and voices utilized in the training relative to the control group but did not demonstrate such improvements in recognizing improvements outside of the tasks.

### **Intensive Behavioral Interventions**

The one study examining an intensive behavioral approach reported on the impact of intensive behavioral treatment from a semi-residential rehabilitation center on adaptive behavior.<sup>64</sup> The study included 34 adolescents (age range not provided) receiving intervention from autism specific centers in Italy. Participants were reported to have improved on measures of socialization and adaptive behavior.

**Table 5. Key outcomes of behavioral studies addressing the core symptoms of ASD**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean/Yrs ± SD IQ, Mean ± SD	Key Outcomes
<b><i>Individual/Group-Based Social Skills Training</i></b>		
<p>Laugeson et al.,<sup>76</sup> 2011 United States</p> <p><b>G1:</b> Immediate socials skills training, 14/12 (28 week followup) <b>G2:</b> Delayed treatment control, 14/14 (14 week followup)</p> <p>Quality: Poor</p>	<p>G1: <b>15.0 ± 1.0</b> G2: <b>14.3 ± 1.4</b></p> <p>IQ (KBIT2) G1: <b>94.1 ± 20.2</b> G2: <b>104.5 ± 18.8</b></p>	<ul style="list-style-type: none"> <li>• 14-week manualized intervention: Program for the Education and Enrichment of Relational Skills with followup 14 weeks postintervention for treatment group participants.</li> <li>• Adolescents with high-functioning ASD (diagnoses not confirmed within study), ranging in age from 12 to 17 (mean = 14.6).</li> <li>• Treatment group showed improvements on parent-reported measures of social skills and interactions compared with control group; limited teacher reports showed no significant differences between groups.</li> <li>• At 14-week followup, most gains maintained for treatment participants; overall social skills continued to improve based on parent-rated measures. Some teacher-rated domains improved also.</li> <li>• Quality considerations: nonrandom assignment to groups; systematic diagnostic approach not reported within study; attrition and treatment fidelity not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>
<p>Laugeson et al.,<sup>61</sup> 2009 United States</p> <p><b>G1:</b> Immediate social skills training, 35 (total)/17 <b>G2:</b> Wait list, 35 (total)/16</p> <p>Quality: Poor</p>	<p>G1: <b>14.6 ± 1.3</b> G2: <b>14.6 ± 1.6</b></p> <p>IQ (KBIT2): G1: <b>96 ± 16.1</b> G2: <b>88.3 ± 21.1</b></p>	<ul style="list-style-type: none"> <li>• 12-week manualized intervention: Program for the Education and Enrichment of Relational Skills.</li> <li>• School-aged children of average intelligence. demonstrated short-term improvements in social skills knowledge, parent rated skills, and reported engagement in social activity.</li> <li>• Teacher-rated outcomes were not different for delayed treatment control.</li> <li>• Quality considerations: randomization method not clearly described; systematic diagnostic approach not reported within study; outcomes not coded by masked assessors.</li> </ul>
<p>Verhoeven et al.,<sup>77</sup> 2011 Netherlands</p> <p><b>G1:</b> Social skills intervention, 28/28</p> <p>Quality: Poor</p>	<p>G1: <b>17.68 ± 3.14</b></p> <p>IQ (WAIS/WISC): <b>G1: 102.82 ± 13.33 (verbal)</b> <b>98.36 ± 12.02 (performance)</b></p>	<ul style="list-style-type: none"> <li>• 12-month intervention associated with psychiatric hospitals, focusing on fostering development, improving behavioral functioning, well-being, and reducing ASD symptoms and understanding role of self-awareness in influencing treatment.</li> <li>• Social and behavioral functioning improved in teacher - and parent-reported measures.</li> <li>• Participants reported decrease in ASD symptoms, but no change in problems of daily behavioral functioning.</li> <li>• Positive correlation between initial self-awareness and improved social functioning; improved self-awareness associated with parent-reported decrease in problems in daily functioning but self-reported increase in problems.</li> <li>• Quality considerations: no comparison group; intervention not fully described; measure of treatment fidelity not reported; outcomes not coded by masked assessors.</li> </ul>

**Table 5. Key outcomes of behavioral studies addressing the core symptoms of ASD (continued)**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean/Yrs ± SD IQ, Mean ± SD	Key Outcomes
<b><i>Individual/Group-based social skills training</i></b>		
<p>Tse et al.,<sup>62</sup> 2007 Canada</p> <p><b>G1:</b> Social skills training with emphasis on learning through role play, 46/32</p> <p>Quality: Poor</p>	<p>G1: <b>14.6 ± 1.7</b></p> <p><b>NR</b></p>	<ul style="list-style-type: none"> <li>• 12-week intervention for adolescents with substantial verbal ability.</li> <li>• Improvement in parent rated skill outcomes.</li> <li>• Nonmanualized intervention, only parent report outcomes noted.</li> <li>• Quality considerations: no comparison group; systematic diagnostic approach not reported within study; participants not clearly characterized (no cognitive or developmental measures); measure of treatment fidelity not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>
<b><i>Computer-based social skills training</i></b>		
<p>Golan et al.,<sup>47</sup> 2006 United Kingdom</p> <p><b>Study 1</b></p> <p><b>G1:</b> Home software users, 19/NR (21% drop out rate)</p> <p><b>G2:</b> Control, 22/NR</p> <p>Quality: Poor</p>	<p>G1: <b>30.5 ± 10.3</b></p> <p>G2: <b>30.9 ± 11.2</b></p> <p>IQ (WASI, verbal):</p> <p>G1: <b>108.3 ± 13.3</b></p> <p>G2: <b>109.7 ± 10.0</b></p>	<ul style="list-style-type: none"> <li>• Individuals participating in home-based program demonstrated improvement related to emotion recognition of faces and voices within the study relative to controls.</li> <li>• Individuals did not perform differently on measures assessing generalization of emotion recognition.</li> <li>• Quality considerations: randomization method not clearly described; systematic diagnostic approach not reported within study; measure of treatment fidelity not reported.</li> </ul>
<p>Golan et al.,<sup>47</sup> 2006 United Kingdom</p> <p><b>Study 2</b></p> <p><b>G1:</b> Software and tutor, 18/13</p> <p><b>G2:</b> Social skills course, 18/13</p> <p>Quality: Poor</p>	<p>G1: <b>25.5 ± 9.3</b></p> <p>G2: <b>24.4 ± 6.4</b></p> <p>IQ (WASI, verbal):</p> <p>G1: <b>105.7 ± 16.1</b></p> <p>G2: <b>96.5 ± 15.5</b></p>	<ul style="list-style-type: none"> <li>• Individuals participating in home-based program plus group intervention demonstrated improvement related to emotion recognition of faces and voices within the study relative to controls.</li> <li>• Individuals did not perform differently on measures assessing generalization of emotion recognition.</li> <li>• Verbal IQ was significantly associated with improvement.</li> <li>• Quality considerations: nonrandom assignment to groups; systematic diagnostic approach not reported within study; inclusion/exclusion criteria not clearly stated; measure of treatment fidelity not reported; differences in concomitant interventions not reported.</li> </ul>

**Table 5. Key outcomes of behavioral studies addressing the core symptoms of ASD (continued)**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean/yr ± SD IQ, Mean ± SD	Key Outcomes
<b>Computer-Based Social Skills Training</b>		
Silver et al., <sup>63</sup> 2001 United Kingdom  <b>G1:</b> Computer sessions + standard lessons, 12/10 <b>G2:</b> Standard lessons only, 12/11  Quality: Poor	G1: 13.9 ± 0.9 G2: <b>14.75 ± 2.0</b>  <b>IQ (BPVS):</b> G1: 10.67 ± 2.25 G2: <b>12.0 ± 3.33</b>	<ul style="list-style-type: none"> <li>• School-aged children and adolescents with substantial verbal abilities demonstrated improvement in emotion recognition after 10 half hour sessions over 2 weeks.</li> <li>• No measures of generalization or outcomes apart from the study session were included.</li> <li>• Quality considerations: randomization method not clearly described; systematic diagnostic approach not reported within study; differences in concomitant interventions not reported; outcomes data not collected from appropriate sources (self-report only).</li> </ul>
<b>Intensive Behavioral Treatment</b>		
Valenti et al., <sup>64</sup> 2010 Italy  <b>G1:</b> ABA-based intensive behavioral therapy, 34/34  Quality: Poor	G1: <b>NR, 34 identified as postpubertal adolescents</b>  <b>25/34 identified as having intellectual disability</b>	<ul style="list-style-type: none"> <li>• Study of treatment received within context of semi-residential facility indexed gains related to adaptive behavior.</li> <li>• No control group was included, the participants were very diverse, and the specific intervention components were not well described.</li> <li>• Parent satisfaction with the treatment program was high on all measures.</li> <li>• Quality considerations: no comparison group; measure of treatment fidelity not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors</li> </ul>

BPVS = British Picture Vocabulary Scale; G = group; IQ = intelligence quotient; KBIT2 = Kaufman Brief Intelligence Test-Second Edition; n = number; NR = not reported; SD = standard deviation; WASI = Wechsler Abbreviated Scale of Intelligence

## Behavioral Studies Addressing Comorbidities and Associated Symptoms

### Individual/Group Social Skills Interventions

One prospective case series examined social outcomes and daily behavioral functioning in 28 high-functioning adolescents (mean verbal IQ = 102.98 ± 13.33, mean age = 17.68 ± 3.14) undergoing individualized treatment at specialized psychiatric hospitals.<sup>77</sup> Greater self-awareness was correlated with increased social functioning; however, improvements in self-awareness after treatment were correlated with increases in reports of problems in daily behavioral functioning and psychological problems by self-report.

### Behavioral Studies Addressing Independent Functioning

#### Intensive Behavioral Interventions

In the poor quality case series assessing the impact of intensive behavioral treatment,<sup>64</sup> participants demonstrated modest improvements in standard measures of adaptive behavior over



a 2-year period. Female participants also had improved daily living and motor skills in this uncontrolled study.

## **Behavioral Studies Addressing Family Outcomes**

### **Intensive Behavioral Interventions**

The same poor quality case series<sup>64</sup> of intensive behavioral intervention reported family satisfaction. The study included both adolescents and younger children and presented satisfaction data for the two groups combined. Overall, parents were highly satisfied with most elements of the program at year 1 and year 2, with median scores in the 4.5 to 10 range on scales ranging from 1 to 6 or 1 to 10. The overall median score for the domain of “family participation” increased slightly (8.0 to 8.5) as did scores on individual domain elements (“feeling of a having a say in the matter,” 5.0 to 5.5; “involvement in school meetings,” 5.0 to 5.5). Scores in the domain of “intervention outcome” remained stable for elements including “service to help participant in facing daily problems” (5.0), “feeling confident about what to do” (5.0), and “service to help participants’ quality of life” (5.0) but declined slightly on “service to help family in coping with problems” (5.0 to 4.5).

## **Studies of Educational Interventions**

### **Key Points**

- Two poor quality studies evaluated educational approaches; the strength of the evidence for effects of educational approaches is insufficient based on few poor quality studies addressing disparate interventions.
- Strategies to increase reading comprehension were reportedly associated with some improvement in one small, poor quality study.
- Neither of two vocabulary teaching methods was more effective in increasing nouns learned by individuals with ASD and intellectual disability.

### **Overview of the Literature**

Two studies, both of poor quality, examined educational interventions. One nonrandomized controlled trial<sup>66</sup> in the United States included 23 individuals ranging in age from 17 to 37 years (mean = 26) with mean mental age scores of 3.3 years and mean language scores of 3.0 years. Participants received language instruction using 2 methods of teaching over the course of 8 weeks, and investigators assessed outcomes including the number of nouns learned and retained. One RCT<sup>65</sup> was conducted in Canada and investigated procedural strategies to promote reading comprehension and included 20 individuals with ASD (mean age = 15.1, mean Stanford-Binet IQ = 88.15 ± 16.06). Appendix G provides the quality ratings for each study.

### **Detailed Analysis**

#### **Educational Studies Addressing Core Symptoms of ASD**

One poor quality nonrandomized trial included 23 adults with ASD and intellectual disability living in a residential treatment facility (Table 6).<sup>66</sup> Participants ranged in age from 17 to 37 (mean = 26) and had mean mental age scores of 3.3 years and mean language scores of 3.0 years.

Investigators matched participants on chronological age, mental age and vocabulary scores, and duration of stays in residential treatment and assigned groups to either analog language teaching for three 15 minute individual sessions/week over 4 weeks or natural language teaching for three 45-minute group sessions/week over 4 weeks. After an assessment, participants crossed over to the alternate training condition.

At the end of this second training phase, investigators assessed vocabulary retention. Neither teaching condition was significantly better at increasing vocabulary (mean number nouns learned in analog condition = 15.7, mean learned in natural language condition = 12.8); as expected, generalization was greater during receptive as compared with expressive testing of noun identification ( $p < 0.001$ ).<sup>66</sup> Participants in both groups retained an average of 92.2 percent of items learned at the final assessment. Participants' level of intelligence was related to the amount of generalization and to order of teaching. Participants in the upper range for mental age scores learned more nouns with analog teaching first (mean nouns learned = 64.8) than did those in the middle range (mean nouns learned = 10.3). Participants in the lowest mental age range performed more poorly than others regardless of teaching condition order.

**Table 6. Key outcomes of educational interventions addressing core symptoms of ASD**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Yrs, Mean $\pm$ SD IQ, Mean $\pm$ SD	Key Outcomes
Elliott et al., <sup>66</sup> 1991 United States  G1: 23/23  Quality: poor	G1: 26  G1: NR	<ul style="list-style-type: none"> <li>• Analog and natural language teaching styles had similar effects on increasing the number of nouns learned by participants.</li> <li>• Quality considerations: nonrandom assignment to groups; inclusion/exclusion criteria not clearly stated; attrition not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>

G = group; NR = not reported; SD = standard deviation

## Educational Studies Addressing Independent Functioning

A poor quality randomized study investigating the use of procedural strategies to promote reading comprehension included 20 individuals with high-functioning ASD (mean age = 15.1, mean Stanford-Binet IQ =  $88.15 \pm 16.06$ ).<sup>65</sup> Investigators presented participants with five stories written at a roughly sixth grade reading level in various procedural facilitation conditions or two control conditions. Procedural facilitation conditions included prereading, in which investigators asked participants questions designed to elicit common knowledge relevant to the main focus of the story; anaphoric cuing, in which a number of pronouns in each passage were underlined with choices for appropriate or inappropriate referent words appearing below them; and a cloze (fill in the blank) condition, in which blanks in sentences in each story could be completed by referring to information presented in the preceding sentences. Passages were not altered in the control condition. Investigators also asked participants questions about the stories' main idea, facts from the stories, and for their own retelling of the stories to gauge their understanding of the content. Participants read and answered questions about all 5 stories, presented in random order for each participant, in approximately 60 minutes, scored independently by masked assessors on a 1 (low) to 25 (high) point scale. Reading comprehension scores ranged from  $12.79 \pm 6.33$  in a control condition to  $15.41 \pm 6.28$  in the anaphoric cuing condition.

Overall, the study reported a medium size effect for procedural facilitation ( $F(4,76) = 2.49$ ,  $\eta^2 = 0.12$ ,  $p = 0.05$ ). Post hoc analyses also revealed a significant effect of anaphoric cuing on passage comprehension with a medium effect size ( $F(1,19) = 5.60$ ,  $\eta^2 = 0.42$ ,  $p = 0.03$ ). No significant effects of prereading questions or cloze (fill in the blank) were apparent in the results. Correlation analyses showed that anaphoric cuing worked best for individuals with lower grammatical ability while prereading questions were most effective for students with high pre-existing comprehension ability (Table 7).<sup>65</sup>

**Table 7. Key outcomes of educational interventions addressing independent functioning**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Yrs, Mean $\pm$ SD IQ, Mean $\pm$ SD	Key Outcomes
O'Connor et al., <sup>65</sup> 2004 Canada  G1: 20/20  Quality: Poor	G1: <b>15.11 <math>\pm</math> 0.99</b>  G1: <b>88.15 <math>\pm</math> 16.06</b>	<ul style="list-style-type: none"> <li>• Medium effect size for procedural facilitation and anaphoric cuing styles as compared with baseline (<math>p = 0.05</math> and <math>p = 0.03</math>, respectively) among high functioning individuals with ASD.</li> <li>• No significant effect of prereading questions or cloze style prompting.</li> <li>• Quality considerations: randomization method not clearly described; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>

ASD = autism spectrum disorders; G = group; SD = standard deviation

## Studies of Adaptive/Life Skills Interventions

### Key Points

- Four poor quality studies reported on disparate adaptive/life skills-focused interventions; most assessed outcomes after short-term (<12 weeks) intervention, and at least two included individuals with intellectual disability and ASD.
- Each study examined a different intervention, precluding a conclusion across studies on the overall effectiveness of life skills interventions. Therefore, with four distinct, poor quality studies, our ability to generate an estimate of effect is insufficient
- Nonetheless, each study reported some improvements in very specific life skills (e.g., shoe lacing, digital device use) after specific short-term interventions.

### Overview of the Literature

We identified four studies, all of poor quality, of adaptive-focused interventions (Table 8).<sup>54-57</sup> Each study examined a different intervention, so the studies could not be combined to assess effectiveness. Appendix G provides the quality ratings for each study. Treatment duration varied from a day-long experiment to roughly 2 years in a residential facility. All studies were conducted in the United States, and at least two included participants with intellectual disability.<sup>54, 55</sup> One crossover RCT assessed the number of trials needed to learn to lace a color coded shoe versus a non-color coded shoe.<sup>55</sup>

One cohort study assessed an implementation of the TEACCH psychoeducational model emphasizing farming and landscaping as vocational modalities and focused on teaching skills and ameliorating behavioral problems.<sup>54</sup> Outcomes assessed included measures of participant

skills and behaviors, level of environmental adaption and individualized programming, and family satisfaction with treatment.

One case series<sup>57</sup> investigated the use of personal digital assistants (PDAs) as memory aids for high school students. Participants were all enrolled in a mainstream high school, had home computers, and could operate a PDA independently. Outcomes measured included self-reported performance of activities of daily living. A final case series addressed the transitioning process by assessing effects related to implementing a classroom process—changing classrooms throughout the school day—that individuals would be likely to encounter as they move to high school or college.<sup>56</sup>

## **Detailed Analysis**

### **Adaptive/Life Skills Studies Addressing Independent Functioning**

A poor quality RCT<sup>55</sup> demonstrated challenges related to utilizing highly salient, non-criterion-related prompts (i.e., color coded targets) in teaching a specific shoe lacing skill to a group of 20 young adolescents (mean age 12.3) with significant cognitive limitations (average developmental age of 3.05). Participants were randomized to attempt to lace a shoe with color coded laces and eyelets or a shoe with no color coding. Participants typically mastered the shoe lace task more quickly in the color-coded condition but were not able to complete lacing a non-color coded shoe as quickly, suggesting that participants may have concentrated more fully on the color-coded prompt than the mechanics of the task.

One poor quality cohort study compared the effects of an experimental treatment setting, a combined residential and vocational TEACCH-based training program model with three control conditions: group homes, institutions, or family homes.<sup>54</sup> The farm-based TEACCH program emphasized farming and landscaping as vocational modalities and focused on teaching skills and ameliorating behavioral problems. All participants were applicants to the TEACCH residential program. Investigators used a part-random, part-clinical/administrative assignment procedure to assign participants, matched on cognitive ability, autism and challenging behavior severity, communication skills, and need for supervision, to the TEACCH treatment group (n = 6). The other participants were living in a control setting (group homes, n = 10; institutions, n = 6; family homes, n = 10). Participants were similar at baseline except in the case of individuals in family homes, who were less likely to have experienced residential placement before age 18. The mean age of all participants at baseline was 25 (range = 16 to 48 years). Eighty-five percent had severe to profound intellectual disability (Vineland Adaptive Behavior Composite mean = 25), and most had moderate to severe autism (mean CARS score = 36, range = 21 to 46). A majority of participants (53%) had experienced residential treatment prior to age 18.

Research assistants measured outcomes at baseline and 12 months after treatment/residence began for the TEACCH group. Outcomes assessed included measures of participant skills and behaviors, level of environmental adaption and individualized programming, and family satisfaction with treatment. The TEACCH program was rated as employing more communication adaptations, socialization programming, preventive behavior management approaches, and visual structure (all  $p < 0.0004$ ) than the other settings. TEACCH was also rated more highly in terms of desirability of the living situation and use of programming ( $p = 0.0001$  for both). Researchers rated group homes as more desirable settings than institutions. Exploratory analyses of changes in skills and behaviors showed variable results with few significant changes in skills or negative behaviors over time across groups.<sup>54</sup>

One poor quality case series<sup>57</sup> investigated the use of PDAs as memory aids for high school students with ASD. While investigators do not report measures of IQ or mental age, participants were all enrolled in a mainstream high school, had home computers, and could operate a PDA independently. All 22 participants (age range 14 to 18, mean = 16.5) reported increases in self-assessed performance of activities of daily living and satisfaction with the PDA after 8 weeks of use following a brief training session ( $p < 0.001$ ). The majority reported independent daily use, and examination of the PDAs showed a variable number of reminders entered. Outcome measures were administered by study investigators who had also provided training in PDA use and included one unvalidated tool.

**Table 8. Summary of outcomes of adaptive/life-skills interventions**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean/Yrs $\pm$ SD IQ, Mean $\pm$ SD	Key Outcomes
Gentry et al., <sup>57</sup> 2010 United States  <b>G1:</b> PDA use, 22/22  Quality: Poor	<b>G1: 16.5 (range 14-18)</b>  <b>NR</b>	<ul style="list-style-type: none"> <li>• Self-rated scores on Canadian Occupational Performance Measure increased from baseline</li> <li>• 22/22 participants used PDA daily and reported wanting to continue use; 16/22 could program device independently.</li> <li>• Quality considerations: no comparison group; systematic diagnostic approach not reported within study; participants not clearly characterized (no cognitive or developmental measures); differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>
Jewell et al., <sup>56</sup> 2007 United States  <b>G1:</b> Adolescents with rotating classroom schedule, 55/55  Quality: Poor	<b>G1: 17.63 (14-22)</b>  <b>NR</b>	<ul style="list-style-type: none"> <li>• Rotating classroom schedule (students change classroom throughout the day) had no significant effect on the number of crisis events (baseline mean = <math>2.44 \pm 6.39</math>, followup = <math>2.22 \pm 5.88</math>) or time in crisis (baseline mean minutes = <math>40.27 \pm 102.08</math>, followup = <math>28.96 \pm 65.47</math>).</li> <li>• Quality considerations: no comparison group; no systematic diagnostic approach reported within study; participants not clearly characterized (no cognitive or developmental measures); attrition not reported; outcomes not coded by masked assessors.</li> </ul>
Von Bourgondien et al., <sup>54</sup> 2003 United States  <b>G1:</b> TEACCH-based program, 6/6 <b>G2:</b> Family home, 10/10 <b>G3:</b> Group home, 10/10 <b>G4:</b> Institutions, 6/6  Quality: Poor	<b>G1:</b> $23.7 \pm 4.4$ <b>G2:</b> $26.6 \pm 5.1$ <b>G3:</b> $27.8 \pm 8.5$ <b>G4:</b> $21.5 \pm 5.0$  <b>85% of all participants had moderate to severe intellectual disability</b>	<ul style="list-style-type: none"> <li>• Outcomes rated by research assistants.</li> <li>• Desirability of living situation and use of programming rated more highly for TEACCH. than other conditions; group homes rated more desirable than institutions.</li> <li>• Few significant changes in skills or negative behaviors reported in exploratory analyses</li> <li>• Parental satisfaction higher for TEACCH than group homes (<math>p \leq 0.05</math>); no difference in parental satisfaction with institutions.</li> <li>• Quality considerations: nonrandom assignment to groups; systematic diagnostic approach not reported within study; inclusion/exclusion criteria not clearly stated; attrition not reported; intervention not fully described; measure of treatment fidelity not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>

**Table 8. Summary of outcomes of adaptive/life-skills interventions (continued)**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Mean/Yrs ± SD IQ, Mean ± SD	Key Outcomes
Nelson et al., <sup>55</sup> 1980 United States  <b>G1:</b> Extra prompts/no extra prompts <b>G2:</b> No extra prompts/extra prompts <b>G1+G2:</b> 20/20  Quality: Poor	G1: <b>11.5 ± 3.0</b> G2: <b>13.1 ± 4.1</b>  IQ (PEP developmental age) G1: <b>3.0 ± 0.7</b> G2: <b>3.1 v 0.9</b>	<ul style="list-style-type: none"> <li>• G1 completed lacing successfully in mean 108.7 trials plus 81.6 trials with the non-color coded shoe.</li> <li>• G2 completed lacing successfully in mean 137.2 trials plus 15.9 trials with the color coded shoe.</li> <li>• Quality considerations: randomization method not clearly described; systematic diagnostic approach not reported within study; attrition not reported; measure of treatment fidelity not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>

ASD = autism spectrum disorders; G = group; IQ = intelligence quotient; n = number; NR = not reported; PDA = personal digital assistant; PEP = PsychoEducational Profile; SD = standard deviation; TEACCH = Treatment and Education of Autistic and Communication related Handicapped Children

### **Adaptive/Life Skills Studies Addressing the Transitioning Process**

One poor quality case series<sup>56</sup> investigated the effect of a rotating classroom schedule (i.e., students change classrooms throughout the day) on behavior warranting crisis intervention among 55 adolescent students at a school for individuals with ASD (mean age = 17.63, range 14 to 22). We considered this study as addressing transitional issues because it was intended to examine the effects of a process (classroom changes) that individuals with ASD are likely to encounter as they transition into high school or higher education settings.

The school used crisis management to handle violent, uncontrollable, self-abusive, or dangerous behaviors. Crisis interventions consisted of progressive behavior management techniques that could include restraint as a last resort. Investigators collected data on the number of crisis interventions and time spent in interventions for 6 months prior to and 6 months following the implementation of a rotating classroom schedule. Twenty-two of 55 adolescent participants had crisis events prior to or after the classroom change. The number of crisis events (mean prerotation = 2.44 ± 6.39, postrotation = 2.22 ± 5.88) and time in crisis were not significantly different across time periods (mean minutes prerotation = 40.27 ± 102.08, postrotation = 28.96 ± 65.47).

### **Adaptive/Life Skills Studies Addressing Family Outcomes**

The cohort study<sup>54</sup> investigating the TEACCH-based residential center<sup>54</sup> also assessed family satisfaction with treatment. Parents were significantly more satisfied with the TEACCH program overall and with individuals' level of community involvement compared with group homes (p≤0.05), but there was no difference in satisfaction with institutions and either the TEACCH program or group homes. Parents of individuals in the TEACCH residence were also more satisfied with the impact of the placement on the family than parents of individuals in other groups.<sup>54</sup>

# Studies of Vocational Interventions

## Key Points

- Five poor quality studies assessed vocational interventions for adolescents and young adults with ASD.
- Individual studies of different on-the-job supports (broadly defined as services to promote job placement and job retention) reported increased rates of employment in the community relative to those without on-the-job supports. Because the individual studies have not been replicated and are of poor quality, the strength of evidence (confidence that future research will not change our understanding of the effect) for the effect seen is insufficient, as more research is needed to quantify the degree to which these interventions are effective, and under what circumstances.
- Despite positive results associated with other outcomes (quality of life, autism symptoms, cognitive development) reported in individual studies, the poor quality of the studies, assessment of unique outcomes in each study, and lack of replication lead to insufficient strength of evidence until further studies are conducted that may confirm the observed effects.

## Overview of the Literature

We identified six papers reporting on five unique study populations and addressing the impact of supported employment/vocational interventions on outcomes for adolescents and young adults with ASD (Table 9). One study was a nonrandomized controlled trial conducted in Spain and Germany.<sup>74, 75</sup> Two prospective cohort studies were conducted in Spain<sup>72</sup> and the United Kingdom,<sup>73</sup> and one case series was conducted in the United Kingdom<sup>17</sup> and one cross-sectional study was conducted in the United States.<sup>48</sup> All studies were considered poor quality. Appendix G provides the quality ratings for each study.

Interventions addressed in the studies all involved finding and implementing on-the-job supports for young adults with ASD. Three of the studies focused on government-funded supports,<sup>17, 48, 73</sup> and two studies conducted in Spain and/or Germany focused on privately-funded supports.<sup>72, 74, 75</sup> Three studies included a comparison or control group that did not receive the employment/vocational intervention,<sup>72-75</sup> and two studies examined the impact of the intervention on employment outcomes without a comparison group.<sup>17, 48</sup>

## Detailed Analysis

### Vocational Studies Addressing Core Symptoms

A poor quality nonrandomized trial reported in two papers<sup>74, 75</sup> examined the impact of supported employment (community-based jobs with no more than two individuals with ASD in the workplace) versus sheltered workshops (defined as “piece work being performed in segregated programs with only disabled coworkers”) on autism symptoms<sup>75</sup> and quality of life<sup>74</sup> of young adults with ASD (Table 9). Participants were 55 young adults who had received a clinical diagnosis of autism. The study did not report participant recruitment procedures clearly. Investigators assigned 26 participants to a sheltered workshop group and 21 to a supported work group. It is unclear why the sum of number of participants in each group does not match the total sample size.

The average age of participants was 21 years (mean =  $21.07 \pm 4.18$ , sheltered workshop group; mean =  $21.64 \pm 3.75$ , supported employment group), and their average IQ scores were in the mid-50s (mean =  $55.52 \pm 14.43$ , sheltered workshop group; mean =  $57.41 \pm 15.01$ , supported employment group). There appeared to be more males in the supported employment group (84%) than in the sheltered workshop group (69.2%), although the study did not assess group differences in gender. Although individuals were matched by gender, autism symptom scores (using the CARS), and IQ, participants were only eligible for the supported employment group if they had an absence of severe behavior problems and acceptable professional and vocational abilities. All of the jobs for those in the supported group were in the community with no more than two individuals with ASD in the same work place. Youth in the supported group worked between 15 to 30 hours a week, were paid competitive wages, and each had a job coach.

The average length of community employment at followup was 30 months. Differences between the supported and sheltered workshop groups in autism symptoms or quality of life were not significant before intervention. However, at followup, young adults who had participated in the supported work program had reduced autism symptom and higher quality of life scores relative to those who were in a sheltered workshop. Further, the autism symptom differences were due to deterioration in the sheltered group over time, whereas the supported group had no difference in autism symptoms scores from before to after intervention. In contrast, the sheltered workshop group had no difference in quality of life over time, whereas the supported group had quality of life scores that improved from before to after intervention. In sum, this study reports that for young adults with autism, supported work in the community may ameliorate increases in autism symptoms and improve quality of life relative to sheltered workshop work.<sup>74, 75</sup>

A related poor quality prospective cohort study from the same research group<sup>72</sup> examined the impact of supported employment in the community (supported work group) versus vocational activities in a sheltered setting (no supported work group) on the cognitive development of young adults with autism (Table 9). Participants included 44 young adults (32 men, 12 women) who were diagnosed according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria and who had CARS scores greater than 30. Participants were randomly selected from the Spanish Program of Employment for Autistic People. The mean age of participants was 25.52 years (SD = 3.35) for the supported work group and 24.32 (SD = 4.34) years for the no supported work group. The average years of schooling was 5.31 (range = 3 to 7 years). The study did not present standardized IQ scores for the participants, but all participants were required to score at about the 35<sup>th</sup> percentile on the Standard Progressive Matrices, a non-verbal IQ test. Similar to earlier studies,<sup>74, 75</sup> participants were eligible for the supported work group if they had an absence of severe behavior problems and acceptable professional and vocational abilities. All of the jobs for those in the supported work group were in the community, with no more than two individuals with autism in the same work place. Youth in the supported work group averaged 20 hours of work a week, were paid competitive wages, and each had a job coach. The average length of community employment at followup was 30 months.

The “no supported work” group was on a waiting list for supported work and participated in non-competitive vocational activities during the study period. It is unclear how many participants were in each group. At the start of the study, there were no significant differences between the supported work and no supported work groups in vocabulary (British Picture Vocabulary Scale), IQ (Raven’s matrices), or autism symptoms (CARS). There were also no differences between groups at this time on any of the 12 cognitive performance tasks which measured constructs such as psychomotor speed, spatial recognition memory, and executive functioning (many of the tasks



were from the Cambridge Neuropsychological Tests: Automatic Battery). Results suggested that, relative to the control group, the supported employment program was associated with improvements over time in 8 of the 12 measures of cognitive functioning.<sup>72</sup>

**Table 9. Key outcomes of vocational studies addressing core symptoms**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Yrs, Mean ± SD IQ, Mean ± SD	Key Outcomes
Garcia-Villamizar et al., <sup>72</sup> 2007 Spain <b>G1:</b> Supported employment <b>G2:</b> Wait list Overall N: 44/44  Quality: Poor	G1: <b>25.52 ± 3.35</b> G2: <b>24.32 ± 4.34</b>  IQ (Raven): G1: <b>41.14 ± 4.45</b> G2: <b>42.23 ± 5.43</b>	<ul style="list-style-type: none"> <li>• Adults with ASD participating in a community work program vs. a waitlisted group who participated in non-competitive (i.e., sheltered) vocational activities.</li> <li>• Followup assessment was approximately 30 months after the start of the intervention.</li> <li>• Relative to the waitlisted group, the supported employment group experienced improvements over time in 8 of the 12 measures of cognitive functioning.</li> <li>• Quality considerations: nonrandom assignment to groups; attrition not reported; intervention not fully described; measure of treatment fidelity not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>
Garcia-Villamizar et al., <sup>74,75</sup> 2000 Spain, Germany  <b>G1:</b> Sheltered work, 26/26 <b>G2:</b> Supported work, 25/21  Quality: Poor	G1: <b>21.07 ± 4.18</b> G2: <b>21.64 ± 3.75</b>  IQ (Leiter): G1: <b>55.52 ± 14.43</b> G2: <b>57.41 ± 15.01</b>	<ul style="list-style-type: none"> <li>• Adults with ASD participating in a community work program had lower autism symptoms and higher quality of life scores relative to those who were in a sheltered workshop.</li> <li>• Followup assessment was approximately 30 months after the start of the intervention.</li> <li>• Quality considerations: nonrandom assignment to groups; inclusion/exclusion criteria not clearly stated; intervention not fully described; measure of treatment fidelity not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>

ASD = autism spectrum disorders; G = group; IQ = intelligence quotient; N = number; SD = standard deviation

## Vocational Studies Addressing Independent Functioning

We identified two cohort studies<sup>17,73</sup> and one cross-sectional study<sup>48</sup> examining the impact of employment/vocational interventions on outcomes for adolescents and young adults with ASD (Table 10). We rated all studies as poor quality.

In one cohort study conducted in the United Kingdom, the authors examined the outcome of a 2-year supported employment scheme for high-functioning adults with autism or Asperger syndrome.<sup>73</sup> Participants in the supported employment scheme included 27 males and 3 females. All participants had a formal diagnosis of autism or Asperger syndrome, a performance or verbal IQ score above 70 (as measured by the Wechsler Adult Intelligence Scale), were actively seeking work and able to travel independently, were capable of eventually maintaining employment with minimal support, and had no psychiatric or physical problems that would adversely affect employment. An additional 20 individuals (all male) who met the study criteria were contacted and enrolled into a no-treatment comparison group. There were no significant differences between the supported employment and comparison groups in age (mean = 31.1 years for the

supported employment group and 28.0 years for the comparison group), IQ, or vocabulary (British Picture Vocabulary Test) at the start of the study.

The supported employment scheme included job finding and work preparation, educating potential and existing employers and colleagues about ASD, and on-the-job supports. On-the-job supports included assistance from a support worker with dealing with the social and occupational requirements of a job and education about ASD for employers and work colleagues. The frequency of supports decreased over the study period. Although the total study period covered two years, and average amount of time that individuals were registered with the scheme was 17.03 months (range from 5 to 24 months). Over the 2-year evaluation period, young adults in the supported employment group were significantly more likely to find paid employment than those in the comparison group (63.3% vs. 25%), and they spent a greater amount of the study time employed (27.09% of time employed for the supported employment group and 12.35% of time employed for the comparison group). For those who were employed, the number of hours worked per week did not differ between the supported work versus comparison group, however the supported work group had higher wages per hour on average. There were no significant differences between those who were and were not able to find work in IQ, vocabulary, social understanding, or age. The investigators noted that the most important aspect of their supported work program—and also the most expensive—was the “job finding” aspect, which included many hours of making presentations to, meeting with, and negotiating with potential employers. The authors also noted that funds are rarely available to subsidize the “job finding” component.

This same research group conducted a longer-term followup of their supported employment scheme, now titled “Prospects.”<sup>17</sup> This prospective cohort study examined whether the gains in employment made during the first two years of the project<sup>73</sup> persisted for up to 8 years and with a larger cohort (recruited from three regional sites in the United Kingdom). In addition to the 30 young adults with ASD reported on in the earlier study,<sup>73</sup> an additional 117 young adults who began receiving services between 2002 and 2003 were added to the cohort. The mean age of individuals added to the cohort was 31.4 years (standard deviation [SD] = 9.3). All had a clinical diagnosis of autism or Asperger syndrome made by a psychiatrist or psychologist, and this diagnosis was confirmed by using the Autism Diagnostic Interview in 20 percent of cases.

Thirteen of the 19 young adults in the original sample who found employment remained employed 7 to 8 years later. For the young adults who were added since the original cohort, the rate of employment remained high, ranging from 70.5 percent to 54.3 percent (depending on regional site). The majority of employed young adults with ASD (84.7%) were generally happy with their job.

A final cross-sectional study examined the impact of vocational/employment interventions conducted in the United States.<sup>48</sup> This study examined the effectiveness of vocational rehabilitative services for adults with ASD compared with adults with other developmental disabilities. The investigators identified 1,707 adults with ASD from national data obtained from the U.S. Department of Education’s Office of Special Education and Rehabilitative Services. Participants with ASD were identified using primary impairment causes for the disability in the vocational rehabilitation dataset. Approximately 73 percent of the sample of adults with ASD was 18 to 25 years of age; 15.5 percent was 25 to 34 years; and 11.1 percent was 35 years of age or older. Eighty-four percent of adults were white, 12.8 percent were black, and 4.2 percent were of Hispanic ethnicity. As this was an administrative database, data were not available about autism symptoms or cognitive abilities. The study reported that the presence of on-the-job supports (which could include counseling, on-the-job training, job search assistance, assessment

and diagnosis, and assistive technology) was associated with a higher likelihood of employment in the community (competitive or supported), and that on-the-job supports were just as effective in promoting employment for adults with ASD as for adults with other developmental disabilities.

**Table 10. Key outcomes of vocational studies addressing independent functioning**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Yrs, Mean ± SD IQ, Mean ± SD	Key Outcomes
<p>Lawer et al.,<sup>48</sup> 2009 United States</p> <p><b>G1:</b> Vocational rehabilitation service users, 1,707/1,707 United States</p> <p>Quality: Poor</p>	<p>Age, range (%): <b>18-25 (73.4)</b> <b>25-34 (15.5)</b> <b>35-44 (8.1)</b> <b>45-54 (2.5)</b> <b>55-65 (0.5)</b></p> <p>IQ: <b>NR</b></p>	<ul style="list-style-type: none"> <li>• Presence of on-the job supports was associated with a higher likelihood of employment in the community (competitive or supported) for adults with ASD.</li> <li>• On-the job supports were as effective in promoting employment for adults with ASD as for adults with other developmental disabilities.</li> <li>• Quality considerations: no comparison group; systematic diagnostic approach note reported within study; participants not clearly characterized (no cognitive or developmental measures); intervention not fully described; measure of treatment fidelity not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>
<p>Howlin et al.,<sup>17</sup> 2005 United Kingdom</p> <p><b>G1a:</b> Pilot supported employment program participants (1995-1996), 30/30</p> <p><b>G1b:</b> Supported employment program participants (2003-2005), 117/89</p> <p>Quality: Poor</p>	<p>G1a: <b>31.1 ± 9.1</b> G1b: <b>31.4 ± 9.3</b></p> <p>IQ (Raven nonverbal): G1a: <b>110.2 ± 17.6</b> G1b: <b>110.7 v 19.5</b></p>	<ul style="list-style-type: none"> <li>• For adults in the 8-year followup (1995-1996 sample), 13 of 19 (68%) who had been previously employed remained employed.</li> <li>• For adults in the additional sample (2003-2005), employment ranged from 70.5% to 54.3%, depending on regional site.</li> <li>• Quality considerations: no comparison group; attrition not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>
<p>Mawhood et al.,<sup>73</sup> 1999 United Kingdom</p> <p><b>G1:</b> Supported employment program, 30/30</p> <p><b>G2:</b> Control, 20/20</p> <p>Quality: Poor</p>	<p>G1: <b>31.1 ± 9.1</b> G2: <b>28.0 ± 6.1</b></p> <p>IQ (WAIS full scale): G1: <b>98.8 ± 16.3</b> G2: <b>97.7 ± 20.4</b></p>	<ul style="list-style-type: none"> <li>• 2-year supported employment scheme for high-functioning adults with autism or Asperger syndrome.</li> <li>• Adults in the supported work group were more likely to find paid employment (63% vs. 25%) and had higher wages per hour on average than a control group.</li> <li>• No differences between groups in number of hours worked per week for those who worked.</li> <li>• Quality considerations: nonrandom assignment to groups; systematic diagnostic approach not reported within study; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>

ASD = autism spectrum disorders; G = group; IQ = intelligence quotient; SD = standard deviation; WAIS = Wechsler Adult Intelligence Scale

# Studies of Medical Interventions

## Key Points

- Eight studies of pharmacologic agents met our review criteria; four of these were RCTs of fair quality. One additional RCT and three case series were poor quality.
- The strength of evidence related to challenging or repetitive behaviors and harms for each of the agents assessed is insufficient based on no good studies and lack of replication.
- Little evidence supports the use of medical interventions in the adolescent and young adult population; most studies focused on the use of medications to address specific challenging behaviors.
- Studies of risperidone reported improvements in aggression, irritability/agitation, repetitive behavior, sensory motor behaviors, and overall behavioral symptoms in participants receiving risperidone.
- A placebo-controlled crossover study reported that haloperidol significantly improved hyperactivity/defiance ratings, but no significant difference was found for irritability/agitation or other symptoms.
- Studies of serotonin reuptake inhibitors (SRIs) had inconsistent results: an RCT of fluvoxamine reported decreases in repetitive behavior, aggression, autistic symptoms, and language usage and case series addressing sertraline, fluoxetine, and clomipramine reported some benefits, while a crossover study of clomipramine versus placebo reported no significant differences in autistic symptoms between groups.
- A crossover study of naltrexone reported no significant improvements in problem behavior and worsening of stereotyped behavior with naltrexone compared with placebo.
- Harms reported across all studies included sedation, weight gain, fatigue, self-injurious behavior, constipation, anxiety, and insomnia.

## Overview of the Literature

We identified a total of eight studies of medical interventions.<sup>50-53, 67-69, 71</sup> All eight of these were studies of pharmacological agents. Overall, no studies were good quality, four were fair quality,<sup>50-53</sup> and four were poor quality.<sup>67-69, 71</sup> Appendix G provides the quality ratings for each study.

Three RCTs addressed the efficacy of antipsychotic medications (Table 11).<sup>50, 51, 67</sup> Two were conducted in the United States, and one in Canada. All of these RCTs were conducted in academic clinic settings using institutional and grant funding, and one was fair quality<sup>51</sup> and two poor.<sup>50, 67</sup>

One fair quality RCT was conducted in an academic clinic in the Netherlands and investigated an opiate antagonist (Table 12).<sup>53</sup> Funding for the study came from institutional and grant sources. Five studies investigated SRIs (Table 13).<sup>50, 52, 68, 69, 71</sup> Two studies were fair quality,<sup>50, 52</sup> and the balance were poor.<sup>68, 69, 71</sup> These studies included two RCTs;<sup>50, 52</sup> one was conducted in the United States and one in Canada. Three poor quality case series were conducted in the United States.<sup>68, 69, 71</sup> All five of these studies were conducted in academic clinic settings using institutional and grant funding.

## Detailed Analysis

### Medical Studies Addressing Comorbidities and Associated Symptoms

We summarize results of studies of medical interventions meeting our criteria below. The Introduction section of the report contains a description of the mechanism of action of these drugs.

#### Antipsychotics

Three studies addressed the efficacy of antipsychotics (Table 11).<sup>50, 51, 67</sup> One fair quality RCT<sup>51</sup> assessed the efficacy and safety of risperidone in adults with autistic disorder or pervasive developmental disorder-not otherwise specified (PDD-NOS). Inclusion criteria were being an adult, having an Autistic Disorder or PDD-NOS diagnosis based on DSM-IV criteria, and at least “moderate” symptom severity on the Clinical Global Impression of Severity (CGI-S) Scale. Participants had either a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) compulsive subscale score greater than 10, a Self-injurious Behavior Questionnaire (SIB-Q) score of 25 or greater, or a Ritvo-Freeman Real-life Rating Scale overall score of 0.20 or more. Exclusion criteria included a diagnosis of schizophrenia or psychosis, or any significant acute medical condition. The experimental design was a 12-week randomized, double-blind, placebo-controlled phase followed by a 12-week open-label risperidone treatment phase for patients from the placebo group. Subjects were off all psychiatric medications for more than 4 weeks before the trial started.

Risperidone dosing began with 1 milligram (mg) at night and advanced to twice daily dosing, increasing every 3 to 4 days by 1 mg/day, up to a maximal clinical effect or a maximum dose of 10 mg/day. Outcome measures included a modified version of the Y-BOCS, the SIB-Q, the Ritvo-Freeman Real-life Rating Scale, visual analog scales of different mood states, the Clinical Global Impression of Improvement (CGI-I), vital signs, and monitoring for extrapyramidal effects or other adverse effects. Subjects with a CGI-I score of “much improved” or “very much improved” were considered responders. The primary outcomes were global improvement (CGI), repetitive behavior (Y-BOCS), aggression (SIB-Q), and social relatedness (Ritvo-Freeman).

The mean age of the 31 subjects who began the trial was 28.1 years (SD 7.3) and mean full-scale IQ was 54.6 (SD 23.9). Only 24 subjects completed the trial. Fifty seven percent (8 of 14 subjects) were considered responders in the risperidone group, while none (0 of 16 subjects) in the placebo group were responders ( $p < 0.002$ ). Repetitive behavior as measured by Y-BOCS improved over time ( $p < 0.001$ ) for the risperidone group compared with the placebo group at each time point. This result was consistent with improvements over time in the open-label phase ( $p < 0.03$ ). Aggressive behavior as measured by SIB-Q improved over time ( $p < 0.001$ ) for the risperidone group compared with the placebo group. This result was consistent with improvements over time in the open-label phase ( $p < 0.05$ ). Symptomatic improvements as measured by the Ritvo-Freeman for the risperidone group compared with placebo were significant over time for sensory motor ( $p < 0.004$ ), affectual reactions ( $p < 0.001$ ), and overall score ( $p < 0.05$ ); however differences for social relationships, sensory responses, or language were not significant.

These results were consistent with the improvements over time in the open label phase except that sensory responses reached significance in the open label phase. Clinician-rated visual analog scales were significantly decreased in the risperidone group compared with placebo for “anxious or nervous” ( $p < 0.02$ ), “depressed” ( $p < 0.03$ ), and “irritable” ( $p < 0.01$ ); however there were no

significant differences for “calm,” “eye contact,” “happy,” “restless,” “social interaction,” “talkative,” or “tired.” Seven subjects did not complete the trial (3 in the risperidone arm and 4 in the placebo arm), with six subjects dropping out due to lack of improvement or agitation, and one subject in the risperidone arm with abnormal gait.

A poor quality crossover study addressed the safety and efficacy of risperidone in children, adolescents, and adults with intellectual disability.<sup>67</sup> Inclusion criteria were age 6 to 65 years; a 6-month or longer history of aggression, property destruction, or self-injury; and Aberrant Behavior Checklist-Community (ABC-C) scales above normal range. Exclusion criteria included a history of hypersensitivity to risperidone, neuroleptic malignant syndrome, seizures within the last year, degenerative brain disease, and problematic living/social situation. Subjects were free of all psychiatric medications for at least 2 weeks prior to entering the trial. The placebo-crossover design began with a placebo run-in phase (3 to 5 weeks). The study randomized participants to low dose risperidone (1 mg/day for children and adolescents, 2 mg/day for adults) or high dose risperidone (0.05 mg/kg/day), divided into a twice-daily schedule. The first treatment period started with 2 weeks of titration followed by 4 weeks at a constant dose. For the second treatment period, subjects crossed over to the other dose with 2 weeks of titration followed by 4 weeks at a constant dose. The crossover study design changed to an open-label design after a second placebo period (3 to 5 weeks) followed by 24 weeks of unblinded maintenance at the better risperidone dose.

Outcome measures included the ABC-C, the Dyskinesia Identification System Condensed User Scale, the Neuroleptic Side Effects Checklist, routine laboratory tests, and weight. Prolactin, hemoglobin A1c, and lipid profile were measured in a subset of the study subjects (n = 20). The primary outcome was the ABC-C Irritability subscale score.

Of the forty subjects, all had intellectual disability, 28 (70%) met DSM-IV criteria for autistic disorder, and 8 (20%) met DSM-IV criteria for PDD-NOS. The mean age was 22.0 years (SD 13.1). Twenty-three (57.5%) of subjects responded fully, and 35 (87.5%) had at least a partial response. The study defined a 50 percent reduction in the ABC-C Irritability/Agitation subscale score as a full response and a 25 percent reduction as a partial response. The mean ABC-C Irritability/Agitation subscale score was significantly different for both treatment periods compared with the second placebo period ( $p = 0.0002$ ). There was no significant dose effect for the ABC-C Irritability/Agitation subscale between low- and high-dose risperidone ( $p = 0.13$ ).

A fair quality crossover study<sup>50</sup> investigated the efficacy of haloperidol for the treatment of autism. Inclusion criteria were a DSM-IV diagnosis of autism; a recommendation for pharmacotherapy based on initial assessments; and never previously having completed an adequate trial of haloperidol or the SRI clomipramine. Exclusion criteria were not reported. The study design was a double-blind, placebo-controlled, crossover with random assignment to 7-week treatment phases of haloperidol, clomipramine, and placebo. Haloperidol dosing started at 0.25 mg at bedtime and increased in 0.25 mg increments every 2 days until the dose was 0.50 mg twice daily, then further 0.25 mg adjustments were made every 3 to 4 days based on clinical assessment. The dose was reduced to the last dose tolerated if adverse effects were experienced. There was a dosage taper during week 7 of each treatment phase. There were one-week placebo washout periods between each treatment phase. No other psychotropic drugs were allowed except benztropine. Outcome measures included the CARS, the Aberrant Behavior Checklist (ABC), the Dosage Treatment Emergent Symptom Scale, and the Extrapyramidal Symptom Rating Scale.

We summarize results for haloperidol and placebo here and address clomipramine results below (see Serotonin Reuptake Inhibitor section). Of the 37 subjects recruited, 36 (mean age = 16.3 years) were included in final analyses. The mean daily dose of haloperidol was 1.3 mg. The mean duration of haloperidol treatment was 5.8 weeks with 23 of 33 (69.7%) subjects completing the 7-week treatment phase. Seven of 10 subjects who discontinued had adverse effects (see Harms section below). The mean duration of placebo treatment was 5.4 weeks with 21 of 32 (65.6%) subjects completing the 7-week phase; 1 of 9 subjects who discontinued had adverse effects which only included nose bleeds (n = 1). The other 8 subjects discontinued due to lack of improvement in symptoms. Haloperidol versus placebo was significant for reductions in ABC Hyperactivity/Defiance scores (p<0.05), but not for the other ABC subscales. The study did not report statistical comparisons of haloperidol versus placebo for the CARS, Extrapyramidal Symptom Rating Scale, or Dosage Treatment Emergent Symptom Scale. The investigators note that carry-over of effects between treatment phases may have affected results in this crossover design, especially with the short one-week washout. Other comparisons between haloperidol and placebo were not discussed.

**Table 11. Key outcomes of studies assessing antipsychotics**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Mean Age, Years ± SD	Mean IQ ± SD	Outcome Measure/ Baseline Scores, Mean ± SD	Outcome Measure/Post-Treatment Scores, Mean ± SD Quality Considerations
<p>Hellings et al.,<sup>67</sup> 2006 United States</p> <p><b>G1+G2:</b> Placebo phase, then dose risperidone, followed by crossover to the other risperidone dose, then another placebo phase</p> <p>Placebo I phase: 3-5 weeks of placebo, n = 40</p> <p>Acute Dose phase: <b>G1</b> Low dose (n = 39) or <b>G2</b> high dose risperidone (n = 36)</p> <p>Placebo II phase: 3-5 weeks of placebo, n = 33</p> <p>Maintenance phase: Optimal dose risperidone, n = 32</p> <p>Quality: Poor</p>	<p><b>G1+G2:</b> 22 ± 13.1</p>	<p>NR, 40/40 with intellectual disability</p>	<p>ABC-C Irritability: <b>G1+G2, Placebo I phase:</b> 19.16 ± 9.96 <b>G1+G2, Placebo II phase:</b> 18.23 ± 12.36</p>	<p>ABC-C Irritability: <b>G1, Low dose acute phase:</b> 11.15 ± 9.28 <b>G2, High dose acute phase:</b> 13.31 ± 8.92 p = 0.13 G1 vs. G2 p = 0.0002 G1+G2 Acute phase vs. G1+G2 Placebo II</p> <p>Maintenance phase scores only reported graphically</p> <p>Quality considerations: inappropriate comparison group; treatment adherence not reported</p>

**Table 11. Key outcomes of studies assessing antipsychotics (continued)**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Mean Age, Years $\pm$ SD	Mean IQ $\pm$ SD	Outcome Measure/ Baseline Scores, Mean $\pm$ SD	Outcome Measure/Post-Treatment Scores, Mean $\pm$ SD Quality Considerations
Remington et al., <sup>50</sup> 2001 Canada  G1: Clomipramine G2: Haloperidol G3: Placebo Overall N: 37/36  Quality: Fair	<b>Overall:</b> 16.3 (SD NR)	NR	CARS Overall: 41.8 $\pm$ 7.1	CARS: G1: 37.8 $\pm$ 8.7 G2: 36.7 $\pm$ 6.1 G3: 39.4 $\pm$ 7.0 p<0.05, G2 vs. baseline  ABC reported only graphically  Quality considerations: participants not clearly characterized (no cognitive or developmental measures); outcomes not coded by masked assessors
McDougle et al., <sup>51</sup> 1998 United States  G1: Risperidone, 15/12 G2: Placebo, 16/12 G2a: Open label risperidone following placebo, n = 15  Quality: Fair	<b>G1+G2:</b> 28.1 $\pm$ 7.3	<b>G1+G2:</b> 54.6 $\pm$ 23.9	Y-BOCS, compulsion: G1: 16.5 $\pm$ 3.58 G2: 14.29 $\pm$ 3.50 G2a: 14.27 $\pm$ 2.92  SIB-Q: G1: 47.8 $\pm$ 19.5 G2: 37.7 $\pm$ 11.9 G2a: 32.43 $\pm$ 15.89	Y-BOCS, compulsion: G1: 12.77 $\pm$ 3.63 G2: 14.35 $\pm$ 3.02 p<.001, G1 vs. G2 G2a: 11.47 $\pm$ 3.64 p<0.03, G2a vs. BL  SIB-Q: G1: 24.2 $\pm$ 9.5 G2: 32.8 $\pm$ 15.0 p<0.001, G2 vs. G1 G2a: 23.07 $\pm$ 13.45 p<0.05, G2a vs. BL Quality considerations: treatment adherence not reported

ABC = Aberrant Behavior Checklist; ABC-I = Aberrant Behavior Checklist-Community Rating Scale-Irritability; ASD = autism spectrum disorders; CARS = Childhood Autism Rating Scale; G = group; IQ = intelligence quotient; n = number; NR = not reported; SD = standard deviation; SIB-Q = Self-Injurious Behavior Questionnaire; Y-BOCS=Yale-Brown Obsessive Compulsive Scale

## Opioid Receptor Antagonists

One study of an opioid receptor antagonist met our review criteria (Table 12).<sup>53</sup> This fair quality randomized, double blind crossover study tested the efficacy and safety of naltrexone on self-injurious behavior and other autistic symptoms in intellectually disabled adults. Inclusion criteria included a diagnosis using the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R) criteria that was agreed upon by two clinicians. The study also required that participants' level of social impairment had to go beyond what was expected by the severity of their intellectual disability, although the details of this determination were not reported. The study also included a subgroup with moderate to high levels of self-injurious behaviors, even though they did not meet criteria for autistic disorder. No exclusion criteria were reported.

Concurrent medications, including antipsychotics, were held stable. The study randomized participants to naltrexone or placebo with a 2-week single-blinded placebo period followed by a single dose of naltrexone (100 mg) with placebo for the remainder of that week. This phase was



followed by a 4-week treatment period, a 4-week washout period, and finally a crossover to the second 4-week treatment period. The first cohort received naltrexone 50 mg/day, but the dose for the second cohort was changed to naltrexone 150 mg/day. Outcome measures included the ABC; a clinician-rated checklist individualized to self-injurious behavior, stereotyped, and compulsive behaviors of each subject; the CGI-I scale; direct observation for a subgroup of 11 subjects; and laboratory analyses (liver function tests, plasma beta-endorphin, and plasma cortisol levels). The primary outcome was self-injurious behavior.

Of the 33 subjects that participated, 24 had autistic disorder and 9 did not. Participants mean age was 29 years (SD = 6), and IQ was not reported. Eleven subjects were taking antipsychotics with the dose held steady during the study. The single dose had no effect on the clinician-rated questionnaire, direct observation, self-injurious behavior, or plasma beta-endorphins. Plasma cortisol was significantly increased (p = 0.006) for naltrexone compared with placebo.

Longer term treatment (4 weeks) with naltrexone resulted in a significant increase in stereotypy as measured by the ABC stereotypy subscale. No changes in any of the other outcome measures were significant. The study did not report comparative statistics, but the CGI scale indicated that placebo was superior to 50 mg/day naltrexone in 12 of 18 subjects. The CGI scale showed that 50 mg/day of naltrexone was better than placebo in only 4 of 18 subjects, while placebo was superior in 12 of 18 subjects. The CGI scale also showed that 150 mg/day of naltrexone was better than placebo in 5 of 14 subjects, while placebo was superior in an equal number of subjects (5 of 14). There were no significant correlations between behavioral changes after the single dose of 100 mg naltrexone and the 4-week treatments with naltrexone (50 mg or 150 mg). Further analyses with groups divided into subjects with concurrent antipsychotic and subjects without did not yield any significant effect for naltrexone versus placebo.

**Table 12. Key outcomes of studies assessing opioid receptor antagonists**

Author, Year, Country, Groups, N Enrollment/N Final Study Quality	Mean Age, Years ± SD	Mean IQ ± SD	Outcome Measure/Baseline Scores, Mean ± SD	Outcome Measure/Post-Treatment Scores, Mean ± SD Quality Considerations
Willemsen-Swinkles et al., <sup>53</sup> 2005 Netherlands  <b>G1+G2:</b> 4 week naltrexone phase for cohorts 1 (50mg daily) and 2 (150mg daily) (ASD patients only) <b>G3+G4:</b> 4 week placebo phase for cohorts 1 and 2 (ASD patients only) Overall N: 33/31  Quality: Fair	<b>Overall:</b> 29 ± 6.0	NR	ABC Stereotypy <b>G1+G2:</b> 9.7 ± 4.7 <b>G3+G4:</b> 8.3 ± 5.2	ABC Stereotypy <b>G1+G2:</b> 10.0 ± 4.7 <b>G3+G4:</b> 9.0 ± 4.8 p = 0.018, G1+G2 vs. G3+G4  Quality considerations: randomization method not clearly described; participants not clearly characterized (no cognitive or developmental measures); treatment adherence not reported; differences in concomitant interventions not reported

ABC = Aberrant Behavior Checklist; ASD = autism spectrum disorders; G = group; IQ = intelligence quotient; mg = milligrams; n = number; NR = not reported; SD = standard deviation

## Serotonin Reuptake Inhibitors

Five studies focused on SRIs met our criteria (Table 13).<sup>50, 52, 68, 69, 71</sup> One fair quality RCT<sup>52</sup> investigated the efficacy of fluvoxamine in adults with autistic disorder. Inclusion criteria were

adults with a diagnosis of autistic disorder based on the DSM-III-R. Exclusion criteria were a DSM-III-R diagnosis of schizophrenia, psychotic symptoms, illicit substance abuse within the prior 6 months, “notable” medical conditions, seizure disorder, or pregnancy. Participants were not on any psychotropic medications for at least 6 weeks prior to starting the trial. The study randomized participants to placebo or fluvoxamine. Fluvoxamine was initiated at 50 mg daily and increased 50 mg every 3 to 4 days to maximum clinical response or a maximum dose of 300 mg/day. Outcome measures included the Y-BOCS, the maladaptive subscales of the Vineland Adaptive Behavior Scales, the Brown Aggression Scale, the CGI-I, and the Ritvo-Freeman Real-Life Rating Scale.

All 30 participants (15 fluvoxamine, 15 placebo) completed the 12-week trial. The mean age was 30.1 years (SD 7.1) for the fluvoxamine group and 30.1 years (SD 8.4) for the placebo group. The mean daily dose was 276.7 mg/day (SD 41.7) for the fluvoxamine group and 283.3 mg/day (SD 36.2) for the placebo group (difference not significant). Global improvement as measured by CGI-I was higher for fluvoxamine compared with placebo ( $p < 0.001$ ). Subjects were classified as responders if the CGI-I scores were “very much improved” or “much improved.” There were significantly more responders ( $p < 0.001$ ) in the fluvoxamine group (8 of 15 subjects) compared with the placebo group (0 of 15). Scores for the fluvoxamine group improved more than those for the placebo group for the Y-BOCS ( $p < 0.001$ ), Vineland maladaptive subscales ( $p < 0.001$ ), Brown Aggression Scale ( $p < 0.03$ ), overall Ritvo-Freeman Scale ( $p < 0.04$ ), and Ritvo-Freeman Scale language usage subscale ( $p < 0.008$ ).

Another fair quality study<sup>50</sup> used a double-blind, placebo-controlled crossover design to investigate the efficacy of clomipramine and haloperidol for the treatment of autism. Inclusion criteria were a DSM-IV diagnosis of autism; a recommendation for pharmacotherapy based on initial assessments; never previously having completed an adequate trial of haloperidol or clomipramine. Exclusion criteria were not reported. Investigators randomized participants to 7-week treatment phases of haloperidol, clomipramine, and placebo. Clomipramine dosing started at 25 mg at bedtime and increased in 25 mg increments every 2 days until the dose was 50 mg twice daily, then further 25 mg adjustments were made every 3 to 4 days based on clinical assessment. The dose was reduced to the last dose tolerated if adverse effects were experienced. There was a dosage taper during week 7 of each treatment phase and 1-week placebo washout periods between each treatment phase. No other psychotropic drugs were allowed except benzotropine. Outcome measures included the CARS, the ABC, the Dosage Treatment Emergent Symptom Scale, and the Extrapyramidal Symptom Rating Scale. Adverse effect outcomes were changes in stereotypy as measured by the Extrapyramidal Symptom Rating Scale and toleration of adverse effects which was measured by continuation of each treatment phase.

We summarize results for clomipramine and placebo here and haloperidol results above (see Antipsychotic section). Of the 37 subjects recruited, 36 (mean age = 16.3 years) were included in final analyses. The mean daily dose of clomipramine was 128.4 mg. The mean duration of clomipramine treatment was 4.5 weeks with 12 of 32 (37.5%) subjects completing the 7-week treatment phase; 12 of 20 subjects who discontinued did so at least partially because of adverse effects (see Harms section below).

The mean duration of placebo treatment was 5.4 weeks with 21 of 32 (65.6%) subjects completing the 7-week treatment phase. One of 9 subjects who discontinued had adverse effects which only included nose bleeds ( $n = 1$ ). The study did not report statistical comparisons for clomipramine versus placebo for the CARS, Extrapyramidal Symptom Rating Scale, or Dosage Treatment Emergent Symptom Scale. The study did not report on the effects of clomipramine

compared with placebo for ABC subscales. The investigators note that carry-over of effects between treatment phases may have affected results in this crossover design, especially with the short 1 week washout.

One poor quality study<sup>69</sup> assessed the efficacy and tolerability of clomipramine using a prospective open-label case series design over 12 weeks. The inclusion criterion was a DSM-IV diagnosis of a pervasive developmental disorder (autistic disorder, Asperger disorder, and PDD-NOS). Subjects were excluded if they had any additional DSM-IV diagnosis other than intellectual disability, had abused illicit drugs within 6 months, were pregnant, or had an acute medical illness. Clomipramine was initially dosed at 50 mg daily, and then increased by 50 mg every 3 to 4 days up to the maximum clinical response or a maximum dose of 250 mg daily. No psychotropic medications were allowed except antiepileptic medication which were held stable and chloral hydrate as needed for agitation. Outcome measures included the Y-BOCS, Brown Aggression Scale, Ritvo-Freeman Real-Life Rating Scale (sensory motor behaviors, social relationship, affectual reactions, sensory responses, and language subscales), and CGI-I. Of the 35 subjects, 33 completed the study and were taking a mean dose of 139 mg (SD 50). There was a significant improvement ( $p < 0.001$ ) in CGI-I global symptoms over time with clomipramine treatment. Of the 33 subjects completing the trial, 18 (55%) were responders as determined by CGI score of “very much improved” or “much improved.” Clomipramine treatment significantly reduced ( $p < 0.001$ ) repetitive thoughts and behaviors as measured by Y-BOCS. Aggression as measured by the Brown Aggression Scale significantly decreased ( $p < 0.001$ ) over time with clomipramine treatment. Clomipramine treatment significantly improved ( $p < 0.001$ ) autistic symptoms as measured by the Ritvo-Freeman Scale overall score, as well as all each subscale. The two subjects not completing the trial withdrew due to agitation in one individual and abdominal cramping in the second participant. There was no placebo control group to compare with the clomipramine treatment group in this open-label trial.

Another poor quality, 12 week open-label prospective case series<sup>68</sup> investigated the efficacy and tolerability of sertraline. Inclusion criteria were a DSM-IV diagnosis of autistic disorder, Asperger disorder, or PDD-NOS; a minimum Y-BOCS score ( $> 15$  for verbal subjects,  $> 7$  for nonverbal subjects); minimum of score of 0.20 on the Ritvo-Freeman scale, minimum score of 25 on the SIB-Q; and a minimum of 5 on the Vineland Maladaptive Behavior Scale, part 2. Sertraline was initially dosed at 50 mg daily, and then increased by 50 mg every week to a maximum clinical response, maximal dose tolerated, or maximum dose of 200 mg daily. The study allowed no psychotropic medications except chloral hydrate as needed for agitation. Outcome measures included the Y-BOCS, SIB-Q, Ritvo-Freeman Real-Life Rating Scale, and CGI-I. Of the 42 subjects, 37 completed the trial. The mean sertraline dose was 122.0 mg (SD 60.5). Of the 42 subjects starting the trial, 24 (57%) were considered responders based on CGI-I score of “very much improved” or “much improved.” Five subjects withdrew from the study: three due to anxiety/agitation, one due to syncope, one due to noncompliance. There was no placebo control group for comparison of possible therapeutic effects or adverse events.

Finally, a poor quality retrospective case series<sup>71</sup> studied the therapeutic effects and tolerability of fluoxetine and included 23 individuals with ASD (mean age  $15.9 \pm 6.2$ ). Most participants (21/23) had concomitant intellectual disability. Participants received up to 80 mg/day of fluoxetine for a mean of  $189 \pm 153$  days. CGI ratings of overall clinical severity improved in 15 participants as did ratings of perseverative or compulsive behavior.

**Table 13. Key outcomes of studies assessing SRIs**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Mean Age, Years $\pm$ SD	Mean IQ $\pm$ SD	Outcome Measure/ Baseline Scores, Mean $\pm$ SD	Outcome Measure/Post-Treatment Scores, Mean $\pm$ SD Quality Considerations
<p>Remington et al.,<sup>50</sup> 2001 Canada</p> <p><b>G1:</b> Clomipramine <b>G2:</b> Haloperidol <b>G3:</b> Placebo Overall N: 37/36</p> <p>Quality: Fair</p>	<p><b>Overall:</b> 16.3 (SD NR)</p>	<p>NR</p>	<p>CARS Overall: 41.8 <math>\pm</math> 7.1</p>	<p>CARS: <b>G1:</b> 37.8 <math>\pm</math> 8.7 <b>G2:</b> 36.7 <math>\pm</math> 6.1 <b>G3:</b> 39.4 <math>\pm</math> 7.0 p&lt;0.05, G2 vs. baseline</p> <p>ABC reported only graphically</p> <p>Quality considerations: participants not clearly characterized (no cognitive or developmental measures); treatment adherence not reported; outcomes not coded by masked assessors</p>
<p>McDougle et al.,<sup>68</sup> 1998 United States</p> <p><b>G1:</b> Sertraline, n = 42/37 <b>G1a:</b> AD <b>G1b:</b> AS <b>G1c:</b> PDD NOS</p> <p>Quality: Poor</p>	<p>26.1 <math>\pm</math> 5.8</p>	<p>60.5 <math>\pm</math> 22.7 (28 with intellectual disability)</p>	<p>Y-BOCS, total score: <b>G1a:</b> 16.5 <math>\pm</math> 6.7 <b>G1b:</b> 25.7 <math>\pm</math> 4.1 <b>G1c:</b> 18.2 <math>\pm</math> 4.8</p> <p>Vineland maladaptive behavior: <b>G1a:</b> 27.0 <math>\pm</math> 9.4 <b>G1b:</b> 19.8 <math>\pm</math> 8.6 <b>G1c:</b> 28.3 <math>\pm</math> 10.8</p> <p>SIB-Q: <b>G1a:</b> 32.7 <math>\pm</math> 16.5 <b>G1b:</b> 17.5 <math>\pm</math> 7.7 <b>G1c:</b> 36.2 <math>\pm</math> 16.4</p>	<p>Y-BOCS, total score: <b>G1a:</b> 11.5 <math>\pm</math> 5.8 <b>G1b:</b> 27.8 <math>\pm</math> 5.3 <b>G1c:</b> 14.8 <math>\pm</math> 5.7 p = 0.005, G1 vs. baseline</p> <p>Vineland maladaptive behavior: <b>G1a:</b> 13.8 <math>\pm</math> 6.0 <b>G1b:</b> 20.2 <math>\pm</math> 8.2 <b>G1c:</b> 19.5 <math>\pm</math> 9.1 p = 0.0001, G1 vs. baseline</p> <p>SIB-Q: <b>G1a:</b> 15.5 <math>\pm</math> 9.5 <b>G1b:</b> 18.8 <math>\pm</math> 7.7 <b>G1c:</b> 20.2 <math>\pm</math> 12.8 p = 0.0001, G1 vs. baseline</p> <p>Quality considerations: no comparison group; treatment adherence not reported; outcomes not coded by masked assessors; differences in concomitant interventions not reported</p>

**Table 13. Key outcomes of studies assessing SRIs (continued)**

Author, Year, Country, Groups, N Enrollment/N Final Study Quality	Mean Age, Years $\pm$ SD	Mean IQ $\pm$ SD	Outcome Measure/ Baseline Scores, Mean $\pm$ SD	Outcome Measure/Post-Treatment Scores, Mean $\pm$ SD Quality Considerations
<p>Brodkin et al.,<sup>69</sup> 1997 United States</p> <p><b>G1:</b> Clomipramine, 35/33 <b>G1a:</b> Responders, n = 18 <b>G1b:</b> Nonresponders, n = 15</p> <p>Quality: Poor</p>	<p><b>G1:</b> 30.2 <math>\pm</math> 7.0</p>	<p><b>G1:</b> 64.6 <math>\pm</math> 27.2</p>	<p>Y-BOCS, total score: <b>G1a:</b> 18.7 <math>\pm</math> 6.8 <b>G1b:</b> 17.9 <math>\pm</math> 6.2</p> <p>Y-BOCS, compulsion subscale: <b>G1a:</b> 13.7 <math>\pm</math> 3.3 <b>G1b:</b> 13.9 <math>\pm</math> 2.5</p> <p>Y-BOCS, obsession subscale: <b>G1a:</b> 10 <math>\pm</math> 6.8 <b>G1b:</b> 6.7 <math>\pm</math> 6.2</p> <p>Brown Aggression Scale: <b>G1a:</b> 10.6 <math>\pm</math> 7.4 <b>G1b:</b> 6.5 <math>\pm</math> 4.1</p>	<p>Y-BOCS, total score: <b>G1a:</b> 9.1 <math>\pm</math> 3.0 <b>G1b:</b> 17.3 <math>\pm</math> 7.8 p&lt;0.001, G1 vs. baseline p&lt;0.001, G1a vs. G1b</p> <p>Y-BOCS, compulsion subscale: <b>G1a:</b> 6.9 <math>\pm</math> 2.1 <b>G1b:</b> 12.5 <math>\pm</math> 3.3 p&lt;0.001, G1 vs. baseline p&lt;0.001, G1a vs. G1b</p> <p>Y-BOCS, obsession subscale: <b>G1a:</b> 4.4 <math>\pm</math> 2.8 <b>G1b:</b> 8 <math>\pm</math> 6.6 p&lt;0.001, G1 vs. baseline p&lt;0.001, G1a vs. G1b</p> <p>Brown Aggression Scale: <b>G1a:</b> 3.7 <math>\pm</math> 3.6 <b>G1b:</b> 6.4 <math>\pm</math> 4.6 p&lt;0.001, G1 vs. baseline p&lt;0.001, G1a vs. G1b</p> <p>Quality considerations: no comparison group; treatment adherence not reported; outcomes not coded by masked assessors</p>
<p>McDougle et al.,<sup>52</sup> 1996 United States</p> <p><b>G1:</b> Fluvoxamine, 15/15 <b>G2:</b> Placebo, 15/15</p> <p>Quality: Fair</p>	<p><b>G1:</b> 30.1 <math>\pm</math> 7.1 <b>G2:</b> 30.1 <math>\pm</math> 8.4</p>	<p><b>G1:</b> 82.5 <math>\pm</math> 26.8 <b>G2:</b> 77.3 <math>\pm</math> 33.1</p>	<p>Y-BOCS, total score: <b>G1:</b> 21.4 <math>\pm</math> 7.3 <b>G2:</b> 21.5 <math>\pm</math> 6.8</p>	<p>Y-BOCS, total score: <b>G1:</b> 13.7 <math>\pm</math> 9.1 <b>G2:</b> 21.9 <math>\pm</math> 6.7 p&lt;.003, G1 vs. G2</p> <p>Data for Vineland Maladaptive Behavior and Brown Aggression Scale were not reported, although statistically significant improvements were noted.</p> <p>Quality considerations: randomization method not clearly described; treatment adherence not reported</p>

**Table 13. Key outcomes of studies assessing SRIs (continued)**

Author, Year, Country, Groups, N Enrollment/N Final Study Quality	Mean Age, Years $\pm$ SD	Mean IQ $\pm$ SD	Outcome Measure/Baseline Scores, Mean $\pm$ SD	Outcome Measure/Post-Treatment Scores, Mean $\pm$ SD Quality Considerations
Cook et al., <sup>71</sup> 1992 United States  <b>G1:</b> Fluoxetine, 23/23  Quality: Poor	15.9 $\pm$ 6.2	NR, 19 with intellectual disability	CGI-S, total: 5.7 $\pm$ 0.8  CGI-S, compulsion: 5.5 $\pm$ 1.5	CGI-S, total: 4.9 $\pm$ 1.1 p<0.002, G1 vs. baseline  CGI-S, compulsion: 4.7 $\pm$ 1.6 p<0.005, G1 vs. baseline  Quality considerations: no comparison group; inclusion and exclusion criteria not clearly stated; treatment adherence not reported; outcomes not coded by masked assessors

ABC = Aberrant Behavior Checklist; ABC-I = Aberrant Behavior Checklist-Community Rating Scale-Irritability; CARS = Childhood Autism Rating Scale; CGI-S = Clinical Global Impression-Severity; G = group; n = number; NR = not reported; PDD-NOS = pervasive developmental disorder-not otherwise specified; SD = standard deviation; SIB-Q = Self-Injurious Behavior Questionnaire; SRIs = serotonin reuptake inhibitors; Y-BOCS = Yale-Brown Obsessive Compulsive Scale

## Medical Studies Reporting Harms

In one study of risperidone<sup>51</sup> the authors describe sedation as the most prominent adverse effect. Seven subjects did not complete the trial (three in the risperidone arm and four in the placebo arm), with six subjects dropping out due to lack of improvement or agitation, and one subject in the risperidone arm with abnormal gait. In another study of risperidone<sup>67</sup> the most common adverse effects during the risperidone periods of the crossover phase were sedation and gastrointestinal complaints. In 13 subjects these adverse effects triggered automatic 50 percent dose reductions per the study protocol. The Dyskinesia Identification System Condensed User Scale scores from the treatment phases were not statistically different when compared either with the first placebo period (p = 0.052) or the second placebo period (p = 0.482). Symptoms on the Neuroleptic Side Effects Checklist that were the most significant (p<0.001) with treatment included drowsiness, weight gain, and increased appetite. Other symptoms were also significant (p<0.05) including “too quiet,” “not themselves,” tremor, “lack of spontaneity,” and nasal congestion. Mean weight gain during the entire study was 8.3 kg for adolescents and 6.0 kg for adults. There were no abnormal laboratory tests.

In a study of haloperidol<sup>50</sup> the mean duration of haloperidol treatment was 5.8 weeks with 23 of 33 (69.7%) subjects completing the 7-week treatment phase; seven of 10 subjects who discontinued had adverse effects, including fatigue (n = 5), dystonia (n = 1), and depression (n = 1). The mean duration of placebo treatment was 5.4 weeks with 21 of 32 subjects (65.6%) completing the 7-week phase; one of nine subjects who discontinued had adverse effects which only included nose bleeds. The other eight subjects discontinued due to lack of improvement in symptoms. There were no significant changes in 12-lead electrocardiogram variables, either in the haloperidol or placebo phases.

In one study of opioid receptor antagonist identified,<sup>53</sup> 11 subjects were taking antipsychotics with the dose held steady during the study. Possible adverse events included one subject with an acute increase in self-injurious behavior, one subject with nausea and tiredness, and three subjects with sedation. Liver function tests remained within normal ranges. The single dose had no effect on the clinician-rated questionnaire, direct observation, self-injurious behavior, or plasma beta-endorphins. Plasma cortisol was significantly increased ( $p = 0.006$ ) for naltrexone compared with placebo. Long-term treatment (4 weeks) with naltrexone resulted in a significant increase in stereotypy as measured by the ABC stereotypy subscale.

One study of clomipramine<sup>50</sup> used a crossover design with a mean duration of clomipramine treatment of 4.5 weeks with 12 of 32 (37.5%) subjects completing the 7-week treatment phase; 12 of 12 subjects that discontinued had adverse effects which included fatigue or lethargy ( $n = 4$ ), tremor ( $n = 2$ ), tachycardia ( $n = 1$ ), insomnia ( $n = 1$ ), diaphoresis ( $n = 1$ ), nausea or vomiting ( $n = 1$ ), decreased appetite ( $n = 1$ ), and preexisting right bundle branch block ( $n = 1$ ). The mean duration of placebo treatment was 5.4 weeks with 21 of 32 (65.6%) subjects completing the 7-week treatment phase; 1 of 9 subjects that discontinued had adverse effects which only included nose bleeds ( $n = 1$ ). There were no significant changes in 12-lead electrocardiogram variables, either in the clomipramine or placebo arms. Statistical comparisons were not reported for the clomipramine versus placebo for the CARS, Extrapyramidal Symptom Rating Scale, or Dosage Treatment Emergent Symptom Scale.

Another study assessing the efficacy and tolerability of clomipramine reported adverse effects in 13 individuals, 3 of whom had seizures during clomipramine treatment.<sup>69</sup> Two of the three participants with seizures had previously diagnosed seizure disorders and were concurrently medicated with antiepileptic medication. The two participants not completing the trial withdrew due to agitation in one individual and abdominal cramping in the second. Other participants who completed the trial experienced constipation ( $n = 3$ ), weight gain ( $n = 3$ ), anorgasmia ( $n = 1$ ), and sedation ( $n = 2$ ). There were no cardiovascular or extrapyramidal adverse effects. There was no placebo control group to compare with the clomipramine treatment group in this open-label trial.

One RCT<sup>52</sup> investigated the efficacy of fluvoxamine in adults with autistic disorder. Adverse effects in the fluvoxamine group included mild sedation ( $n = 2$ ) and nausea ( $n = 3$ ). There were no significant changes in anticholinergic effects, vital signs, routine lab analyses, or electrocardiogram.

In a case series<sup>68</sup> assessing the efficacy and tolerability of sertraline, five subjects withdrew from the study: three due to anxiety/agitation, one due to syncope, one due to noncompliance. There were no cardiovascular, extrapyramidal, or seizure adverse effects. There was no placebo control group for comparison of possible therapeutic effects or adverse events. Finally, another case series<sup>71</sup> examined fluoxetine and reported that six of 23 participants experienced side effects that “significantly” interfered with function or outweighed therapeutic benefits. Harms reported overall included agitation ( $n = 5$ ), insomnia ( $n = 4$ ), elated affect ( $n = 4$ ), decreased appetite ( $n = 4$ ), and increased screaming ( $n = 2$ ). Additional harms were reported in at least one individual (inappropriate behavior, crying, yawning, rash).

# Studies of Allied Health Interventions

## Key Points

- Five studies, one fair and four poor quality, investigated disparate allied health approaches. Three studies included individuals with ASD and intellectual disability.
- A leisure/recreation program reported positive effects on stress and quality of life in a fair quality RCT.
- Facilitated communication did not increase participants' communication or literacy abilities over their independent abilities.
- Some positive effects on social skills were reported in studies of music therapy, but outcome measures were unvalidated and largely subjective.
- No two studies assessed the same intervention; therefore, although individual studies report promising results, without replication, and with no studies of good quality, the strength of evidence for the body of literature is insufficient that any allied health approach is associated with positive outcomes.

## Overview of the Literature

We identified five studies of allied health interventions<sup>49, 58-60, 70</sup> including one fair quality RCT investigating a leisure/recreation program.<sup>49</sup> Appendix G provides the quality ratings for each study. The RCT, conducted in Spain, included 71 individuals ranging from 17 to 49 years of age with mean Leiter mental age scores of  $64.36 \pm 21.33$  months in the intervention group and  $61.44 \pm 9.37$  months in the control group. Assessments included measures of quality of life and stress. Two poor quality prospective case series addressed facilitated communication,<sup>59, 70</sup> and two poor quality retrospective case series addressed music therapy.<sup>58, 60</sup> Studies were conducted in the United States<sup>58-60</sup> and Canada<sup>70</sup> and included participants ranging in age from 2 to 40 across the studies. The duration of treatment ranged from 20 hours to 7 months in three studies;<sup>59, 60, 70</sup> one study of music therapy reviewed data from participants who had participated in varying hours of therapy.<sup>58</sup> Studies of facilitated communication<sup>59, 70</sup> employed outcome measures gauging the number of correct responses to a given task with and without the aid of a facilitator. Facilitators helped to steady or physically support the hand of an individual with ASD either typing responses on a keyboard or pointing to images. Study evaluating a music therapy program<sup>58, 60</sup> reported on the number of goals met and social outcomes or social outcomes using largely subjective measures. Tables 14 and 15 summarize key study outcomes.

## Detailed Analysis

### Allied Health Studies Addressing Core Symptoms of ASD

#### Music Therapy

A poor quality case series addressing music therapy<sup>58</sup> used 2 years of therapist database records to assess the number of goals met and types of music therapy employed with 40 clients. Participants ages ranged from 2 to 49 years (mean age = 13.9) and all had diagnoses on the autism spectrum. Diagnoses were not reported as confirmed within the study. Music therapy involved individual or small or large group sessions and occurred in settings including a community music school or group home. The number of sessions varied for each client.



Therapists assessed each client's "level of difficulty" related to aggression, property destruction, on-task behavior, and other domains on a scale with a maximum value of 14 points (highest level of difficulty); participants' level of difficulty ratings averaged 2.5. Therapists also set and tracked goals met in areas including behavioral/psychosocial skills, language/communication skills, perceptual/motor skills, and cognitive skills. Therapists defined meeting a goal as an increase or decrease of 25 percent from a client's baseline level of performance. Parents also completed annual questionnaires to assess generalizations of skills to other settings. All participants achieved their initial goal within 1 year as well as achieved 77 percent of intermediate goals. Attainment of goals was not affected by client level of difficulty or session type. Thirty caregivers returned generalization surveys, which reported that all participants used skills practiced in music therapy in nontherapy settings occasionally or frequently.

### **Facilitated Communication**

Two poor quality case series addressed facilitated communication,<sup>59, 70</sup> and included 41 individuals with ASD ranging in age from 8 to 21. Both studies included individuals with limited literacy, and one assessed the effects of facilitated communication via a series of picture recognition tasks performed with and without a facilitator and with the facilitator informed and uninformed of the object presented.<sup>70</sup> Facilitators, staff members of a school for individuals with autism, all received 2 days of facilitated communication training. In one task involving participants' pointing to the picture of a word displayed previously, the number of correct responses was greatest when facilitators were aware of the word displayed. Facilitated communication did not enhance participant performance beyond participants' independent communication abilities, and facilitator influence was evident for at least 12 of 20 participants. In a second task using headphones and requiring responses to auditory cues, facilitators heard the same message as participants, a different message, or white noise. Responses across all 3 trials were not significantly different, and facilitator influence was evident for 14/20 participants.

In a third task participants completed segments of the Peabody Picture Vocabulary Test with and without facilitated communication. Scores on the test did not differ significantly between conditions; all 12 participants completing the test showed receptive language difficulties, and there were no clear patterns of facilitator influence. The investigators also collected followup data for seven participants after 5 to 7 additional months of facilitated communication use. Additional time with facilitated communication did not increase participants' accuracy of responding and was associated with increased facilitator influence in one task ( $p < 0.03$ ).

A second case series addressing facilitated communication included 21 participants (mean age = 15.5) with ASD and mild to profound intellectual disability and language development age equivalent ranging from 1.6 to 5.1 years.<sup>59</sup> Study tasks involved both facilitated and non-facilitated communication. In the non-facilitated condition, facilitators were screened from stimuli or investigator cues visible or audible to participants. Facilitators were trained in the history and principles of facilitated communication for roughly 4 hours before participating in the study, and facilitators unfamiliar to participants spent at least 2 weeks prior to the study helping participants acclimate. Participants completed baseline measures without facilitation and pretest measures with the assistance of screened facilitators. These tests were followed by 20 hours of facilitated communication exposure and training prior to completing post-test outcome measures.

Investigators scored participant responses liberally, counting as correct partial words, misspellings, and recognizable character strings embedded in other text (e.g., the characters “OSY” were scored correctly for “yes”). Performance on initial test measures declined from baseline (14/21 participants able to answer some questions correctly) to pretest (2/21 participants able to answer some questions correctly). At post-test, conducted after facilitated communication training and with screened facilitation, 2 of 21 participants were able to answer some questions correctly. Scores for a test session during which facilitators were not screened were higher, with 6 out of 21 participants able to answer some questions correctly. No participants demonstrated improved communication abilities or literacy.

**Table 14. Key outcomes of studies of allied health interventions addressing core symptoms of ASD**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Yrs, Mean ± SD IQ, Mean ± SD	Key Outcomes
<b>Music Therapy</b>		
Kaplan et al., <sup>58</sup> 2005 United States  <b>G1:</b> Music therapy, 40/40  Quality: Poor	<b>G1: 13.9 (range 2-49)</b>  <b>NR</b>	<ul style="list-style-type: none"> <li>• Retrospective review of client database records; music therapists set goals and determined percentage increase/decrease in skills/behavior relevant to goal.</li> <li>• 40/40 participants with ASD met initial goals within 12 months of therapy; over 70% of participants met intermediate goals.</li> <li>• All caregivers returning generalization surveys (n = 30) reported use of skills practiced in therapy sessions in non-therapy sessions occasionally or frequently.</li> <li>• Quality considerations: no comparison group; systematic diagnostic approach not reported within study; participants not clearly characterized (no cognitive or developmental measures); attrition not reported; intervention not fully described; measure of treatment fidelity not reported; outcome measures not valid/reliable; outcomes not coded by masked assessors.</li> </ul>
<b>Facilitated Communication</b>		
Bebko et al., <sup>70</sup> 1996 Canada  <b>G1:</b> Facilitated communication  Quality: Poor	<b>G1: 13 (range 6-21)</b>  <b>G1: 1.3 years - 4 years (mental age range)</b>	<ul style="list-style-type: none"> <li>• 6 weeks of FC training and practice with up to 7months followup data for 7 participants.</li> <li>• Scores on visual stimulus experiment increased from baseline when FC used and facilitator aware of word being prompted (56.86% correct responses vs. 75%); scores decreased from baseline when FC used and facilitator not informed of word prompted (30% correct responses vs.25.57%).</li> <li>• Visual stimulus scores increased from baseline when no FC used and facilitator was informed of word being prompted (36.71% correct responses vs. 53.57%) and decreased when no FC used and facilitator not informed of word (35.71% correct vs. 32.57%).</li> <li>• FC did not enhance communication beyond participants' independent abilities.</li> <li>• Quality considerations: no comparison group; inclusion and exclusion criteria not clearly stated; measure of treatment fidelity not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>

**Table 14. Key outcomes of studies of allied health interventions addressing core symptoms of ASD (continued)**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Yrs, Mean ± SD IQ, Mean ± SD	Key Outcomes
<b>Facilitated Communication (continued)</b>		
Eberlin et al., <sup>59</sup> 1993 United States  <b>G1:</b> Facilitated communication, 21/21  Quality: Poor	<b>G1: 15.5 (range 11.3-20.2)</b>  <b>G1:</b> <b>Mild to moderate intellectual disability, n = 2</b> <b>Moderate to severe intellectual disability, n = 11</b> <b>Severe to profound intellectual disability, n = 8</b>	<ul style="list-style-type: none"> <li>• 20 total hours FC training.</li> <li>• Median correct answers declined from baseline (no FC) after testing using FC with facilitator not informed of words prompted (8 correct answers vs. 0); median score at testing with FC and facilitator informed of word prompted = 1.</li> <li>• Communication ability or literacy did not improve for any participants.</li> <li>• Quality considerations: no comparison group; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>

ASD = autism spectrum disorders; FC = facilitated communication; G = group; IQ = intelligence quotient; N = number; SD = standard deviation

## Allied Health Studies Addressing Independent Functioning

One fair quality RCT investigating a leisure/recreation program randomized individuals with ASD to either a waiting list control group (n = 34) or a 12-month leisure program emphasizing engagement in exercise, playing games and completing crafts, interacting with media, and attending social events (n = 37) (Table 15).<sup>49</sup> ASD diagnoses were confirmed within the study. Participants ranged in age from 17 to 49 years and had mean Leiter mental age scores of 64.36 ± 21.33 months in the intervention group and 61.44 ± 9.37 months in the control group. Assessments included measures of quality of life and stress completed at baseline and after 12 months by participants with adequate verbal skills or by individuals familiar with the participant.

Scores on the stress assessment improved for individuals in the intervention group compared with those in the control group (p<0.001). Overall quality of life scores similarly improved for intervention participants compared with the waiting list group; however, scores on empowerment/independence and social/integration subscales did not improve significantly between groups.

One poor quality case series investigated music therapy interventions using largely subjective measures. One study addressed a university-based program aimed at assessing the feasibility of a music program in promoting social skills in adolescents and young adults with ASD.<sup>60</sup> The 22 participants ranged from age 13 to 29 (mean = 18), and diagnoses were not reported as confirmed within the study. The program's curriculum included sessions in learning about music, music appreciation, video production, and storytelling with music over 8 weeks. Investigators assessed participants' and parents' impressions of social benefits gained via a 1 (low) to 10 (high) scale and open-ended questions. Both parents and participants rated the program highly with mean scores of nearly 7. Nineteen participants indicated that they had made friends during the program, and 11 parents noted that their children had made friends.

**Table 15. Summary of outcomes of studies of allied health interventions addressing independent functioning**

Author, Year, Country Groups, N Enrollment/N Final Study Quality	Age, Yrs, Mean ± SD IQ, Mean ± SD	Key Outcomes
<p>Garcia-Villamizar et al.,<sup>49</sup> 2010 Spain</p> <p><b>G1:</b> Leisure/recreation program, 37/37 <b>G2:</b> Wait list control, 34/34</p> <p>Quality: Fair</p>	<p><b>G1: 31.49 ± 4.83</b> <b>G2: 30.06 ± 3.44</b></p> <p><b>IQ (Leiter)</b> <b>G1: 63.46 ± 21.33</b> <b>G2: 61.44 ± 9.37</b></p>	<ul style="list-style-type: none"> <li>• Participants randomized to 12-month recreation/leisure program or waiting list.</li> <li>• Stress and total quality of life scores improved for treatment group compared with wait list group (p&lt;0.001).</li> <li>• Scores on empowerment/independence and social/integration subscale improved for treatment group vs. control but not significantly.</li> <li>• Quality considerations: randomization method not clearly described; attrition not reported; measure of treatment fidelity not reported; differences in concomitant interventions not reported.</li> </ul>
<p>Greher et al.,<sup>60</sup> 2010 United States</p> <p><b>G1:</b> Music therapy (SoundScape), 22/22</p> <p>Quality: Poor</p>	<p><b>G1: 18 (range: 13-29)</b></p> <p><b>NR</b></p>	<ul style="list-style-type: none"> <li>• 8-week program emphasizing understanding elements of music and recording music.</li> <li>• Participants and parents rated social benefits of program highly.</li> <li>• 11 participants and 19 parents reported that they/their child had developed friendships through the program.</li> <li>• Quality considerations: no comparison group; systematic diagnostic approach not reported within study; participants not clearly characterized (no cognitive or developmental measures); measure of treatment fidelity not reported; differences in concomitant interventions not reported; outcomes not coded by masked assessors.</li> </ul>

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

# Discussion

## State of the Literature

Despite a growing population of adolescents and young adults who have diagnoses of an autism spectrum disorder (ASD) and the need for effective intervention across the lifespan, very little research is available to guide therapy in adolescents and young adults with ASD. The available research is lacking in scientific rigor. We identified 32 studies (one paper reported two separate studies), of which 10 were randomized controlled trials (RCTs). Nonetheless, most studies were of poor quality; only five were fair quality and none was good quality.

Studies typically addressed the core symptoms (impairments in communication, social interaction, or behavior) of ASD (Key Question 1) and the effects of interventions on functional and adaptive behavior (Key Question 3). One study addressed the transition process (Key Question 4), and two addressed family outcomes (Key Question 6). Harms of interventions (Key question 5) were only discussed in studies of medical approaches. Eight studies of medical approaches and one behavioral study addressed Key Question 2, which examined the effects of interventions on comorbid medical or mental health conditions (e.g., epilepsy, sleep disorders, motor impairments, obesity, depression, anxiety, acute and episodic aggression, attention deficit hyperactivity disorder, etc.).

## Summary of Outcomes

### Studies of Behavioral Interventions

Six poor quality studies of targeted social skills interventions representing different individual/group- and computer-based paradigms met our inclusion criteria.<sup>47, 61-63, 76, 77</sup> Research involving individual or group-based interventions<sup>61, 62, 76, 77</sup> reported improvements across a variety of social skills as rated by parents. Research on computer assisted interventions suggested improvements associated with emotion recognition.<sup>47, 63</sup> However, each study employed a different approach and paradigm, making synthesis of the results into one estimate of effect impossible. Likewise, such social skills interventions have yet to demonstrate consistent generalization of skills across settings and often circumscribe interventions to individuals with average to above average verbal and/or cognitive abilities. As such, the strength of evidence for social skills interventions is insufficient, meaning that future research is needed to establish one effect.

A single poor quality case series of a semi-residential, intensive behavior-based intervention included 34 adolescents and focused on changes in adaptive behavior after 2 years of program attendance.<sup>64</sup> Overall, both male and female participants improved on measures of socialization, and females also improved in daily living and motor skills. While the authors reported that there was a positive impact across a fairly heterogeneous group, the study did not involve a control group and did not clearly define an intervention; parental satisfaction data reported were positive.

### Studies of Educational Interventions

Research into language and communication strategies for adolescents and young adults with ASD is very limited, with only two small crossover studies identified in this population. There is little evidence to support selection among various educational strategies, with one study finding

similar vocabulary acquisition between analog and natural language approaches.<sup>66</sup> Procedural facilitation and anaphoric cuing showed some promise for increasing vocabulary in high-functioning ASD but were addressed in only one small, short term study.<sup>65</sup>

## **Studies of Adaptive/Life Skills Interventions**

Studies of adaptive-focused interventions meeting our criteria were of poor quality, addressed disparate interventions, and included few participants. No study included more than 81 individuals with ASD, and at least two studies included individuals with concomitant intellectual disability. Interventions addressing teaching self-care skills (shoe lacing),<sup>55</sup> digital memory aids,<sup>57</sup> and a residential, Treatment and Education of Autistic and Communication related handicapped Children (TEACCH)-based program<sup>54</sup> reported some positive effects. Studies were typically uncontrolled and of short duration, however.

One poor quality study assessed the effects of a classroom rotation schedule on crisis events in a residential school<sup>56</sup> and reported no significant increase in events after the implementation of classroom rotation. The few studies addressing family-focused outcomes reported parent or family satisfaction with treatment approaches. One study of a TEACCH-based residential program compared with group homes and institutions reported greater satisfaction with treatment and program participants' community involvement among parents of individuals in the TEACCH-based facility compared with group homes.<sup>54</sup> Parents of individuals in the TEACCH residence were also more satisfied with the impact of the placement on the family than parents of individuals in other groups. Assignment to the TEACCH program, however, was not random; thus individuals in the group may have differed meaningfully from individuals in group homes, family homes, or institutions.

## **Studies of Vocational Interventions**

Our search identified five studies focused on supported employment/vocational interventions.<sup>17, 48, 72-75</sup> It is important to note that all of the identified studies focused on on-the-job supports as the employment/vocational intervention; no other vocational interventions were reported in the literature meeting our study criteria. Our ability to assess the benefit of supported employment programs is limited, given the existing research. No study utilized random assignment, making it difficult to draw conclusions about the effectiveness of the programs. The majority of the studies were small, and all were poor quality thus the strength of the evidence is insufficient at this time.

Supported employment interventions are particularly understudied. For example, only one study examined rates of employment for programs that lasted 3 years or longer.<sup>17</sup> Further, this longer-term study did not include a control group, making it impossible to determine the rates of employment over time for young adults with ASD who were not participating in the supported employment intervention. Finally, none of the studies examined whether increased employment rates or improvements in other outcomes were sustained after the termination of the supported employment intervention.

## **Studies of Medical Interventions**

The use of medical interventions in adolescents and young adults with ASD is common.<sup>78</sup> However, there is little evidence that supports the use of medical interventions specifically in this population. We identified three studies of antipsychotic medications,<sup>50, 51, 67</sup> five studies of

serotonin reuptake inhibitors (SRIs),<sup>50, 52, 68, 69, 71</sup> and one study of an opiate antagonist.<sup>53</sup> Overall, most of these studies focused on the use of medications to address specific challenging behaviors (i.e., aggression or irritability). Four studies were fair quality,<sup>50-53</sup> and four were poor.<sup>67-69, 71</sup>

The most consistent findings were identified for antipsychotic medications. An RCT studying risperidone found improvements in aggression, repetitive behavior, sensory motor behaviors, and overall behavioral symptoms.<sup>51</sup> A crossover study of risperidone also showed a significant reduction of irritability/agitation ratings with risperidone treatment, but the control was indirect.<sup>67</sup> A placebo-controlled crossover study found that haloperidol significantly improved hyperactivity/defiance ratings, but no significant difference was found for irritability/agitation or other symptoms.<sup>50</sup> While limited literature supports the use of risperidone in adolescents or young adults with ASD, the efficacy of risperidone in studies including mostly children has moderate strength of evidence<sup>32</sup> that is consistent with the results of the one fair RCT and one poor crossover study in adults with ASD. There is therefore no evidence to suggest that the effects of risperidone for irritability/agitation in ASD is specific to a particular age range.

A number of studies of SRIs were identified but with limited consistency across studies as a whole. An RCT of fluvoxamine showed decreases in repetitive behavior, aggression, autistic symptoms, and language usage.<sup>52</sup> In contrast, no significant differences were observed in a crossover study of clomipramine versus placebo.<sup>50</sup> Three case series of SRIs were also identified, including sertraline, fluoxetine, and clomipramine, with each study reporting some benefit to treatment.<sup>68, 69, 71</sup> A recent study not meeting criteria for this review contributes to the limited data on SRIs: the placebo-controlled RCT<sup>79</sup> of fluoxetine included 37 individuals with ASD with a mean age of 34.31 and reported improvements in repetitive behavior and ASD symptoms in the treatment group and mild harms. This study used a different medication than the one fair quality study in our age range, so it would be unlikely to influence the strength of evidence for a specific medication. It is possible, however, that a systematic review of SRIs in the broader age range of adults with ASD could provide data that might increase our confidence in the effect.

A crossover study of the opioid receptor antagonist naltrexone found no significant improvements in problem behavior and showed worsening of stereotyped behavior with naltrexone treatment compared with placebo.<sup>53</sup>

Based upon the published studies in adolescents and adults with ASD, the strength of evidence is insufficient regarding harms associated with medications tested in this population. As in the case of efficacy, the data on adverse effects associated with risperidone, including sedation and weight gain, are consistent with the high strength of evidence for the association of treatment with these adverse effects in children with ASD.<sup>32</sup> The available evidence therefore appears consistent in supporting our understanding of the risk of these adverse events in ASD without being limited to a specific age range. Of course, this does not mean that other medications tested in ASD are free of adverse effects. It is reasonable to expect that, in contrast to efficacy, which is more likely to be specific to disorder and symptom, adverse effects are more likely to extend across diverse groups of subjects studied. Clinicians evaluating the evidence and sharing information with families routinely take this perspective, as does the Food and Drug Administration in mandating that all adverse events be listed for a drug, rather than just those for a particular indication.

As one example, the limited studies of adults with ASD treated with risperidone indicate weight gain as an adverse effect but in too few studies to draw a clear conclusion about the strength of evidence. There is, however, high strength of evidence for weight gain in children with ASD treated with risperidone, as noted in a previous comparative effectiveness review.<sup>32</sup>

Similarly, recent Cochrane reviews found substantial evidence for weight gain in adults with schizophrenia or bipolar disorder treated with risperidone.<sup>80,81</sup> When the broader evidence base is considered, the consistency of these findings supports an association of weight gain with risperidone in adults with ASD, just as is true in children with ASD and adults with other disorders. This approach to assessing the evidence for harms is outside of the scope of this review, but similar conclusions could be drawn with respect to sedation and extrapyramidal symptoms with risperidone or haloperidol.

## **Studies of Allied Health Interventions**

Few studies of allied health interventions met our criteria.<sup>49, 58-60, 70</sup> One fair quality RCT assessed a 12-month recreation program<sup>49</sup> and reported improved quality of life and lower stress scores in individuals participating in the leisure/recreation program compared with those on a waiting list. One poor quality case series<sup>60</sup> included 22 young adults engaged in a music therapy intervention. Nearly all participants reported making friends during the program and were generally satisfied with the program. Both studies assessed outcomes shortly after treatment, so longer-term effects of the interventions are not known.

Two studies of facilitated communication<sup>59,70</sup> used approaches designed to assess the effects of facilitation both with and without facilitators' awareness of the word being prompted. Both studies demonstrated some facilitator influence and limited effects on participants' independent ability to communicate. One retrospective study of a music therapy program reported some positive effects on participants' social skills using largely subjective outcome measures.<sup>58</sup>

## **Strength of the Evidence for Effectiveness of Therapies**

### **Overview**

We assessed the literature 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 Effective Health Care Program's Methods Guide for Effectiveness and Comparative Effectiveness Reviews<sup>46</sup> 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. Table 3 in the Methods section of the report includes a description of these domains.

We determined the strength of evidence for outcomes including social skills, adaptive behavior, autism symptom, challenging and repetitive behavior, harms of treatment, employment, and parent satisfaction. Tables 16 through 21 document the strength of evidence for each domain of the major intervention-outcome combinations.



## Strength of the Evidence

### Behavioral Interventions

All studies assessing behavioral interventions were poor quality. The strength of the evidence for all interventions targeting social skills is insufficient as it is for an intensive behavioral intervention (Table 16).

**Table 16. Intervention, strength of evidence domains, and strength of evidence for outcomes of behavioral studies**

Outcome/Intervention	Study Type (N Studies of Type Reporting Outcome)	Domains Pertaining to Strength of Evidence (SOE)				SOE
		Risk of Bias	Consistency	Directness	Precision	
<b>Adaptive Behavior</b>						
Intensive behavioral treatment	Case series (1) <sup>64</sup>	High	Unknown	Direct	Imprecise	Insufficient
<b>Problem Behavior</b>						
Social skills individual/group training	Case series (1) <sup>77</sup>	High	Unknown	Direct	Imprecise	Insufficient
<b>Social Skills/Social Behaviors</b>						
Social Skills groups	RCT (1) <sup>61</sup> Case series (1) <sup>62</sup>	High	Consistent	Direct	Imprecise	Insufficient
Computer-based social skills intervention <sup>a</sup>	RCT (3) <sup>47, 63</sup> nRCT (1) <sup>47</sup>	Medium	Inconsistent	Indirect	Imprecise	Insufficient
<b>Parent Satisfaction</b>						
Intensive behavioral treatment	Case series (1) <sup>64</sup>	High	Unknown	Direct	Imprecise	Insufficient

N = number; RCT = randomized controlled trial; SOE = strength of evidence

<sup>a</sup>Paper includes two unique studies reported in one publication.

### Educational Interventions

Only two poor quality studies investigated educational interventions targeting communication skills thus we assessed the strength of the evidence as insufficient (Table 17).

**Table 17. Intervention, strength of evidence domains, and strength of evidence for key outcomes of educational studies**

Outcome/Intervention	Study Type (N Studies of Type Reporting Outcome)	Domains Pertaining to Strength of Evidence (SOE)				SOE
		Risk of Bias	Consistency	Directness	Precision	
<b>Language/Communication</b>						
Teaching strategies	RCT (1) <sup>65</sup> nRCT (1) <sup>66</sup>	High	Inconsistent	Direct	Imprecise	Insufficient

N = number; nRCT = nonrandomized controlled trial; RCT = randomized controlled trial; SOE = strength of evidence

### Adaptive/Life Skills Interventions

With four poor quality studies targeting disparate outcomes using disparate adaptive/life skills-focused interventions focused on highly specific tasks/skills, we rated the strength of the evidence overall as insufficient (Table 18).

**Table 18. Intervention, strength of evidence domains, and strength of evidence for outcomes of adaptive/life skills studies**

Outcome/Intervention	Study Type (N Studies of Type Reporting Outcome)	Domains Pertaining to Strength of Evidence (SOE)				SOE
		Risk of Bias	Consistency	Directness	Precision	
<b>Adaptive/Functional Behavior</b>						
Self-care/ADL training	RCT (1) <sup>55</sup> Prospective cohort (1) <sup>54</sup> Case series (2) <sup>56, 57</sup>	High	Consistent	Direct	Imprecise	Insufficient
<b>Parent Satisfaction</b>						
TEACCH-based program	Prospective cohort (1) <sup>54</sup>	High	Unknown	Direct	Imprecise	Insufficient

ADL = activities of daily living; N = number; RCT = randomized controlled trial; SOE = strength of evidence; TEACCH = Treatment and Education of Autistic and Communication related Handicapped Children

## Vocational Interventions

Five studies assessed employment-related outcomes as well as outcomes related to cognition and autism symptoms. All studies were poor quality, and we assessed the strength of the evidence as insufficient for all outcomes (Table 19).

**Table 19. Intervention, strength of evidence domains, and strength of evidence for supported employment/vocational interventions**

Outcome/Intervention	Study Type (N Studies of Type Reporting Outcome)	Domains Pertaining to Strength of Evidence (SOE)				SOE
		Risk of Bias	Consistency	Directness	Precision	
<b>Employment</b>						
Supported employment/vocational	Prospective cohort (1) <sup>73</sup> Case series (1) <sup>17</sup> Cross-sectional (1) <sup>48</sup>	High	Consistent	Direct	Imprecise	Insufficient
<b>Autism Symptoms</b>						
Supported employment/vocational	nRCT (1) <sup>74, 75</sup>	High	Unknown	Direct	Imprecise	Insufficient
<b>Quality of Life</b>						
Supported employment/vocational	nRCT (1) <sup>74, 75</sup>	High	Unknown	Direct	Imprecise	Insufficient
<b>Cognitive Development</b>						
Supported employment/vocational	nRCT (1) <sup>72</sup> Prospective cohort	High	Unknown	Direct	Imprecise	Insufficient

N = number; nRCT = nonrandomized controlled trial; SOE = strength of evidence

## Medical Interventions

There were no good studies identified for antipsychotics, serotonin reuptake inhibitors, or opioid receptor antagonists in adolescents or young adults with ASD. The strength of evidence

for each of these medication classes is insufficient. Similarly the strength of evidence for adverse effects is also insufficient (Table 20).

The strength of evidence for the use of risperidone to treat irritability and repetitive behaviors in ASD is insufficient based on a single fair RCT<sup>51</sup> and a single poor crossover study.<sup>67</sup> The strength of evidence for the use of haloperidol to treat hyperactivity/defiance in ASD is insufficient based on a single fair study.<sup>50</sup> The strength of evidence for the use of naltrexone for the treatment of either problem behaviors or core ASD symptoms is insufficient based on a single fair crossover trial. The strength of evidence for the use of clomipramine for the treatment of ASD symptoms is insufficient based on a single fair study,<sup>50</sup> and a single poor case series study.<sup>69</sup> The strength of evidence for the use of fluvoxamine for repetitive behaviors, aggression, or other ASD symptoms is insufficient based on a single fair RCT.<sup>52</sup>

**Table 20. Intervention, strength of evidence domains, and strength of evidence for outcomes of medical studies**

Outcome/Intervention	Study Type (N Studies of Type Reporting Outcome)	Domains Pertaining to Strength of Evidence (SOE)				SOE
		Risk of Bias	Consistency	Directness	Precision	
<b>Challenging Behavior</b>						
Risperidone	RCT (2) <sup>51, 67</sup>	Medium	Consistent	Direct	Imprecise	Insufficient
Haloperidol	RCT (1) <sup>50</sup>	Medium	Unknown	Direct	Imprecise	Insufficient
Clomipramine	RCT (1) <sup>50</sup> Case series (1) <sup>69</sup>	Medium	Inconsistent	Direct	Imprecise	Insufficient
Fluvoxamine	RCT (1) <sup>52</sup>	Medium	Unknown	Direct	Imprecise	Insufficient
Sertraline	Case series (1) <sup>68</sup>	High	Unknown	Direct	Imprecise	Insufficient
<b>Repetitive Behavior</b>						
Risperidone	RCT (1) <sup>51</sup>	Medium	Consistent	Direct	Imprecise	Insufficient
Naltrexone	RCT (1) <sup>53</sup>	Medium	Unknown	Direct	Imprecise	Insufficient
Haloperidol	RCT (1) <sup>50</sup>	Medium	Unknown	Direct	Imprecise	Insufficient
Clomipramine	RCT (1) <sup>50</sup> Case series (1) <sup>69</sup>	Medium	Inconsistent	Direct	Imprecise	Insufficient
Sertraline	Case series (1) <sup>68</sup>	High	Unknown	Direct	Imprecise	Insufficient
Fluoxetine	Case series (1) <sup>71</sup>	High	Unknown	Indirect	Imprecise	Insufficient
<b>Harms</b>						
Risperidone	RCT (2) <sup>51, 67</sup>	Medium	Consistent	Direct	Imprecise	Insufficient
Naltrexone	RCT (1) <sup>53</sup>	Medium	Unknown	Direct	Imprecise	Insufficient
Haloperidol	Case series (1) <sup>68</sup>	Medium	Unknown	Direct	Imprecise	Insufficient
Clomipramine	RCT (1) <sup>50</sup> Case series (1) <sup>69</sup>	Medium	Inconsistent	Direct	Imprecise	Insufficient
Sertraline	Case series (1) <sup>68</sup>	High	Unknown	Direct	Imprecise	Insufficient
Fluoxetine	Case series (1) <sup>71</sup>	High	Unknown	Indirect	Imprecise	Insufficient
Fluvoxamine	RCT (1) <sup>52</sup>	Medium	Unknown	Direct	Imprecise	Insufficient

N = number; RCT = randomized controlled trial; SOE = strength of evidence

## Allied Health Interventions

With only one fair quality RCT of a leisure program addressing quality of life outcomes, we rated the strength of the evidence as insufficient for this outcome. Similarly, the strength of the evidence was insufficient for other allied health interventions and outcomes (Table 21).

**Table 21. Intervention, strength of evidence domains, and strength of evidence for outcomes of allied health studies**

Outcome/Intervention	Study Type (N Studies of Type Reporting Outcome)	Domains Pertaining to Strength of Evidence (SOE)				SOE
		Risk of Bias	Consistency	Directness	Precision	
<b>Quality of Life</b>						
Recreation program	RCT (1) <sup>49</sup>	High	Unknown	Direct	Imprecise	Insufficient
<b>Social Skills/Social Behaviors</b>						
Music therapy	Case series (1) <sup>60</sup>	High	Unknown	Indirect	Imprecise	Insufficient
<b>Language</b>						
Music therapy	Case series (1) <sup>58</sup>	High	Unknown	Indirect	Imprecise	Insufficient
Facilitated communication	Case series (2) <sup>59, 70</sup>	High	Consistent	Direct	Imprecise	Insufficient

N = number; RCT = randomized controlled trial; SOE = strength of evidence

## Applicability

### Applicability of the Evidence

By definition, ASDs are heterogeneous. Characterizing a “typical” individual with an ASD is not possible, although certain symptoms are central to the range of individuals 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. We describe the applicability of the evidence for interventions represented in this review below.

### Behavioral Interventions

Studies of behavioral interventions to date have been limited in scope. The single investigation of an intensive, comprehensive behavioral intervention was conducted across a broad age range of individuals (4 to 18) within a residential rehabilitation center. While numerous studies of younger children have focused on intensive behavioral and developmental interventions, quite often behavioral interventions for adolescents and young adults with ASD have been limited to social skills interventions. Social skills interventions in turn have been limited to investigations conducted with individuals with substantial cognitive and verbal abilities, often individuals with high-functioning autism or Asperger syndrome. Therefore the evidence of social skills interventions is likely applicable only to older, higher functioning individuals. The range of approaches studied also does not always match what is available in practice—that is, either the studies were conducted in highly controlled environments (e.g., university-supported manualized intervention trials), the actual methodology was not well described (i.e., approaches lacking treatment manuals), or the computer based intervention is not widely available. 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. Ultimately, the effectiveness of social skills interventions within and outside of these limited samples and setting is currently unknown.

## **Educational Interventions**

The two studies of educational interventions included in this review were conducted in the United States and Canada in the home and educational environments. Characteristics of participants in the studies (intelligence quotient [IQ], language skills) likely represented a wide spectrum and were not categorized well enough to assess their applicability to the larger population. Educational approaches targeted acquisition of vocabulary and included individual- and group-based strategies; the intensity of interventions varied from a single session to multiple sessions across several weeks. Outcomes examined in this literature primarily focused on reading comprehension and acquisition of vocabulary among individuals exposed to various teaching approaches.

## **Adaptive/Life Skills Interventions**

Two adaptive/life skills studies explicitly included individuals with ASD and intellectual disability,<sup>54, 55</sup> however specific measures of developmental and behavioral profiles of included individuals were quite variable and often lacked adequate description across studies. One study explicitly included high school students able to use a computer and program a digital device,<sup>57</sup> but specific cognitive and behavioral characteristics of this group were not well described. The remaining study included individuals attending a special school and likewise did not report explicit standardized measurements of the developmental and behavioral characteristics of the group apart from ASD diagnosis.<sup>56</sup>

Studies of certain adaptive/life skills interventions based on intensive application of highly specified programs focused on individuals with ASD with profound cognitive impairments, while specific technological and educational structure-related interventions targeted individuals with cognitive abilities closer to developmental expectations. However, given the variability and limited information concerning developmental, cognitive, and behavioral characteristics of study populations in this category, it is unclear how findings from these studies might apply across varying individuals with ASD. Furthermore, given methodological limitations in study design and time frame, it is not only unclear how adaptive/life skills interventions apply to varying groups of individuals, but it is unclear whether they represent intervention enhancements with meaningful effect over time.

## **Vocational Interventions**

Although often not well characterized, the populations from studies examining the efficacy of supported employment/vocational interventions likely represent higher-functioning adults with ASD. Studies were conducted in the United States, United Kingdom, Spain, and Germany, and two specifically targeted adults with high-functioning autism or Asperger syndrome. One study included those who had nonverbal IQ scores above the 35th percentile. Although a fourth study included adults with a range of intellectual functioning, all adults were required to have “acceptable professional and vocational abilities.” The final study did not report on the intellectual functioning of the sample.

Supported work interventions ranged in duration from 2 years to 8 years, and included job finding services and job coaches who accompanied adults with ASD to the worksite. Comparators included adults in a sheltered work setting (i.e., sheltered workshop) as well as

adults who were receiving no supported employment services. The most common outcome assessed was the presence/absence of a job in the community. Other aspects of employment that were sometimes examined included the length of time employed, number of hours working per week, and wages. One study each assessed autism symptoms, quality of life, and cognitive functioning. Overall, participants in these studies were drawn from the community and thus reflect characteristics of the larger population of higher functioning individuals. Interventions also took place within the larger community. Jobs located were typically support or service positions and do not reflect the scope of employment possibilities potentially available for individuals with ASD with more developed cognitive abilities or social and communication skills.

## **Medical Interventions**

### **Studies of Antipsychotics**

Three RCTs, including mostly adolescents and young adults (age 13 to 30 years) but not limited to this range, examined antipsychotics. Although the mean age was within this range the populations include younger children and older adults. All of the studies used Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria-based diagnoses of autistic disorder as an inclusion criterion. One risperidone study also included individuals with pervasive developmental disorder-not otherwise specified (PDD-NOS). Inclusion criteria for the two risperidone studies also included a minimum level of problem behaviors. The mean IQ of the patients was in the range of intellectual disability in the two risperidone studies, while the haloperidol study did not report IQ. Doses of risperidone or haloperidol in all three RCTs were within the range of doses used clinically for some adolescents and young adults with ASD.

All three RCTs assessed aggressive behavior, repetitive behaviors, and general autism symptoms. All of the studies monitored for adverse effects (extrapyramidal and others) either clinically or with specific assessments. Some, but not all, of the studies specifically assessed repetitive behaviors, self-injurious behavior, social relationships, or language. All three of these RCTs were conducted in academic clinic settings in the United States and Canada. The characteristics of these settings may limit applicability.

### **Studies of Opioid Receptor Antagonists**

One placebo-controlled RCT assessed naltrexone and included adult subjects with Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R) criteria-based diagnoses of autistic disorder. Participants also reportedly had intellectual disabilities. Naltrexone dose in one cohort was 50 mg/day but in the second cohort was increased to 150 mg/day. The increased dose was slightly higher than other studies cited, and the clinical applicability of these doses to patients with ASD has not been established.

The primary outcome was self-injurious behavior. Additional outcomes included irritability, stereotypy, hyperactivity, inappropriate speech, social withdrawal, and global clinical improvement. This RCT was conducted in an academic clinic setting in the Netherlands, and the applicability may be limited by this setting.

### **Studies of SRIs**

Five studies (two placebo-controlled RCTs and four case series) investigated SRIs including clomipramine, fluvoxamine, sertraline, and fluoxetine. All participants had DSM-IV or DSM-III-

R criteria-based diagnoses of autistic disorder. Two of studies also included other types of ASD (e.g., PDD-NOS and Asperger syndrome). Most of the subjects in these studies were adolescents and young adults (ages 13 to 30 years). The mean age was within this range, although some younger children and older adults were included. Drug dosages used in these studies were consistent with doses used clinically for some adolescents and young adults; however, the clinical applicability of these doses to patients with ASD has not been established.

Most of the studies assessed repetitive behaviors, aggressive behavior, and general autism symptoms. Some, but not all of the studies specifically assessed self-injurious behavior, social relationships, or language. All studies were conducted in academic clinic settings in the United States and Canada. The applicability of these studies may be limited by these settings.

## **Allied Health Interventions**

The five studies<sup>49, 58-60, 70</sup> of allied health interventions meeting our criteria included disparate groups of individuals and interventions. Three of the studies explicitly included individuals with intellectual disability,<sup>49, 59, 70</sup> and participant ages ranged widely, though most were in the adolescent range. With the exception of an RCT of a recreation program<sup>49</sup> employing a waiting list control condition, studies were case series and thus lacked comparison groups. In studies of facilitated communication, all participants engaged in communication trials in which the facilitator was either aware or not aware of the word or image being prompted. Outcomes included quality of life and stress level in the recreation program RCT, social skills-related outcomes in studies of music therapy, and language/vocabulary in studies of facilitated communication. Interventions occurred in university-based or specialized developmental disabilities treatment centers and may not be widely available to the larger community with ASD. Studies were short term with the exception of the recreation program RCT,<sup>49</sup> which assessed individuals after 12 months of participation.

## **Gaps in the Evidence**

### **Methodologic Considerations**

A number of methodologic considerations may be helpful for understanding the current state of the literature and for guiding future research. Of the 32 studies included in the report, 18 used a comparison group. Of those, 11 applied random assignment, and of those 11, 3 were assessed to have randomized appropriately. The rest of the studies were case series or cross-sectional. Few studies in this area are prospective trials, most being retrospective program evaluations, which have substantial risks of bias.

Growth in the number of studies with greater attention to rigorous design for the purpose of studying effectiveness will provide additional information for those making decisions about care in the future. Over half (18 of 32) of the studies reported use of an adequate diagnostic approach, and we suggest that future research attend to improved reporting about the basis for diagnosis of individuals included in the studies. Most, but not all (26 of 32) fully described inclusion and exclusion criteria, which is helpful for characterizing the population and assessing the applicability of the evidence. Reporting of either fidelity (for behavioral studies) or treatment adherence was low, with eight studies reporting fidelity and five studies reporting adherence. Again, this information is important to end users of the research for assessing applicability and understanding the implications of the results.

Methodologic strengths in this literature included the use of valid outcomes measures (29 of 32 studies), appropriate sources (e.g., teacher or parent report) of outcome data (31 of 32 studies), and appropriate statistical analysis (26 of 32) for the study design.

## **Future Research**

The period of development representing the transition from adolescence to early adulthood presents numerous challenges for individuals with and without neurodevelopmental challenges. During this same interval individuals with ASD are presented with additional complexities that require efforts to maximize the possibility of a positive transition and achievement of individual goals for independence. Nonetheless, and despite increasing numbers of adolescents facing this transition, no area of research provides sufficient strength of evidence for the impact of specific intervention strategies in terms of improving important outcomes for specific groups of individuals with ASD.

Overall, there is a dearth of evidence in all areas of care for adolescents and young adults with ASD, and it is urgent that more rigorous studies be developed and conducted. It is unlikely that large scale implementation of interventions will be considered until a stronger evidence base is developed, despite growing numbers of individuals with need, and some small studies demonstrating initial promise. A fruitful area for consideration may be identifying programs/interventions that are appropriate candidates for developing treatment manuals to encourage standardized replication of promising approaches.

Basic understanding of the effects of aging on health, cognitive skills and other domains of functioning is absent, and evaluations of interventions are rare. The lack of randomized, controlled trials is notable in all categories of intervention, but especially so in medical interventions, where substantial adverse events may be associated with medication use in adolescence. Only three studies reported more than 12 months of followup<sup>17, 54, 74</sup>; longer term data are needed in all areas of therapy. Furthermore, although early intervention for individuals with ASD is often delivered in the home or at specialized agencies, behavioral and educational interventions for adolescents and adults with ASD are likely to take place in existing community-based settings such as schools and businesses, with non-specialists having a key role in implementation. Thus, another critical issue is to design interventions for implementation in such settings.

The behavioral literature generally focuses on subsets of individuals with ASD, often those who are higher functioning, and may not be representative of the range of individuals with ASD. In particular, more attention is warranted to understanding the impact of behavioral interventions in the lives of individuals and how these interventions generalize to real-world impact and outcome. Few studies addressing educational interventions in the adolescent and young adult population have been conducted, and studies focusing on life skills or adaptive behaviors have included few individuals in typically short-term studies focused on very specific short-term intermediate outcomes. More research in both areas over a broader time frame with more clearly defined populations is critical for helping individuals with ASD transition to greater independence.

In vocational research, studies are needed that illuminate which aspects of multifaceted supported employment programs have the greatest impact. Studies that do show evidence of effectiveness in this area should collect longer-term data to describe the degree to which findings, including the duration of employment, continue after the intervention itself is removed. These studies should also broaden the outcomes measured, to include other functional outcomes



such as quality of life, educational attainment, residential outcomes and social outcomes. Similarly, allied health studies are needed to understand best approaches to fostering independent living skills and ways in which improvements in motor skills may affect communication and other domains.

Medical studies conducted in adolescents and young adults have focused largely on problem behaviors, and additional data are needed on medical comorbidities in adolescents with ASD. Clear evidence from earlier studies of antipsychotics, which included mostly younger children, supports the use of risperidone and aripiprazole in children with ASD. The only fair quality study of risperidone in adults is consistent with the findings in children, but the strength of evidence based upon the adult literature alone is insufficient to draw firm conclusions. Population studies may be helpful to empirically group ASD patients by age in a way that fosters more effective studies of treatments. Understanding the age-appropriateness of potential medical treatments as based on social, physiological, pharmacological, and functional characteristics of the population would help to prioritize future research, including the ways in which medical comorbidities arise or increase as children with ASD move into adolescence and adulthood. Increased use of standardized age groupings would facilitate comparisons of effectiveness within medical intervention categories as well as with non-medical therapies. One way to support accomplishing this is by developing treatment networks with adequate numbers of patients of varying ages to participate in research.

Thus far, medication research in adolescents and young adults with ASD has been limited to compounds that are already approved for other indications. As targeted treatments for ASD emerge, initial studies will need to study adult populations to establish safety before moving into studies of adolescents and finally children. Study of compounds not yet on the market could be facilitated with partnerships between the academic and pharmaceutical communities. It will be critical to consider the appropriate outcome measures and settings in which to study medication response in adults. The heterogeneity in settings for adults with ASD is a significant impediment to assessing symptom response. Ideally, medications would be combined with an educational or psychosocial intervention that would mirror the school and therapeutic settings in which children with ASD show improvements in social, communication, or behavioral function. Without some level of educational or social challenge, it may be quite difficult to assess medication response.

Across all intervention types, research is needed on which outcomes to use in future studies. The Aberrant Behavior Checklist is a widely used, easily repeatable, and highly sensitive outcome measure for behavioral symptoms in ASD, but it does not directly index anxiety, mood, social, or communication function, nor does it capture broader outcomes such as quality of life. More outcome measures are needed to allow assessment of a broader range of symptoms, particularly in individuals who may be higher functioning. No studies provide adequate information on longer-term outcomes, and particularly on outcomes related to achieving goals for independence and quality of life. To some degree, this reflects a lack of understanding and consensus about optimal outcomes and how to measure them. We know little about which outcome measures are most appropriate and valid for this population specifically; nor do we have good, empirical evidence about which outcomes are valued by individuals and their families. Furthermore, it is unclear which outcomes are most likely to change as a result of the very different types of interventions assessed in this population. Substantial, foundational research should be done to identify and validate outcome measures in the adolescent and young adult population with ASD.

Research is also necessary to understand how individuals' expression of ASD symptoms and the severity of symptoms may affect treatment over the lifespan. Foundational research is necessary to understand the goals of individuals with autism and their families as future research studies are planned. Similarly, little research addressing the effects of family and caregiver interactions and characteristics on the responses of individuals' with ASD to interventions exists. Finally, for all research in this area, we encourage greater transparency in reporting, particularly as it relates to reporting of randomization approaches, characterization of study participants, description of the intervention and measures of fidelity and adherence. These are all necessary to understand correctly the potential impact of the interventions being reported.

## **Conclusions**

Given the number of individuals affected by ASD, there is a dramatic lack of evidence on best approaches to therapies for adolescents and young adults with these conditions. In particular, families have little in the way of evidence-based approaches to support interventions capable of optimizing the transition of teens with autism into adulthood. Most of the studies identified were poor quality; while the five fair quality studies were primarily of medical interventions. Behavioral, educational, and adaptive/life skills studies were typically small and short term and suggested some improvements in social skills and functional behavior.

Individual studies also suggested that vocational programs may increase employment success, but the studies were small. By the same token, few data address the effectiveness and harms of medical or allied health interventions in the adolescent and young adult population. Although the studies that have been conducted focused on the use of medications to address specific challenging behaviors, the effectiveness in managing irritability and aggression in this age group remains largely unknown and can at best be inferred from studies including mostly younger children.

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## Acronyms and Abbreviations

ABC	Aberrant Behavior Checklist
ABC-C	Aberrant Behavior Checklist-Community Rating Scale
ABC-I	Aberrant Behavior Checklist-Community Rating Scale-Irritability
AHRQ	Agency for Healthcare Research and Quality
ASD	Autism spectrum disorders
BPVS	British Picture Vocabulary Scale
CARS	Childhood Autism Rating Scale
CGI-I	Clinical Global Impressions-Improvement
CGI-S	Clinical Global Impressions-Severity
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
FC	Facilitated communication
G	Group
IQ	Intelligence quotient
KBIT2	Kaufman Brief Intelligence Test-Second Edition
KQ	Key Question
mg	Milligram
N, n	Number
NA	Not applicable
NR	Not reported
nRCT	Nonrandomized controlled trial
PDA	Personal digital assistant
PDD-NOS	Pervasive developmental disorder-not otherwise specified
PEP	PsychoEducational Profile
RCT	Randomized controlled trial
SD	Standard deviation
SIB-Q	Self-Injurious Behavior Questionnaire
SRI	Serotonin reuptake inhibitor
TEACCH	Treatment and Education of Autistic and Communication related Handicapped Children
TEP	Technical Expert Panel
TOO	Task Order Officer
U.K.	United Kingdom
U.S.	United States
WAIS	Wechsler Adult Intelligence Scale
WASI	Wechsler Abbreviated Scale of Intelligence
Y-BOCS	Yale Brown Obsessive Compulsive Scale



## Appendix A. Exact Search Strings and Results

**Table A-1. PubMed search strategies (all searches last updated December 13, 2011)**

Search Terms	Search Results
<b>#1</b> Autistic[tiab] OR autism[tiab] OR autistic disorder[mh] OR asperger syndrome[mh] OR child development disorders, pervasive[mh:noexp] OR asperger[tiab] OR asperger's[tiab] OR aspergers[tiab] OR pervasive development[tiab] OR pervasive developmental[tiab]	20485
<b>#2</b> therapy[sh] OR therapeutics[mh] OR teaching[mh] OR psychotherapy[mh] OR treatment outcome[mh] OR vocational education[mh] OR vocational guidance[mh] OR rehabilitation, vocational[mh] OR vocational[tiab] OR transition[tiab] OR transitional[tiab] OR transitioning[tiab] OR transitions[tiab] OR occupational[tiab] OR employment, supported[mh]	6387748
<b>#3</b> #1 AND #2 AND eng[la] AND humans[mh]	5206
<b>#4</b> #3 AND newspaper article[pt]	1
<b>#5</b> #3 AND letter[pt]	301
<b>#6</b> #3 AND comment[pt]	184
<b>#7</b> #3 AND case reports[pt]	891
<b>#8</b> #3 AND review[pt]	962
<b>#9</b> #3 AND practice guideline[pt]	7
<b>#10</b> #3 AND news[pt]	53
<b>#11</b> #3 AND editorial[pt]	96
<b>#12</b> #3 AND historical article[pt]	33
<b>#13</b> #3 AND meta-analysis[pt]	33
<b>#14</b> #3 AND legal cases[pt]	7
<b>#15</b> #3 AND jsubsetk	29
<b>#16</b> #3 NOT (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15)	2961
<b>#17</b> #16 AND 1980:2012[dp]	2574

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

\*Note: numbers do not tally as some articles are excluded in more than one category.

**Table A-2. PsycINFO search strategies (CSA interface)**

Search Terms	Search Results
#1	DE=("pervasive developmental disorders" or "aspergers syndrome" or "autism") 20109
#2	DE=("treatment" or "adjunctive treatment" or "aftercare" or "alternative medicine" or "acupuncture" or "aromatherapy" or "faith healing" or "folk medicine" or "behavior modification" or "behavior therapy" or "aversion therapy" or "covert sensitization" or "conversion therapy" or "dialectical behavior therapy" or "exposure therapy" or "implosive therapy" or "systematic desensitization therapy" or "reciprocal inhibition therapy" or "response cost" or "biofeedback training" or "classroom behavior modification" or "contingency management" or "token economy programs" or "fading conditioning" or "omission training" or "overcorrection" or "self management" or "self instructional training" or "time out" or "bibliotherapy" or "cognitive techniques" or "cognitive restructuring" or "cognitive therapy" or "self instructional training" or "computer assisted therapy" or "creative arts therapy" or "art therapy" or "dance therapy" or "music therapy" or "poetry therapy" or "recreation therapy" or "crisis intervention services" or "hot line services" or "suicide prevention centers" or "cross cultural treatment" or "cross cultural counseling" or "disease management" or "health care services" or "continuum of care" or "long term care" or "mental health services" or "community mental health services" or "palliative care" or "primary health care" or "interdisciplinary treatment approach" or "involuntary treatment" or "medical treatment general" or "gene therapy" or "milieu therapy" or "movement therapy" or "multimodal treatment approach" or "online therapy" or "outpatient treatment" or "outpatient commitment" or "partial hospitalization" or "personal therapy" or "physical treatment methods" or "acupuncture" or "artificial respiration" or "deep brain stimulation" or "drug therapy" or "hormone therapy" or "narcoanalysis" or "sleep treatment" or "polypharmacy" or "vitamin therapy" or "electrosleep treatment" or "gene therapy" or "phototherapy" or "psychosurgery" or "thalamotomy" or "radiation therapy" or "shock therapy" or "electroconvulsive shock therapy" or "insulin shock therapy" or "surgery" or "brain stimulation" or "brain self stimulation" or "chemical brain stimulation" or "electrical brain stimulation" or "spreading depression" or "transcranial magnetic stimulation" or "preventive medicine" or "psychotherapeutic techniques" or "animal assisted therapy" or "autogenic training" or "cotherapy" or "dream analysis" or "guided imagery" or "mirroring" or "morita therapy" or "motivational interviewing" or "mutual storytelling technique" or "paradoxical techniques" or "psychodrama" or "psychotherapy" or "adlerian psychotherapy" or "adolescent psychotherapy" or "analytical psychotherapy" or "autogenic training" or "behavior therapy" or "aversion therapy" or "covert sensitization" or "conversion therapy" or "dialectical behavior therapy" or "exposure therapy" or "implosive therapy" or "systematic desensitization therapy" or "reciprocal inhibition therapy" or "response cost" or "brief psychotherapy" or "child psychotherapy" or "play therapy" or "client centered therapy" or "cognitive behavior therapy" or "acceptance and commitment therapy" or "eclectic psychotherapy" or "emotion focused therapy" or "existential therapy" or "experiential psychotherapy" or "expressive psychotherapy" or "eye movement desensitization therapy" or "feminist therapy" or "geriatric psychotherapy" or "gestalt therapy" or "group psychotherapy" or "encounter group therapy" or "marathon group therapy" or "therapeutic community" or "guided imagery" or "humanistic psychotherapy" or "hypnotherapy" or "age regression hypnotic" or "individual psychotherapy" or "insight therapy" or "integrative psychotherapy" or "interpersonal psychotherapy" or "logotherapy" or "narrative therapy" or "persuasion therapy" or "primal therapy" or "psychoanalysis" or "dream analysis" or "self analysis" or "psychodrama" or "psychodynamic psychotherapy" or "psychotherapeutic counseling" or "family therapy" or "conjoint therapy" or "rational emotive behavior therapy" or "reality therapy" or "relationship therapy" or "solution focused therapy" or "supportive psychotherapy" or "transactional analysis" or "rehabilitation" or "cognitive rehabilitation" or "neuropsychological rehabilitation" or "occupational therapy" or "physical therapy" or "psychosocial rehabilitation" or "therapeutic social clubs" or "vocational rehabilitation" or "supported employment" or "vocational evaluation" or "work adjustment training" or "relaxation therapy" or "progressive relaxation therapy" or "social casework" or "social group work" or "sociotherapy" or "speech therapy" or "treatment guidelines" or "self help techniques" or "self management" or "self instructional training" or "therapeutic social clubs" or "medicinal herbs and plants" or "hypericum perforatum" or "dietary supplements" or "diets" or "nutrition" or "vitamins" or "ascorbic acid" or "choline" or "lecithin" or "folic acid" or "nicotinamide" or "nicotinic acid" or "vocational education" or "occupational guidance" or "school to work transition" or "group homes" or "residential care institutions" or "independent living programs" or "institutional schools" or "assisted living" or "therapeutic camps" or

	"mainstreaming" or "mainstreaming (educational)" or "special education")	
#3	#1 and #2 and PT=(journal article) and (ME=(empirical study) or ME=(field study) or ME=(followup study) or ME=(longitudinal study) or ME=(prospective study) or ME=(qualitative study) or ME=(quantitative study) or ME=(retrospective study) or ME=(treatment outcome/clinical trial)), limited to English language and human and peer-reviewed journals, citations from 1980 to present	1738

Key: DE = subject descriptor; PT = publication type; ME = methodology

**Table A-3. ERIC search strategies (CSA interface)**

Search Terms	Search Results	
#1	("pervasive developmental disorders") or autism or ("asperger syndrome")	8044
#2	DE=("therapy" or "educational therapy" or "group therapy" or "hearing therapy" or "music therapy" or "occupational therapy" or "physical therapy" or "psychotherapy" or "milieu therapy" or "relaxation training" or "speech therapy" or "therapeutic recreation" or "play therapy" or "art therapy" or "bibliotherapy" or "drug therapy" or "intervention" or "crisis intervention" or "early intervention" or "individualized family service plans" or "prereferral intervention" or "outcomes of treatment" or "rehabilitation" or "special education" or "adapted physical education" or "therapeutic environment" or "Dietetics" or "Food" or "Nutrition" or "vocational education" or "adult vocational education" or "prevocational education" or "individualized transition plans" or "vocational rehabilitation" or "vocational schools" or "vocational training centers" or "transitional programs" or "education work relationship" or "supported employment" or "residential care" or "residential schools" or "residential programs" or "residential institutions" or "boarding schools" or "resident camp programs" or "group homes")	138853
#3	#1 and #2, limited to peer reviewed journals, English only, and citations from 1980 to present	977

Key: DE = subject descriptor

**Table A-4. CINAHL search strategies (EBSCO interface)**

Search Terms	Search Results
#1 (MH "Child Development Disorders, Pervasive") OR (MH "Asperger Syndrome") OR (MH "Autistic Disorder"), limited to English language, human, research studies, and peer-reviewed journals, excluding MEDLINE records	398
#2 #1 AND PT systematic review	16
#3 #1 AND PT review	1
#4 #1 AND PT case study	49
#5 #1 NOT (#2 OR #3 OR #4)	332

Key: MH = subject term

Note: CINAHL includes citations from 1981 to present so date limiting unnecessary for this search

## Appendix B. Categorization of Study Designs

- Cohort, prospective: studies in which subjects receive more than one type of treatment or exposure (e.g. ABA therapy or DIR/floortime compared with another treatment or no treatment) in order to make comparisons of the outcomes of treatment, in which the investigator(s) does not assign the treatment or non-treatment states for the purposes of comparing them. For the purpose of this review, we termed studies with more than one “exposure” group prospective cohorts to distinguish them from case series. Analysis is focused on estimating the risk or odds of the outcome(s) based on the participants’ exposure (treatment group status). These would include comparative studies in which the treatment is set based on "happenstance" conditions such as availability of a therapist, or parental choice. These types of studies can also be described as employing a nonrandomized pre-post group comparison design.
- Cohort, retrospective: studies in which subjects having more than one type of treatment (more than one “exposure”) are identified after having had intervention (e.g., chart review of children with ASD receiving either risperidone or olanzapine). Studies that have some component of follow-up should be classified as retrospective if the intent to follow-up the cohort was not designed and future data collection planned prior to the time of the treatment under investigation. Analysis estimates the risk or odds of the outcome(s) based on the participants’ exposure (treatment group status).
- Randomized clinical trials: special instances of prospective cohorts in which the “exposure” or treatment group is assigned by the investigator through use of an allocation method; treatment and nontreatment are assigned by study investigators using an a priori protocol.
- Controlled trials (nonrandomized): special instances of prospective cohorts in which the exposure or treatment group is assigned by the investigator but without using a randomization scheme.
- Case-control studies: studies that identify cases based on the outcome under study. A control, comparison population is identified that is intended to be a representative sample of similar children. In order to assure similar characteristics overall with respect to covariates not being studied, matching is often used, such as matching on age or race to assure a similar distribution of these potential confounders. Analysis is technically estimating the odds of having had a particular exposure or characteristic given known presence or absence of the outcome.
- Case series, prospective: studies in which subjects (ideally consecutive participants) having the same type of treatment for symptoms of ASD are identified prior to treatment and consented to participate (i.e., all participants receive the same treatment). The components of the study and outcome follow-up are designed before the participants are enrolled. Data analysis is descriptive including the full range of potential outcome measures such as reduction in problem behaviors, changes in IQ, etc. Analysis may include construction of predictive models that seek to examine influences on outcomes, such as IQ at intake, etc. Studies may also present data for groups of participants (e.g., males vs. females) though all participants received the same treatment. Case series might include experimental approaches

or analyses such as multiple baseline, reversal, ABAB, alternating treatments, or changing criterion studies in this literature. Group designed studies from which we could only collect data from one arm (e.g., studies that inappropriately compared the effects of an intervention in children with ASD with normally developing children) were considered case series.

- Case series, retrospective: studies in which investigators obtain permission to review existing clinical records in order to summarize the outcomes from a sequence (ideally consecutive patients) receiving the same treatment. Followup of the members of a case series identified from medical records or databases using methods such as surveys should still be counted as “retrospective” if the design of the study and future data collection were not established prior to the time of the treatment under study. Analysis is descriptive.

# Appendix C. Sample Data Extraction Forms

## Interventions for Adolescents and Young Adults with Autism Comparative Effectiveness Review -- Abstract Review Form

First Author, Year: \_\_\_\_\_ Reference ID #: \_\_\_\_\_ Abstractor Initials: \_\_\_\_\_

<b>Primary Inclusion/Exclusion Criteria</b>			
1. Includes: ___ participants diagnosed with ASD (Autism, Aspergers, PDD-NOS) between the ages of 13-30 ___caregivers/family members of individuals ages 13-30 with ASDs	Yes  (if at least 1 marked, circle Yes)	No	Cannot Determine
2. Original research (exclude editorials, commentaries, letters, reviews, etc.)	Yes	No	Cannot Determine
3. Eligible study size ( $\geq 20$ individuals with ASDs between ages 13-30) N ages 13-30= _____	Yes	No	Cannot Determine
4. Addresses any of the following in individuals with ASD between the ages of 13-30: a. ___treatment modality intended to modify core symptoms of ASD b. ___treatment modality intended to modify medical or mental health comorbidities (e.g., epilepsy, sleep disorders, depression, anxiety, acute and episodic aggression, motor skills, etc.) c. ___treatment modality intended to affect functional behavior, attainment of goals toward independence, educational attainment, occupational attainment, life satisfaction, residential outcomes, social outcomes, and relationship-focused outcomes d. ___treatment modality intended to assist with transitional issues (e.g., attainment of goals toward independence, educational attainment, occupational attainment, life satisfaction, access to services, legal outcomes, and social outcomes) e. ___treatment modality intended to affect family adaptation or family outcomes f. ___ harms/adverse effects associated with treatment	Yes  (if at least 1 element marked, circle Yes)	No	Cannot Determine

Retain for: \_\_\_\_\_BACKGROUND/DISCUSSION \_\_\_\_\_REVIEW OF REFERENCES  
 \_\_\_\_\_Other\_\_\_\_\_

**COMMENTS:**



**Interventions for Adolescents and Young Adults with Autism Comparative Effectiveness Review --  
Full Text Review Form**

First Author, Year: \_\_\_\_\_ Reference ID #: \_\_\_\_\_ Abstractor Initials: \_\_\_\_\_

1. Includes one of the following: 1a. Only individuals between the ages 13 and 30 with ASD	Yes	No
1b. Mean age of participants with ASD is within range of 13-30	Yes	No
1c. At least 50% of participants with ASD in age range 13-30	Yes	No
1d. Family members of individuals in the target population	Yes	No
2. Original research (exclude editorials, commentaries, letters, reviews, systematic reviews, meta analyses, etc.)	Yes	No
3. Eligible study size $N \geq 20$ <b>TOTAL</b> in target age range	Yes	No
4. Study addresses one or more of the following questions (check applicable KQ below):	Yes	No
<p>__KQ1: Among adolescents and young adults with autism spectrum disorders (ASDs), what are the effects of available interventions* on the core symptoms of ASD?</p> <p>__KQ2: Among adolescents and young adults with ASD, what are the effects of available interventions (see KQ1*) on common medical and mental health comorbidities (e.g., epilepsy, sleep disorders, obesity, motor impairments, depression, anxiety, acute and episodic aggression, ADHD etc.)?</p> <p>__KQ3: Among adolescents and young adults with ASD, what are the effects of available interventions (see KQ1*) on functional behavior, attainment of goals toward independence, educational attainment, occupational/vocational attainment, life satisfaction, access to health and other services, legal outcomes, and social outcomes?</p> <p>__KQ4: Among adolescents and young adults with ASD, what is the effectiveness of interventions designed to support the transitioning process, specifically to affect attainment of goals toward independence, educational attainment, occupational/vocational attainment, life satisfaction, access to health and other services, legal outcomes, and social outcomes?</p> <p>__KQ5: Among adolescents and young adults with ASD, what harms are associated with available interventions (see KQ1*)?</p> <p>__KQ6: What are the effects of interventions on family outcomes?</p>		
<p><b>Treatment area studied (circle applicable):</b> behavioral, educational, medical, allied health,</p>		

CAM, transitional support, family-focused, vocational, crisis management, sex education, exercise/recreational, residential supports, other:\_\_\_\_\_ )

5. Study published in English

Yes

No

*EXCLUDE IF AN ITEM IN A GRAY BOX IS SELECTED*

6. If excluded, retain for \_\_\_Background/Discussion \_\_\_Review of references \_\_\_Other:

\_\_\_\_\_

**Comments:**

\* Available interventions may include the following broad categories: social skills, psychopharmacology, functional behavioral interventions, psychoeducational interventions, vocational and independent living skills training, targeted educational interventions, transition support, complementary and alternative medicine (CAM), diet/nutrition therapies, crisis management, sexual education, case management, family-focused interventions, exercise/recreational interventions, applied behavior analysis, allied health (e.g., speech/language, physical, and occupational therapies), and residential supports.

## Appendix D. Evidence Tables

Tables are sorted by year, then last name of first author.

**Table D-1. Interventions for adolescents and young adults with autism evidence table**

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
<p><b>Author:</b> Garcia-Villamizar et al., 2010</p> <p><b>Country:</b> Spain</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NR</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> RCT</p>	<p><b>Intervention:</b> Leisure/recreation program including interaction with media, exercise, game playing, and other recreational activities for 2 hrs/day</p> <p><b>Intervention target:</b> Quality of life and stress</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> <b>G1:</b> leisure program <b>G2:</b> wait list control</p> <p><b>Treatment duration:</b> 12 months</p> <p><b>Frequency of contact during study:</b> Baseline and after 12 months</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1:</b> 37 <b>G2:</b> 34</p> <p><b>N at followup:</b> <b>G1:</b> 37 <b>G2:</b> 34</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Attendance at day program for adults with special needs</li> <li>• Consent to participate in study</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• See inclusion criteria</li> </ul> <p><b>Age, yrs, mean ± SD, (range):</b> <b>G1:</b> 31.49 ± 4.83 (17-39) <b>G2:</b> 30.06 ± 3.44 (24-38)</p> <p><b>Mental age (Leiter), months, mean ± SD:</b> <b>G1:</b> 63.46 ± 21.33 <b>G2:</b> 61.44 ± 9.37</p> <p><b>Gender, n:</b> Male: <b>G1:</b> 22 <b>G2:</b> 19 Female: <b>G1:</b> 15 <b>G2:</b> 15</p> <p><b>DSM-based diagnostic approach reported:</b> No</p>	<p><b>Leiter test, mean ± SD:</b> <b>G1:</b> 63.46 ± 21.33 <b>G2:</b> 61.44 ± 9.37</p> <p><b>Stress Survey Schedule, mean ± SD:</b> <b>G1:</b> 114.03 ± 19.90 <b>G2:</b> 116.94 ± 18.61</p> <p><b>Quality of Life Questionnaire, mean ± SD:</b> Total score: <b>G1:</b> 50.59 ± 2.93 <b>G2:</b> 54.17 ± 2.90</p> <p>Empower/independence: <b>G1:</b> 12.13 ± 1.18 <b>G2:</b> 13.06 ± 1.81</p> <p>Satisfaction: <b>G1:</b> 15.29 ± 2.32 <b>G2:</b> 16.23 ± 1.21</p> <p>Competence/productivity: <b>G1:</b> 7.62 ± 1.08 <b>G2:</b> 7.64 ± .73</p> <p>Social/integration: <b>G1:</b> 15.54 ± 2.06 <b>G2:</b> 17.23 ± 2.04</p>	<p><b>Leiter test, mean ± SD:</b> <b>G1:</b> 62.16 ± 18.84 <b>G2:</b> 61.79 ± 14.87</p> <p><b>Stress Survey Schedule, mean ± SD:</b> <b>G1:</b> 103.19 ± 19.27 <b>G2:</b> 117.67 ± 16.25 <b>G1/G2:</b> <i>P</i> &lt; 0.001</p> <p><b>Quality of Life Questionnaire, mean ± SD:</b> Total score: <b>G1:</b> 63.62 ± 8.99 <b>G2:</b> 55.29 ± 3.45 <b>G1/G2:</b> <i>P</i> &lt; 0.001</p> <p>Empower/independence: <b>G1:</b> 13.24 ± 1.88 <b>G2:</b> 14.26 ± 1.60 <b>G1/G2:</b> <i>P</i> = NS</p> <p>Satisfaction: <b>G1:</b> 22.03 ± 2.92 <b>G2:</b> 15.03 ± 0.93 <b>G1/G2:</b> <i>P</i> &lt; 0.001</p> <p>Competence/productivity: <b>G1:</b> 11.35 ± 4.08 <b>G2:</b> 7.82 ± 7.33 <b>G1/G2:</b> <i>P</i> &lt; 0.001</p> <p>Social/integration: <b>G1:</b> 17.00 ± 2.40 <b>G2:</b> 18.17 ± 2.11 <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Harms:</b> NR</p>

**Interventions for adolescents and young adults with autism evidence table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Gentry et al., 2010</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> Commonwealth Neurotrauma Initiative</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Prospective case series</p>	<p><b>Intervention:</b> Four home-based training visits on the use of a personal digital assistant as a cognitive aid.</p> <p><b>Intervention target:</b> Executive function-related tasks (memory, organization, planning, and goal-direction).</p> <p><b>Primary outcome:</b> Occupational performance and satisfaction (COPM); satisfaction, usage, and retention (FATCAT).</p> <p><b>Groups:</b> <b>G1:</b> PDA training</p> <p><b>Treatment duration:</b> 10-14 days</p> <p><b>Frequency of contact during study:</b> As needed via phone or email (only initiated by participants)</p> <p><b>Last followup post-treatment:</b> 8 weeks</p> <p><b>Measure of treatment fidelity/adherence reported:</b> Yes</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1:</b> 22</p> <p><b>N at followup:</b> <b>G1:</b> 22</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Autism diagnosis and current IEP</li> <li>• At least 14 years old</li> <li>• Attending public school in Virginia</li> <li>• Demonstrate sufficient dexterity</li> <li>• Functional vision and hearing</li> <li>• Caregiver willing to participate in assessment</li> <li>• Home personal computer</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• See inclusion criteria</li> </ul> <p><b>Age, yrs, mean (range):</b> <b>G1:</b> 16.5 (14-18)</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, n (%):</b> Male: <b>G1:</b> 18 (82) Female: <b>G1:</b> 4 (18)</p> <p><b>DSM-based diagnostic approach reported:</b> No</p>	<p><b>COPM score, mean:</b> Performance: <b>G1:</b> 2.82</p> <p>Satisfaction: <b>G1:</b> 2.05</p>	<p><b>COPM score, mean:</b> Performance: <b>G1:</b> 6.64 <b>G1/BL:</b> <math>P &lt; 0.001</math></p> <p>Satisfaction: <b>G1:</b> 6.32 <b>G1/BL:</b> <math>P &lt; 0.001</math></p> <p><b>FATCAT, n (%):</b> Used PDA daily: <b>G1:</b> 22 (100)</p> <p>Want to continue using: <b>G1:</b> 22 (100)</p> <p>Can program without help: <b>G1:</b> 16 (73)</p> <p>Device is a waste of time: <b>G1:</b> 0 (0)</p> <p><b>Harms:</b> NR</p>

Interventions for adolescents and young adults with autism evidence table (continued)

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
<p><b>Author:</b> Greher et al., 2010</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NR</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Prospective case series</p>	<p><b>Intervention:</b> SoundScape music intervention, 90 minutes per week</p> <p><b>Intervention target:</b> NR</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> <b>G1:</b> music intervention <b>G2:</b> parental evaluations</p> <p><b>Treatment duration:</b> 8 weeks</p> <p><b>Frequency of contact during study:</b> Weekly</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1:</b> 22</p> <p><b>N at followup:</b> <b>G1:</b> 22</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Autism spectrum diagnosis</li> <li>Aged between 13-30</li> <li>No severe behavioral challenges</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>See inclusion criteria</li> </ul> <p><b>Age, yrs, mean (range):</b> <b>G1:</b> 18 (13-29)</p> <p><b>Mental age:</b> NR</p> <p><b>Gender:</b> NR</p> <p><b>DSM-based diagnostic approach reported:</b> No</p>	NR	<p><b>Feedback questionnaire ratings (scale 1-10), mean:</b></p> <p>How enjoyable have you [your child] found the music program? <b>G1:</b> 7.86 <b>G2:</b> 7.91</p> <p>How interesting have you [your child] found the music program? <b>G1:</b> 7.82 <b>G2:</b> 7.95</p> <p>How much do you believe you [your child] have benefited socially from the music program? <b>G1:</b> 6.95 <b>G2:</b> 6.86</p> <p><b>Feedback questionnaire, n:</b></p> <p>Have you [your child] made any friends in the music program? Yes: <b>G1:</b> 19 <b>G2:</b> 11 Kind of/not sure: <b>G1:</b> 1 <b>G2:</b> 4 No: <b>G1:</b> 2 <b>G2:</b> 6</p> <p><b>Harms:</b> NR</p>

Interventions for adolescents and young adults with autism evidence table (continued)

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
<p><b>Author:</b> Valenti et al., 2010</p> <p><b>Country:</b> Italy</p> <p><b>Enrollment period:</b> April 2007 to March 2009</p> <p><b>Funding:</b> Italian National Health System</p> <p><b>Author industry relationship disclosures:</b> None</p> <p><b>Design:</b> Prospective case series</p>	<p><b>Intervention:</b> Intensive behavioral treatment at a semi-residential rehabilitation center for autism.</p> <p><b>Intervention target:</b> Adaptive functioning</p> <p><b>Primary outcome:</b> Adaptive functioning (VABS)</p> <p><b>Groups:</b> <b>G1:</b> intensive behavioral treatment <b>G1a:</b> female adolescents <b>G1b:</b> male adolescents</p> <p><b>Treatment duration:</b> 2 years</p> <p><b>Frequency of contact during study:</b> Yearly</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> Yes</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies, n (%):</b> Psychoactive drugs: <b>G1:</b> 12 (35.3)</p> <p><b>N at enrollment:*</b> <b>G1:</b> 34</p> <p><b>N at followup:*</b> <b>G1:</b> 34</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Diagnosis of ASD</li> <li>• Regular public school attendance</li> <li>• Consent of parent or tutor</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• See inclusion criteria</li> </ul> <p><b>Age, range:</b> <b>G1:</b> post-pubescent adolescents up to 18 yrs</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, n (%):</b> Male: <b>G1:</b> 23 (68) Female: <b>G1:</b> 11 (32)</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>VABS score, mean ± SD:</b></p> <p>Communication: <b>G1a:</b> 72.59 ± 9.78 <b>G1b:</b> 84.18 ± 7.20</p> <p>Daily living <b>G1a:</b> 80.77 ± 8.64 <b>G1b:</b> 80.66 ± 8.66</p> <p>Socialization: <b>G1a:</b> 68.18 ± 8.82 <b>G1b:</b> 75.84 ± 6.53</p> <p>Motor skills: <b>G1a:</b> 74.88 ± 8.39 <b>G1b:</b> 94.93 ± 9.57</p>	<p><b>VABS score, year 1, mean ± SD:</b></p> <p>Communication: <b>G1a:</b> 70.40 ± 7.97 <b>G1b:</b> 84.31 ± 7.75</p> <p>Daily living: <b>G1a:</b> 78.21 ± 9.27 <b>G1b:</b> 86.57 ± 8.26</p> <p>Socialization: <b>G1a:</b> 73.04 ± 8.99 <b>G1b:</b> 77.60 ± 8.20</p> <p>Motor skills: <b>G1a:</b> 84.07 ± 7.80 <b>G1b:</b> 99.41 ± 8.80</p> <p><b>VABS score, year 2, mean ± SD:</b></p> <p>Communication: <b>G1a:</b> 73.23 ± 8.64 <b>G1b:</b> 87.93 ± 7.44 <b>G1a/BL:</b> ES = 0.02 <b>G1b/BL:</b> ES = 0.11</p> <p>Daily Living: <b>G1a:</b> 87.08 ± 8.38 <b>G1b:</b> 88.67 ± 8.87 <b>G1a/BL:</b> ES = 0.22 <b>G1b/BL:</b> ES = 0.19</p> <p>Socialization: <b>G1a:</b> 75.60 ± 8.02 <b>G1b:</b> 83.20 ± 8.92 <b>G1a/BL:</b> ES = 0.26 <b>G1b/BL:</b> ES = 0.23</p> <p>Motor Skills: <b>G1a:</b> 85.16 ± 6.37 <b>G1b:</b> 102.42 ± 8.39 <b>G1a/BL:</b> ES = 0.20 <b>G1b/BL:</b> ES = 0.16</p> <p><b>Harms:</b> NR</p>

Interventions for adolescents and young adults with autism evidence table (continued)

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
<p><b>Author:</b> Laugeson et al., 2009</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NIH, NIMH</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> RCT</p>	<p><b>Intervention:</b> Program for the Education and Enrichment of Relational Skills (PEERS) outpatient social skills program; weekly 90 minute sessions</p> <p><b>Groups:</b> <b>G1:</b> PEERS <b>G2:</b> delayed treatment control</p> <p><b>Intervention target:</b> Improve friendship quality and social skills in teens</p> <p><b>Primary outcome:</b> NR</p> <p><b>Treatment duration:</b> 12 weeks</p> <p><b>Frequency of contact during study:</b> Weekly visits</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> Yes</p> <p><b>Co-interventions held stable during treatment:</b> Yes</p> <p><b>Concomitant therapies, n:</b> Lithium carbonate, quetiapine <b>G1:</b> 1 <b>G2:</b> 0 Dexamethylphenidate, bupropion: <b>G1:</b> 1 <b>G2:</b> 0 Methylphenidate: <b>G1:</b> 1 <b>G2:</b> 0 Fluoxetine: <b>G1:</b> 0 <b>G2:</b> 1 Atomoxetine, aripiprazole, oxycarbazepine: <b>G1:</b> 0 <b>G2:</b> 1</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Chronological age 13-17 years</li> <li>• Social problems as reported by the parent</li> <li>• Previous diagnosis of either high functioning Autism, Asperger's Disorder, or PDD-NOS</li> <li>• English fluency of the teen</li> <li>• Parent or family member who was a fluent English speaker and who was willing to participate in the study</li> <li>• Verbal IQ <math>\geq 70</math> on the K-BIT-2</li> <li>• No history of major mental illness (e.g., bipolar disorder, schizophrenia, psychosis)</li> <li>• Absence of hearing, visual, or physical impairments which precluded teen from participating in outdoor sports activities</li> <li>• Teens who verbally expressed an interest in participating in the intervention during the eligibility appointment</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• See inclusion criteria</li> </ul> <p><b>Age, yrs, mean <math>\pm</math> SD:</b> <b>G1:</b> 14.6 <math>\pm</math> 1.3 <b>G2:</b> 14.6 <math>\pm</math> 1.6</p> <p><b>IQ, mean <math>\pm</math> SD:</b> <b>G1:</b> 96 <math>\pm</math> 16.1 <b>G2:</b> 88.3 <math>\pm</math> 21.1</p> <p><b>Gender, %:</b> Male: <b>G1:</b> 88.2 <b>G2:</b> 81.2 Female: <b>G1:</b> 11.8 <b>G2:</b> 18.8</p>	<p><b>VABS score, mean <math>\pm</math> SD:</b> Communication: <b>G1:</b> 72.2 <math>\pm</math> 6.2 <b>G2:</b> 70.6 <math>\pm</math> 6.6 Socialization: <b>G1:</b> 65.8 <math>\pm</math> 8.5 <b>G2:</b> 65.9 <math>\pm</math> 7.0 Composite: <b>G1:</b> 70.3 <math>\pm</math> 8.5 <b>G2:</b> 68.6 <math>\pm</math> 6.2</p> <p><b>TASSK score, teen report, mean <math>\pm</math> SD:</b> <b>G1:</b> 13.3 <math>\pm</math> 2.4 <b>G2:</b> 12.6 <math>\pm</math> 3.6</p> <p><b>QPQ score, teen report, mean <math>\pm</math> SD:</b> Host: <b>G1:</b> 1.1 <math>\pm</math> 1.4 <b>G2:</b> 0.6 <math>\pm</math> 0.9 Guest: <b>G1:</b> 0.9 <math>\pm</math> 1.3 <b>G2:</b> 1.3 <math>\pm</math> 2.3 Conflict: <b>G1:</b> 4.1 <math>\pm</math> 5.2 <b>G2:</b> 4.3 <math>\pm</math> 4.5</p> <p><b>FQS score, teen report, mean <math>\pm</math> SD:</b> <b>G1:</b> 16.8 <math>\pm</math> 3.4 <b>G2:</b> 18.1 <math>\pm</math> 3.9</p> <p><b>QPQ score, parent report, mean <math>\pm</math> SD:</b> Host: <b>G1:</b> 1.5 <math>\pm</math> 2.7 <b>G2:</b> 0.6 <math>\pm</math> 0.9 Guest: <b>G1:</b> 0.9 <math>\pm</math> 1.3 <b>G2:</b> 1.3 <math>\pm</math> 2.5 Conflict: <b>G1:</b> 6.5 <math>\pm</math> 5.0 <b>G2:</b> 6.9 <math>\pm</math> 5.6</p> <p><b>SSRS score, parent report, mean <math>\pm</math> SD:</b> Social skills: <b>G1:</b> 80.2 <math>\pm</math> 8.8 <b>G2:</b> 77.9 <math>\pm</math> 12.1 Problem behaviors: <b>G1:</b> 114.9 <math>\pm</math> 14.2 <b>G2:</b> 120.7 <math>\pm</math> 13.6</p>	<p><b>TASSK score, teen report, mean <math>\pm</math> SD:</b> <b>G1:</b> 19.6 <math>\pm</math> 1.4 <b>G2:</b> 13.3 <math>\pm</math> 3.8 <b>G1/G2:</b> <math>P &lt; 0.0001</math> <b>G1/BL:</b> <math>P &lt; 0.01</math> <b>G2/BL:</b> <math>P = NS</math></p> <p><b>QPQ score, teen report, mean <math>\pm</math> SD:</b> Host: <b>G1:</b> 3.2 <math>\pm</math> 2.2 <b>G2:</b> 1.1 <math>\pm</math> 1.3 <b>G1/G2:</b> <math>P &lt; 0.025</math> <b>G1/BL:</b> <math>P &lt; 0.01</math> <b>G2/BL:</b> <math>P = NS</math></p> <p><b>FQS score, teen report, mean <math>\pm</math> SD:</b> <b>G1:</b> 17.2 <math>\pm</math> 4.0 <b>G2:</b> 16.6 <math>\pm</math> 4.6 <b>G1/G2:</b> <math>P &lt; 0.05</math> <b>G1/BL:</b> <math>P = NS</math> <b>G2/BL:</b> <math>P &lt; 0.05</math></p> <p><b>SSRS score, parent report, mean <math>\pm</math> SD:</b> Social skills: <b>G1:</b> 89.7 <math>\pm</math> 12.1 <b>G2:</b> 79.8 <math>\pm</math> 11.7 <b>G1/G2:</b> <math>P &lt; 0.05</math> <b>G1/BL:</b> <math>P &lt; 0.01</math> <b>G2/BL:</b> <math>P = NS</math></p> <p><b>Harms:</b> NR</p>

Interventions for adolescents and young adults with autism evidence table (continued)

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Laugeson et al., 2009 (continued)	Paroxetine: <b>G1:</b> 0 <b>G2:</b> 1  <b>N at enrollment:</b> <b>Total:</b> 35*  <b>N at followup:</b> <b>G1:</b> 17 <b>G2:</b> 16	<b>DSM-based diagnostic approach reported:</b> NR (diagnosis by community/university/school psychologists)	<b>SSRS score, teacher report, mean ± SD:</b> Social skills: <b>G1:</b> 83.6 ± 7.3 (n=8) <b>G2:</b> 86.6 ± 14.8 (n=5)  Problem behavior: <b>G1:</b> 96.5 ± 16.7 (n=8) <b>G2:</b> 85.4 ± 21.3 (n=5)	



Interventions for adolescents and young adults with autism evidence table (continued)

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
<p><b>Author:</b> Lawer et al., 2009</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NR</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Cross-sectional study</p>	<p><b>Intervention:</b> NA</p> <p><b>Intervention target:</b> NR</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> <b>G1:</b> Individuals with ASD in US Vocational Rehabilitation System</p> <p><b>Treatment duration:</b> NA</p> <p><b>Frequency of contact during study:</b> NA</p> <p><b>Last followup post-treatment:</b> NA</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1:</b> 1,707</p> <p><b>N at followup:</b> <b>G1:</b> 1,707</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Age 18-65</li> <li>Individuals receiving vocational rehabilitation services from the US Rehabilitation Services Administration whose cases were closed in 2005 for reasons other than death or lack of need for services</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>See inclusion criteria</li> </ul> <p><b>Age, yrs, n (%):</b> 18-25: <b>G1:</b> 1,253 (73.4) 25-34: <b>G1:</b> 265 (15.5) 35-44: <b>G1:</b> 138 (8.1) 45-54: <b>G1:</b> 43 (2.5) 55-65: <b>G1:</b> 8 (0.5)</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, n (%):</b> Male: <b>G1:</b> 1,434 (84)</p> <p><b>DSM-based diagnostic approach reported:</b> No</p>	<p>NR</p>	<p><b>Case deemed too severe to benefit from services, n (%):</b> <b>G1:</b> 74 (4.3)</p> <p><b>Vocational outcomes at closure, n (%):</b> Not employed: <b>G1:</b> 909 (55.7) Employed in sheltered setting: <b>G1:</b> 35 (2.1) Competitive employment: <b>G1:</b> 689 (42.2)</p> <p><b>Received on-the-job supports at any time, by vocational outcome, n (%):</b> Not employed: <b>G1:</b> 115 (12.7) Employed in sheltered setting: <b>G1:</b> 23 (65.7) Competitive employment: <b>G1:</b> 391 (56.8)</p> <p><b>Education at closure, n (%):</b> &lt; high school: <b>G1:</b> 739 (43.7) High school or GED: <b>G1:</b> 642 (38.0) &gt; high school: <b>G1:</b> 309 (18.3)</p> <p><b>Cost of services among those with any expenditures, median:</b> <b>G1:</b> \$2,380 (n=1,229)</p> <p><b>Average expenditure for purchased services, mean ± SD:</b> <b>G1:</b> \$3,324 ± \$5,662</p> <p><b>Harms:</b> NR</p>

Interventions for adolescents and young adults with autism evidence table (continued)

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
<p><b>Author:</b> Jewell et al., 2007</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NA</p> <p><b>Funding:</b> NR</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Retrospective case series</p>	<p><b>Intervention:</b> Rotating classroom schedule in a not-for-profit school for children with autism.</p> <p><b>Intervention target:</b> NR</p> <p><b>Primary outcome:</b> Number of crisis interventions and the time spent in crisis intervention</p> <p><b>Groups:</b> <b>G1:</b> Adolescent students with rotating classroom schedule</p> <p><b>Treatment duration:</b> NR</p> <p><b>Frequency of contact during study:</b> Daily</p> <p><b>Last followup post-treatment:</b> NA</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1:</b> 55</p> <p><b>N at followup:</b> <b>G1:</b> 55</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Enrolled at the study school</li> <li>Primary diagnosis of autism</li> <li>Diagnosed by a psychologist from the student's home school</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Other primary diagnosis (e.g. behavior disorder or Rhett's)</li> </ul> <p><b>Age, yrs, mean (range):</b> <b>G1:</b> 17.63 (14-22)</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, n (%):</b> Male: <b>G1:</b> 44 (80) Female: <b>G1:</b> 11 (20)</p> <p><b>DSM-based diagnostic approach reported:</b> No</p>	<p><b>Number of crisis events, mean ± SD:</b> <b>G1:</b> 2.44 ± 6.39</p> <p><b>Time in crisis, min, mean ± SD:</b> <b>G1:</b> 40.27 ± 102.08</p>	<p><b>Number of crisis events, mean ± SD:</b> <b>G1:</b> 2.22 ± 5.88 <b>G1/BL:</b> <i>P</i> = 0.84</p> <p><b>Time in crisis, min, mean ± SD:</b> <b>G1:</b> 28.96 ± 65.47 <b>G1/BL:</b> <i>P</i> = 0.83</p> <p><b>Harms:</b> NR</p>

**Interventions for adolescents and young adults with autism evidence table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Tse et al., 2007</p> <p><b>Country:</b> Canada</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NR</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Prospective case series</p>	<p><b>Intervention:</b> Social skills training for adolescents with Asperger's syndrome and high-functioning autism in psychiatry clinic. Psycho-educational and experiential methods of teaching social skills, with emphasis on learning through role play. Each group enrolled 7-8 adolescents.</p> <p><b>Intervention target:</b> Social competence and problem behaviors</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> G1: Social skills group</p> <p><b>Treatment duration:</b> 12 weeks</p> <p><b>Frequency of contact during study:</b> Weekly</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies, n (%):</b> Psychotropic medication: 17 (37) Atypical antipsychotics: 6 (NR) Selective serotonin reuptake inhibitors: 5 (NR) Methylphenidate: 5 (NR)</p> <p><b>N at enrollment:</b> G1: 46</p> <p><b>N at followup:</b> G1: 32</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Diagnosis of an autism spectrum disorder by a child psychiatrist</li> <li>• Adequate language skills for participation in activities; being able to talk about their interests and to verbalize some goals for participation and willingness to attend</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• See inclusion criteria</li> </ul> <p><b>Age, yrs, mean ± SD (range):</b> G1: 14.6 ± 1.7 (13-18)</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, %:</b> Male: G1: 61 Female: G1: 39</p> <p><b>DSM-based diagnostic approach reported:</b> NR</p>	<p><b>SRS score, mean ± SD (n = 32):</b> Total: G1: 95.9 ± 27.9</p> <p>Social awareness: G1: 12.0 ± 4.0</p> <p>Social cognition: G1: 16.9 ± 5.8</p> <p>Social communication: G1: 32.9 ± 9.8</p> <p>Social motivation: G1: 15.8 ± 5.7</p> <p>Autistic mannerisms: G1: 18.2 ± 7.3</p> <p>DSM social aspects: G1: 69.1 ± 19.4</p> <p>DSM language aspects: G1: 8.5 ± 3.4</p> <p>DSM preoccupations/mannerisms: G1: 18.2 ± 7.3</p> <p><b>N-CBRF Positive Social score, mean ± SD (n = 30):</b> Total: G1: 13.9 ± 4.4</p> <p>Compliant/calm: G1: 8.6 ± 3.1</p> <p>Adaptive social: G1: 5.3 ± 2.0</p> <p><b>ABC score, mean ± SD (n = 30):</b> Total: G1: 41.9 ± 22.1</p> <p>Irritability: G1: 8.9 ± 6.8</p> <p>Lethargy/withdrawal: G1: 12.8 ± 7.5</p> <p>Stereotypic behavior: G1: 4.7 ± 3.8</p>	<p><b>SRS score, mean ± SD (n = 32):</b> Total: G1: 84.9 ± 28.3 G1/BL: P = 0.003, ES = 0.39</p> <p>Social awareness: G1: 11.5 ± 4.1 G1/BL: P = 0.321, ES = 0.12</p> <p>Social cognition: G1: 15.0 ± 5.4 G1/BL: P = 0.009, ES = 0.34</p> <p>Social communication: G1: 28.3 ± 10.1 G1/BL: P = 0.002, ES = 0.46</p> <p>Social motivation: G1: 13.6 ± 5.8 G1/BL: P = 0.013, ES = 0.38</p> <p>Autistic mannerisms: G1: 16.5 ± 6.8 G1/BL: P = 0.058, ES = 0.24</p> <p>DSM social aspects: G1: 60.7 ± 19.8 G1/BL: P = 0.001, ES = 0.43</p> <p>DSM language aspects: G1: 7.7 ± 3.5 G1/BL: P = 0.107, ES = 0.23</p> <p>DSM preoccupations/mannerisms: G1: 16.5 ± 6.8 G1/BL: P = 0.058, ES = 0.24</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
Tse et al., 2007 (continued)			<p>Hyperactivity: <b>G1:</b> 12.1 ± 8.9</p> <p>Inappropriate speech: <b>G1:</b> 3.5 ± 2.6</p> <p><b>N-CBRF Problem Behavior score, mean ± SD (n = 30):</b> Total: <b>G1:</b> 51.3 ± 24.7</p> <p>Conduct problems: <b>G1:</b> 10.2 ± 7.8</p> <p>Insecure/anxious: <b>G1:</b> 13.0 ± 6.2</p> <p>Hyperactive: <b>G1:</b> 8.3 ± 5.4</p> <p>Self-injure/ stereotypic: <b>G1:</b> 1.3 ± 1.8</p> <p>Self-isolated/ ritualistic: <b>G1:</b> 7.9 ± 5.2</p>	<p><b>N-CBRF Positive Social score, mean ± SD (n = 30):</b> Total: <b>G1:</b> 16.0 ± 5.5 <b>G1/BL:</b> <i>P</i> = 0.024, <i>ES</i> = 0.42 Compliant/calm: <b>G1:</b> 10.0 ± 3.8 <b>G1/BL:</b> <i>P</i> = 0.052, <i>ES</i> = 0.40</p> <p>Adaptive social: <b>G1:</b> 6.0 ± 2.3 <b>G1/BL:</b> <i>P</i> = 0.060, <i>ES</i> = 0.32</p> <p><b>ABC score, mean ± SD (n = 30):</b> Total, <b>G1:</b> 27.9 ± 16.5 <b>G1/BL:</b> <i>P</i> = 0.001, <i>ES</i> = 0.72</p> <p>Irritability: <b>G1:</b> 4.9 ± 4.0 <b>G1/BL:</b> <i>P</i> = 0.002, <i>ES</i> = 0.72</p> <p>Lethargy/ withdrawal: <b>G1:</b> 9.0 ± 7.5 <b>G1/BL:</b> <i>P</i> = 0.008, <i>ES</i> = 0.51</p> <p>Stereotypic behavior: <b>G1:</b> 2.8 ± 2.9 <b>G1/BL:</b> <i>P</i> = 0.005, <i>ES</i> = 0.56</p> <p>Hyperactivity: <b>G1:</b> 9.0 ± 7.4 <b>G1/BL:</b> <i>P</i> = 0.029, <i>ES</i> = 0.38</p> <p>Inappropriate speech: <b>G1:</b> 2.2 ± 1.8 <b>G1/BL:</b> <i>P</i> = 0.003, <i>ES</i> = 0.58</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
Tse et al., 2007 (continued)				<p><b>N-CBRF Problem Behavior score, mean ± SD (n = 30):</b>                      Total:  <b>G1: 38.6 ± 19.7</b>  <b>G1/BL: P = 0.005, ES = 0.57</b></p> <p>Conduct problems:  <b>G1: 7.7 ± 6.7</b>  <b>G1/BL: P = 0.046, ES = 0.34</b></p> <p>Insecure/ anxious:  <b>G1: 10.5 ± 5.6:</b>  <b>G1/BL: P = 0.040, ES = 0.42</b></p> <p>Hyperactive:  <b>G1: 7.0 ± 4.9</b>  <b>G1/BL: P = 0.257, ES = 0.25</b></p> <p>Self-injure/ stereotypic:  <b>G1: 0.7 ± 1.1</b>  <b>G1/BL: P = 0.022, ES = 0.40</b></p> <p>Self-isolated/ ritualistic:  <b>G1: 5.5 ± 3.7</b>  <b>G1/BL: P = 0.003, ES = 0.53</b></p> <p><b>Feedback surveys, teen report, n:</b>                      Liking the group: 10/13                      Liked it a lot: 5/13                      Disliking the group: 1/13</p> <p>Improvement in “having a conversation”:                      A lot: 7/13                      Some: 5/13</p> <p>Made friends in the group: 12/13</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Tse et al., 2007 (continued)				<b>Feedback surveys, parent report, n:</b> Child seemed happy to attend the group: 15/17  Overall improvement in their child's social behavior: A little: 10 The same: 3 Much better or very much better: 3  <b>Harms: NR</b>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Garcia-Villamizar et al., 2006</p> <p><b>Country:</b> Spain</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> Fondo Social Europeo, Cosejería de Asuntos Sociales de la Comunidad Autónoma de Madrid (Spain)</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Prospective cohort</p>	<p><b>Intervention:</b> Sheltered and supported community-based work environments</p> <p><b>Intervention target:</b> Cognitive performance</p> <p><b>Groups:</b> <b>G1:</b> Supported employment <b>G2:</b> Unemployed</p> <p><b>Primary outcome:</b> NR</p> <p><b>Treatment duration:</b> Average length of community employment: 30 months for an average of 20 hours/week</p> <p><b>Frequency of contact during study:</b> Beginning and end of program</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> Yes</p> <p><b>Co-interventions held stable during treatment:</b> NR with exception of medication free at testing</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1+G2:</b> 44</p> <p><b>N at followup:</b> <b>G1+G2:</b> 44</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Diagnosis of autism</li> <li>• For G2, sheltered workshops enrollment prior to participation in supported work program</li> <li>• No severe behavior problems</li> <li>• Acceptable professional and vocational abilities</li> <li>• Medication free at the time of testing</li> <li>• Score above 35<sup>th</sup> percentile point on the Standard Progressive Matrices (SPM)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• History of psychiatric disorder, neurological disorder or head injury</li> </ul> <p><b>Age, yrs, mean ± SD:</b> <b>G1:</b> 25.52 ± 3.35 <b>G2:</b> 24.32 ± 4.34</p> <p><b>IQ, Leiter (total score), mean ± SD:</b> NR</p> <p><b>Gender, n:</b> Male: <b>G1+G2:</b> 32 Female: <b>G1+G2:</b> 12</p> <p><b>DSM-based diagnostic approach reported:</b> Yes (DSM-IV &amp; CARS)</p>	<p><b>Big Circle/Little Circle score, mean ± SD:</b> <b>G1:</b> 39.38 ± 0.97 <b>G2:</b> 39.52 ± 0.73 <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Spatial Span Task score, mean ± SD:</b> <b>G1:</b> 3.90 ± 0.14 <b>G2:</b> 3.78 ± 1.17 <b>G3:</b> <i>P</i> = NS</p> <p><b>Spatial Working Memory Task score, mean ± SD:</b> Between errors: <b>G1:</b> 68.14 ± 14.55 <b>G2:</b> 67.91 ± 13.2 <b>G1/G2:</b> <i>P</i> = NS</p> <p>Strategy: <b>G1:</b> 38.19 ± 2.11 <b>G2:</b> 39.26 ± 2.84 <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Intradimensional/ Extradimensional score, mean ± SD:</b> Stages completed: <b>G1:</b> 7.48 ± 5.11 <b>G2:</b> 7.39 ± 0.94 <b>G1/G2:</b> <i>P</i> = NS</p> <p>Errors: <b>G1:</b> 16.90 ± 10.94 <b>G2:</b> 19.69 ± 10.75 <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Planning task ‘Stockings of Cambridge’ score, mean ± SD:</b> Problems solved in minimum moves: <b>G1:</b> 5.10 ± 2.47 <b>G2:</b> 5.91 ± 2.45 <b>G1/G2:</b> <i>P</i> = NS</p> <p>Average planning time: <b>G1:</b> 6.71 ± 3.02 <b>G2:</b> 6.91 ± 3.38 <b>G1/G2:</b> <i>P</i> = NS</p>	<p><b>Big Circle/Little Circle score, mean ± SD:</b> <b>G1:</b> 39.48 ± 0.87 <b>G2:</b> 39.25 ± 0.96 <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Spatial Span Task score, mean ± SD:</b> <b>G1:</b> 4.85 ± 0.79 <b>G2:</b> 3.96 ± 0.93 <b>G1/G2:</b> <i>P</i> &lt; 0.05</p> <p><b>Spatial Working Memory Task score, mean ± SD:</b> Between errors: <b>G1:</b> 61.91 ± 12.38 <b>G2:</b> 66.13 ± 13.19 <b>G1/G2:</b> <i>P</i> &lt; 0.001</p> <p>Strategy: <b>G1:</b> 34.00 ± 2.19 <b>G2:</b> 37.43 ± 2.92 <b>G1/G2:</b> <i>P</i> &lt; 0.001</p> <p><b>Intradimensional/ Extradimensional score, mean ± SD:</b> Stages completed: <b>G1:</b> 7.43 ± 0.51 <b>G2:</b> 7.30 ± 0.47 <b>G1/G2:</b> <i>P</i> = 0.02</p> <p>Errors: <b>G1:</b> 12.71 ± 6.71 <b>G2:</b> 17.13 ± 9.15 <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Planning task ‘Stockings of Cambridge’ score, mean ± SD:</b> Problems solved in minimum moves: <b>G1:</b> 7.38 ± 1.80 <b>G2:</b> 5.57 ± 1.88 <b>G1/G2:</b> <i>P</i> &lt; 0.01</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
Garcia-Villamizar et al., 2006 (continued)			<p><b>Trail Making Test – part B score, mean ± SD:</b>  <b>G1:</b> 55.48 ± 18.27  <b>G2:</b> 66.22 ± 23.75  <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Matching Familiar Figures Test score, mean ± SD:</b>  Time of 1<sup>st</sup> answer:  <b>G1:</b> 16.33 ± 4.86  <b>G2:</b> 17.43 ± 3.91  <b>G1/G2:</b> <i>P</i> = NS</p> <p>Errors:  <b>G1:</b> 7.76 ± 2.84  <b>G2:</b> 7.96 ± 3.62  <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Word fluency test score, mean ± SD:</b>  <b>G1:</b> 39.38 ± 0.97  <b>G2:</b> 39.52 ± 0.73  <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>CARS score, mean ± SD:</b>†  <b>G1:</b> 34.81 ± 5.19  <b>G2:</b> 33.19 ± 6.65</p>	<p>Average planning time:  <b>G1:</b> 4.86 ± 2.54  <b>G2:</b> 7.61 ± 3.04  <b>G1/G2:</b> <i>P</i> &lt; 0.001</p> <p><b>Trail Making Test – part B score, mean ± SD:</b>  <b>G1:</b> 51.14 ± 15.19  <b>G2:</b> 66.43 ± 23.03  <b>G1/G2:</b> <i>P</i> &lt; 0.001</p> <p><b>Matching Familiar Figures Test score, mean ± SD:</b>  Time of 1<sup>st</sup> answer:  <b>G1:</b> 10.76 ± 4.30  <b>G2:</b> 15.96 ± 4.14  <b>G1/G2:</b> <i>P</i> &lt; 0.001</p> <p>Errors:  <b>G1:</b> 5.05 ± 1.47  <b>G2:</b> 8.04 ± 2.88  <b>G1/G2:</b> <i>P</i> &lt; 0.001</p> <p><b>Word fluency test score, mean ± SD:</b>  <b>G1:</b> 39.48 ± 0.87  <b>G2:</b> 39.26 ± 0.96  <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Harms:</b>  NR</p>



**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Golan et al., 2006 Study 1</p> <p><b>Country:</b> UK</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> National Alliance for Autism Research, Corob Charitable Trust, Cambridge Overseas Trust, B'nai B'rith Leo Baeck, Shirley Foundation, Medical Research Council, Three Guineas Trust</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Controlled study</p>	<p><b>Intervention:</b> Mind Reading computer program used at home for 2 hr/wk over 10 weeks</p> <p><b>Intervention target:</b> Emotion recognition skills</p> <p><b>Primary outcome:</b> Emotion recognition</p> <p><b>Groups:</b> <b>G1:</b> computer program <b>G2:</b> no computer program</p> <p><b>Treatment duration:</b> 10-15 weeks</p> <p><b>Frequency of contact during study:</b> Beginning and end of study, with 1 followup phone call during the study</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> Yes</p> <p><b>Co-interventions held stable during treatment:</b> Yes</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1:</b> 24 <b>G2:</b> 22</p> <p><b>N at followup:</b> <b>G1:</b> 19 <b>G2:</b> 22</p>	<p><b>Inclusion criteria:</b> Diagnosed with AS/HFA in specialist centers using established criteria</p> <p>No participation in any related intervention during the last 3 months</p> <p>No plans for engaging in another intervention while the study was ongoing</p> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>Age, yrs, mean ± SD:</b> <b>G1:</b> 30.5 ± 10.3 <b>G2:</b> 30.9 ± 11.2</p> <p><b>Mental age:</b> NR</p> <p><b>Verbal IQ, mean ± SD:</b> <b>G1:</b> 108.3 ± 13.3 <b>G2:</b> 109.7 ± 10.0</p> <p><b>Performance IQ, mean ± SD:</b> <b>G1:</b> 112.0 ± 12.6 <b>G2:</b> 115.3 ± 12.3</p> <p><b>Gender, n (%):</b> Male: <b>G1:</b> 14 (74) <b>G2:</b> 17 (73) Female: <b>G1:</b> 5 (26) <b>G2:</b> 5 (23)</p> <p><b>DSM-based diagnostic approach reported:</b> No</p> <p><b>AQ, mean ± SD</b> <b>G1:</b> 37.2 ± 8.4 <b>G2:</b> 38.2 ± 7.5</p>	<p><b>CAM score, mean ± SD:</b> Face mask: <b>G1:</b> 31.3 ± 8.8 <b>G2:</b> 32.5 ± 8.4 Voice task: <b>G1:</b> 33.8 ± 6.6 <b>G2:</b> 35.2 ± 7.4 Number of concepts recognized: <b>G1:</b> 9.8 ± 5.2 <b>G2:</b> 10.5 ± 5.2</p> <p><b>Reading the Mind in the Eyes, mean ± SD:</b> <b>G1:</b> 23.1 ± 6.7 <b>G2:</b> 23.9 ± 6.7</p> <p><b>Reading the Mind in the Voice, mean ± SD:</b> <b>G1:</b> 16.1 ± 2.9 <b>G2:</b> 16.1 ± 3.9</p> <p><b>Reading the Mind in Films:</b> NR</p>	<p><b>CAM score, mean ± SD:*</b> Face mask: <b>G1:</b> 37.5 ± 7.8 <b>G2:</b> 36.6 ± 7.9 <b>G1/G2:</b> <math>P &lt; 0.002</math></p> <p>Voice task: <b>G1:</b> 38.9 ± 6.2 <b>G2:</b> 36.6 ± 7.9 <b>G1/G2:</b> <math>P &lt; 0.01</math></p> <p>Number of concepts recognized:** <b>G1:</b> 13.6 ± 4.8 <b>G2:</b> 11.3 ± 5.4 <b>G1/G2:</b> <math>P &lt; 0.01</math></p> <p><b>Reading the Mind in the Eyes, mean ± SD:*</b> <b>G1:</b> 23.8 ± 4.7 <b>G2:</b> 23.0 ± 7.3 <b>G1/G2:</b> <math>P = NS</math></p> <p><b>Reading the Mind in the Voice, mean ± SD:*</b> <b>G1:</b> 16.7 ± 3.9 <b>G2:</b> 17.4 ± 3.5 <b>G1/G2:</b> <math>P = NS</math></p> <p><b>Reading the Mind in Films, mean ± SD:*</b> <b>G1:</b> 11.8 ± 3.8 <b>G2:</b> 12.8 ± 3.4 <b>G1/G2:</b> <math>P = NS</math></p> <p><b>Harms:</b> NR</p>

**Comments:**

Typical controls included in study as well but data not extracted.

\* Significance is time X group interaction from a MANCOVA with covariates age, verbal, and performance IQ.

\*\* ANOVA for CAM concepts showed significant individual between group effects for the following concepts: grave ( $P < 0.05$ ), lured ( $P < 0.05$ ), uneasy ( $P < 0.05$ ), intimate ( $P < 0.05$ ), and nostalgic ( $P < 0.001$ ) (data NR).

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Golan et al., 2006 Study 2</p> <p><b>Country:</b> UK</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> National Alliance for Autism Research, Corob Charitable Trust, Cambridge Overseas Trust, B'nai B'rith Leo Baeck, Shirley Foundation, Medical Research Council, Three Guineas Trust</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Prospective cohort study</p>	<p><b>Intervention:</b> Computer program group: Mind Reading computer program 2 hr/wk for 10 weeks and 10 weekly small group sessions with a tutor</p> <p>Social skills training: 10 weekly sessions of small group social skills training facilitated by a clinical psychologist</p> <p><b>Intervention target:</b> Emotion recognition skills</p> <p><b>Primary outcome:</b> Emotion recognition</p> <p><b>Groups:</b> G1: computer program and tutor G2: social skills training</p> <p><b>Treatment duration:</b> 10 weeks</p> <p><b>Frequency of contact during study:</b> Weekly</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> Yes</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> G1: 18 G2: 18</p> <p><b>N at followup:</b> G1: 13 G2: 13</p>	<p><b>Inclusion criteria:</b> Diagnosed with AS/HFA in specialist centers using established criteria No participation in any related intervention during the last 3 months Had no plans for engaging in another intervention while the study was ongoing</p> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>Age, yrs, mean ± SD:</b> G1: 25.5 ± 9.3 G2: 24.4 ± 6.4</p> <p><b>Mental age:</b> NR</p> <p><b>Verbal IQ, mean ± SD:</b> G1: 105.7 ± 16.1 G2: 96.5 ± 15.5</p> <p><b>Performance IQ, mean ± SD:</b> G1: 103.9 ± 19.8 G2: 95.5 ± 6.0</p> <p><b>Gender, n (%):</b> Male: G1: 12 (92) G2: 10 (77) Female: G1: 1 (8) G2: 3 (23)</p> <p><b>DSM-based diagnostic approach reported:</b> No</p>	<p><b>CAM scores, mean ± SD:</b> Face mask: G1: 32.3 ± 8.1 G2: 26.8 ± 9.7 Voice task: G1: 33.2 ± 9.1 G2: 31.1 ± 9.1 Number of concepts recognized: G1: 10.2 ± 4.9 G2: 7.7 ± 5.8</p> <p><b>Reading the Mind in the Eyes, mean ± SD:</b> G1: 21.6 ± 6.3 G2: 21.5 ± 5.6</p> <p><b>Reading the Mind in the Voice, mean ± SD:</b> G1: 15.1 ± 2.8 G2: 13.9 ± 4.5</p> <p><b>Reading the Mind in Films:</b> NR</p>	<p><b>CAM scores, mean ± SD:*</b> Face mask: G1: 36.2 ± 8.9 G2: 29.3 ± 9.5 G1/G2: <i>P</i> = NS</p> <p>Voice task: G1: 38.9 ± 7.6 G2: 31.8 ± 10.9 G1/G2: <i>P</i> &lt; 0.012</p> <p>Number of concepts recognized:** G1: 13.5 ± 5.2 G2: 8.5 ± 6.3 G1/G2: <i>P</i> &lt; 0.016</p> <p><b>Reading the Mind in the Eyes, mean ± SD:*</b> G1: 23.8 ± 4.2 G2: 19.2 ± 6.8 G1/G2: <i>P</i> &lt; 0.01</p> <p><b>Reading the Mind in the Voice, mean ± SD:*</b> G1: 16.2 ± 3.5 G2: 14.7 ± 4.6 G1/G2: <i>P</i> = NS</p> <p><b>Reading the Mind in Films, mean ± SD:</b> G1: 11.9 ± 3.7 G2: 10.5 ± 3.2</p> <p><b>Harms:</b> NR</p>

**Comments:**

\* Significance is time X group interaction from a MANCOVA with covariate verbal IQ.

\*\* ANOVA for CAM concepts showed significant individual between group effects for the following concepts: vibrant (*P* < 0.05) and mortified (*P* < 0.01) (data NR).

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Hellings et al., 2006</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NIH</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Randomized crossover study</p>	<p><b>Intervention:</b> Blinded phase: Randomized subjects to 3, 4 or 5 weeks placebo; then randomized to low or high dose risperidone phase; risperidone gradually increased to target dose over 2 weeks then maintained for 4 weeks, then crossover to other study arm; dose then gradually tapered down for 2 weeks, followed by 3, 4 or 5 week phase of placebo, then open label phase for 24 weeks.</p> <p>Low dose risperidone: children and adolescents 1 mg/day; adults 2 mg/day</p> <p>High dose risperidone: children and adolescents 2.0 mg/day (range 1.2-2.9 mg/day); adults 3.6 mg/day (range 2.4-5.2 mg/day)</p> <p>Open label phase: optimal dose of risperidone, adjusted monthly as needed</p> <p><b>Intervention target:</b> Persistent aggression, property destruction and self-injury</p> <p><b>Primary outcome:</b> ABC-C Irritability subscale score</p> <p><b>Groups:</b> G1: all participants</p> <p><b>Treatment duration:</b> 46 weeks</p> <p><b>Frequency of contact during study:</b> Every second week and at the end of each sub-phase during the acute phase; monthly during the maintenance phase</p>	<p><b>Inclusion criteria:</b> Age 6-65 years Mental retardation (IQ &lt; 70) History of aggression, property destruction or self-injury ≥ 6 months by caregiver report Baseline Irritability subscale scores above norms for age, gender and setting as rated by the primary caregiver Drug-free period lasting ≥ 2 weeks</p> <p><b>Exclusion criteria:</b> Previous risperidone hypersensitivity History of neuroleptic malignant syndrome Seizures in past year Degenerative brain disease as assessed by history Problematic living situation such as lack of reliable caregiving</p> <p><b>Age, yrs, mean ± SD:</b> G1: 22 ± 13.1</p> <p><b>Age, years, n:</b> 8-12 (children): G1: 13 13-18 (adolescents): G1: 8 22-56 (adults): G1: 19</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, n (%):</b> Male: G1: 23 (58) Female: G1: 17 (42)</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>ABC-C subscale scores, 1<sup>st</sup> placebo period, mean ± SD:</b> Irritability: G1: 19.16 ± 9.96 Lethargy: G1: 7.61 ± 6.85 Stereotypy: G1: 5.72 ± 5.63 Hyperactivity: G1: 19.51 ± 11.10 Excessive speech: G1: 4.42 ± 3.25</p> <p><b>ABC-C subscale scores, 2<sup>nd</sup> placebo period, mean ± SD:</b> Irritability: G1: 18.22 ± 12.35 Lethargy: G1: 7.04 ± 7.62 Stereotypy: G1: 6.47 ± 6.84 Hyperactivity: G1: 19.95 ± 15.05 Excessive speech: G1: 3.97 ± 15.05</p>	<p><b>ABC-C Subscales scores, low dose phase, mean ± SD:</b> Irritability:* G1: 11.15 ± 9.28 Lethargy: G1: 5.06 ± 5.96 Stereotypy: G1: 4.07 ± 4.86 Hyperactivity: G1: 12.79 ± 11.38 Excessive speech: G1: 3.11 ± 3.15</p> <p><b>ABC-C Subscales scores, high dose phase, mean ± SD:</b> Irritability:* G1: 13.31 ± 8.91 Lethargy: G1: 6.98 ± 6.36 Stereotypy: G1: 5.14 ± 5.51 Hyperactivity: G1: 14.59 ± 12.44 Excessive speech: G1: 3.35 ± 3.50</p> <p><b>Harms, n:</b> Weight gain &gt; 3.0 kg: G1: 28/40 Sedation and gastrointestinal side effects:** G1: 13/40 Seizure (maintenance phase): G1: 1</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
Hellings et al., 2006 (continued)	<p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> All: 40</p> <p><b>N at followup:</b> All: 33</p>			

**Comments:**

\* ABC-C irritability scores across both acute drug phases were significantly different than placebo ( $P = 0.0002$ ). The pattern of results for the children and adolescents was similar (data only available in figures).

The linear decreasing trend in irritability scores across the maintenance phase approached significance ( $P = 0.09$ ).

Age group was a significant predictor of mean irritability scores across the maintenance phase ( $P < 0.0001$ ).

DISCUS scores in the acute drug phase was more significant versus the 1<sup>st</sup> placebo period ( $P = 0.052$ ) than versus the 2<sup>nd</sup> placebo period ( $P = 0.482$ ).

NSEC side effects significant at the 0.05 level were: drowsiness, increased weight gain, appetite, too quiet, not themselves, tremor, lack of spontaneity and nasal congestion.

\*\* These side effects lead to study withdrawal for 6/13 subjects.

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Howlin et al., 2005</p> <p><b>Country:</b> UK</p> <p><b>Enrollment period:</b> NA</p> <p><b>Funding:</b> The National Autistic Society, UK Department for Work and Pensions, New Deal for Disabled People, Student Support Service, British Telecom</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Retrospective case series</p> <p>See related study Mawhood et al., 1999</p>	<p><b>Intervention:</b> Supported employment program</p> <p><b>Intervention target:</b> Preparation for work and obtaining employment</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> <b>G1:</b> Supported employment program participants <b>Ga:</b> 1995-1996 (pilot) <b>Gb:</b> 2003-2005</p> <p><b>Treatment duration:</b> NR</p> <p><b>Frequency of contact during study:</b> NR</p> <p><b>Last followup post-treatment:</b> NR</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1a:</b> 30 <b>G1b:</b> 117</p> <p><b>N at followup:</b> <b>G1a:</b> 30 <b>G1b:</b> 89</p>	<p><b>Inclusion criteria:</b> Participation in supported employment program from 1995-2003</p> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>Age, yrs, mean <math>\pm</math> SD:</b> <b>G1a:</b> 31.1 <math>\pm</math> 9.1 <b>G1b:</b> 31.4 <math>\pm</math> 9.3</p> <p><b>Mental age, Raven nonverbal IQ, mean <math>\pm</math> SD (range):</b> <b>G1a:</b> 110.2 <math>\pm</math> 17.6 (70-135) <b>G1b:</b> 110.7 <math>\pm</math> 19.5 (60-139)</p> <p><b>Gender, male:female ratio:</b> <b>G1a:</b> 9.0:1 <b>G1b:</b> 4.2:1</p> <p><b>DSM-based diagnostic approach reported:</b> Yes (20% of client diagnoses confirmed with ADI or ADI-R)</p>	<p><b>BPVS score, mean <math>\pm</math> SD (range):</b> <b>G1a:</b> 94.7 <math>\pm</math> 21.2 (41-127) <b>G1b:</b> 121.6 <math>\pm</math> 32.3 (48-160)</p> <p><b>EOWPVT score, mean <math>\pm</math> SD (range):</b> <b>G1a:</b> 99.3 <math>\pm</math> 19.1 (59-132) <b>G1b:</b> 91.2 <math>\pm</math> 16.1 (50-122)</p> <p><b>Benefits received, n:</b> Severe disability allowance: <b>G1:</b> 6 Income support: <b>G1:</b> 26 Housing benefit: <b>G1:</b> 37 Job seekers allowance: <b>G1:</b> 36 Incapacity benefit: <b>G1:</b> 16 Council tax: <b>G1:</b> 19 Tax credit: <b>G1:</b> 1 Other: <b>G1:</b> 6 Disability allowance: <b>G1:</b> 37</p> <p><b>Employed, n (%):</b> <b>G1b:</b> 31/89 (39)</p> <p><b>Living independently, n:</b> <b>G1b:</b> 25</p>	<p><b>Benefits received, n:</b> Severe disability allowance: <b>G1:</b> 1 Income support: <b>G1:</b> 7 Housing benefit: <b>G1:</b> 11 Job seekers allowance: <b>G1:</b> 0 Incapacity benefit: <b>G1:</b> 5 Council tax: <b>G1:</b> 8 Tax credit: <b>G1:</b> 9 Other: <b>G1:</b> 2 Disability allowance: <b>G1:</b> 44</p> <p><b>Employed, n (%):</b> <b>G1b:</b> 59/89 (66) <b>G1b/BL:</b> <math>P &lt; 0.001</math></p> <p><b>Living independently, n:</b> <b>G1b:</b> 34</p> <p><b>Job satisfaction and social outcomes among those employed, n:</b> Generally satisfied with job: <b>G1b:</b> 50/59 Job lives up to expectations: <b>G1b:</b> 45/59 Satisfied with work hours: <b>G1b:</b> 47/59 Satisfied with pay: <b>G1b:</b> 38/59 Liked boss: <b>G1b:</b> 49/59</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
Howlin et al., 2005 (continued)				<p>Considered supported employment program helpful: <b>G1b:</b> 58/59</p> <p>Could not have managed without supported employment program help: <b>G1b:</b> 44/59</p> <p>Get along with colleagues: <b>G1b:</b> 52/59</p> <p>Made friendships as a result of jobs: <b>G1b:</b> 32/59</p> <p>Meet with colleagues outside of work: <b>G1b:</b> 7/59</p> <p><b>Jobs found meeting criteria of 16+ hrs/week for ≥ 13 weeks, n (%):</b> <b>G1:</b> 134/192 (70)</p> <p><b>Classification of jobs found, n (%):*</b></p> <p>Permanent contracts: <b>G1:</b> 107/185 (58)</p> <p>Short-term contracts: <b>G1:</b> 12/185 (6)</p> <p>Temporary: <b>G1:</b> 66/185 (36)</p> <p><b>Line managers satisfaction with supported employment program, n:</b></p> <p>Satisfied with service offered: <b>G1b:</b> 50/63</p> <p>No problems with participants' work performance: <b>G1b:</b> 26/63</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
Howlin et al., 2005 (continued)				<p>Experienced some difficulties with participants' work performance: <b>G1b:</b> 37/63</p> <p>Program helped to address performance difficulties: <b>G1b:</b> 61/63</p> <p>Personally gained from working with supported employment program: <b>G1b:</b> 51/63</p> <p><b>Senior manager or employers' satisfaction with supported employment program:</b> Very satisfied: <b>G1b:</b> 47/61 Satisfied: <b>G1b:</b> 13/61</p> <p><b>Harms:</b> NR</p>

**Comments:**

Data were collected on clients enrolled from April 1995 to March 2003; new data were collected for clients registered between 2002 and 2003 and for area 3 were available for the years 2000-2003.

\* Data missing for 7 of the 192 jobs found.

Among 19/30 participants in 1995-1996 who found jobs, 13 remained in permanent jobs in 2002-2003, and 2 had re-enrolled with the supported employment program. Of the 11/30 not finding jobs in 1995-1996, 2 located employment by 2002-2003, 1 acted as a volunteer, and 1 had re-enrolled with the supported employment program.

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Kaplan et al., 2005</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> 2002 to 2003</p> <p><b>Funding:</b> NR</p> <p><b>Author industry relationship disclosures:</b> NA</p> <p><b>Design:</b> Retrospective case series</p>	<p><b>Intervention:</b> Music therapy in varying group sizes; sessions occurred in community music school, suburban satellite, group home settings</p> <p><b>Intervention target:</b> Behavioral/psychosocial skills; language/communication skills; perceptual/motor skills; cognitive skills; musical skills; modifying physiological responses</p> <p><b>Primary outcome:</b> Specific to client</p> <p><b>Groups:</b> G1: Music therapy</p> <p><b>Treatment duration:</b> 2 program years</p> <p><b>Frequency of contact during study:</b> NR</p> <p><b>Last followup post-treatment:</b> NR</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> G1: 40*</p> <p><b>N at followup:</b> G1: 40</p>	<p><b>Inclusion criteria:</b> Children and adults with ASD diagnosis receiving music therapy</p> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>Age, yrs, mean (range):</b> G1: 13.9 (2-49)</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, n (%):</b> Male: G1: 28 (70) Female: G1: 12 (30)</p> <p><b>DSM-based diagnostic approach reported:</b> No</p>	<p>NR</p>	<p><b>Met initial objectives, %:</b> G1: 100</p> <p><b>Met intermediate objectives, %:</b> G1: 77</p> <p><b>Met Intermediate objectives, by category, %:</b> Behavioral/psychosocial skills: G1: 74</p> <p>Language/communication skills: G1: 74</p> <p>Perceptual/motor skills: G1: 80</p> <p>Cognitive skills: G1: 100</p> <p>Musical skills: G1: 100</p> <p><b>Generalization of skills learned in primary goal areas to nonmusic therapy settings, by category, %:</b> Behavioral/psychosocial: G1: 14/16 (88)</p> <p>Language/communication: G1: 9/9 (100)</p> <p>Perceptual/motor: G1: 1/2 (50)</p> <p>Cognitive: G1: 2/2 (100)</p> <p>Musical: G1: 1/1 (100)</p> <p><b>Harms:</b> NR</p>

**Comments:**

\* If a client was served both years, each year with that client was treated separately in the data.



**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> O'Connor et al., 2004</p> <p><b>Country:</b> Canada</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NR</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Randomized trial with crossover design</p>	<p><b>Intervention:</b> In one session, students read 5 passages written in 3 different procedural facilitation styles (pre-reading questions, anaphoric cuing, and cloze task) and one control style.</p> <p>Order and style randomly varied (approximately 10 min/passage, including 1 passage in each facilitation style and 2 control passages); experiments took place at home (n=14) or school (n=6).</p> <p><b>Intervention target:</b> Comprehension of text</p> <p><b>Primary outcome:</b> Comprehension of text</p> <p><b>Groups:</b> G1: all participants</p> <p><b>Treatment duration:</b> Single session</p> <p><b>Frequency of contact during study:</b> NA</p> <p><b>Last followup post-treatment:</b> Immediately post treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> G1: 20</p> <p><b>N at followup:</b> G1: 20</p>	<p><b>Inclusion criteria:</b> Moderate to high levels of decoding Lower levels of reading comprehension</p> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>Age, yrs, mean ± SD:</b> G1: 15.11 ± 0.99</p> <p><b>Mental age, Stanford-Binet Intelligence, mean ± SD:</b> G1: 88.15 ± 16.06</p> <p><b>Gender, n (%):</b> Male: G1: 19 (95) Female: G1: 1 (5)</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>Total Reading Comprehension score, mean ± SD;</b> Control passage 1: G1: 12.79 ± 6.33 Control passage 2: G1: 12.86 ± 6.27</p>	<p><b>Total Reading Comprehension score, mean ± SD;</b> Anaphoric cuing passage: G1: 15.41 ± 6.28 G1/BL: P = 0.03</p> <p>Prereading questions passage: G1: 13.88 ± 5.47 G1/BL: P = 0.29</p> <p>Cloze passage: G1: 13.83 ± 5.14 G1/BL: P = 0.32</p> <p><b>Improvement of ≥ 0.50 SD, score vs. control, n:</b> Anaphoric cuing passage: G1:11</p> <p>Prereading questions passage: G1: 7</p> <p>Cloze passage: G1: 7</p> <p><b>Harms:</b> NR</p>

**Comments:**

Repeated measures ANOVA showed a significant effect of procedural facilitation (combined) vs. control (P = 0.05).

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Van Bourgondien et al., 2003</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NIMH</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Prospective Cohort</p>	<p><b>Intervention:</b> Experimental treatment program (combined residential &amp; vocational training program) using TEACCH psychoeducational model</p> <p>Part-random, part-clinical/administrative assignment of subjects to the treatment group; the remaining participants were living in one of three control conditions: group homes institutions or family home</p> <p><b>Intervention target:</b> Family satisfaction, measures of participant skills &amp; behaviors</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> <b>G1:</b> TEACCH-based program <b>G2:</b> Family home <b>G3:</b> Group homes <b>G4:</b> Institutions</p> <p><b>Treatment duration:</b> 24 hour programs assessed 6 and 12 months after participants' entry into TEACCH program</p> <p><b>Frequency of contact during study:</b> 4 time periods of 6 month intervals</p> <p><b>Last followup post-treatment:</b> 12 months after moving into G1</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> No</p>	<p><b>Inclusion criteria:</b> • Adolescents and adults with autism selected from applicants to the TEACCH-based program*</p> <p><b>Exclusion criteria:</b> • See inclusion criteria</p> <p><b>Age, yrs, mean ± SD:</b> <b>G1:</b> 23.7 ± 4.4 <b>G2:</b> 26.6 ± 5.1 <b>G3:</b> 27.8 ± 8.5 <b>G4:</b> 21.5 ± 5.0</p> <p><b>Mental age, functioning in the moderate to severe/profound ranges of mental retardation, %:</b> <b>Total:</b> 85</p> <p><b>Gender, n:</b> Male: <b>G1:</b> 6 <b>G2:</b> 8 <b>G3:</b> 8 <b>G4:</b> 4 Female: <b>G1:</b> 0 <b>G2:</b> 2 <b>G3:</b> 2 <b>G4:</b> 2</p> <p><b>DSM-based diagnostic approach reported:</b> Yes (CARS)</p>	<p><b>CARS score, mean ± SD:</b> <b>G1:</b> 37.3 ± 5.3 <b>G2:</b> 35.6 ± 6.9 <b>G3:</b> 34.7 ± 3.9 <b>G4:</b> 37.2 ± 2.9</p> <p><b>ERS score, mean ± SD:</b> Communication: <b>G1:</b> 3.0 ± 0.65 Structure: <b>G1:</b> 2.58 ± 0.62 Socialization: <b>G1:</b> 2.81 ± 0.76 Developmental: <b>G1:</b> 3.00 ± 0.63 Behavior: <b>G1:</b> 3.31 ± 0.38 Total: <b>G1:</b> 3.09 ± 0.43</p> <p><b>Aggression and/or self-injury, n:</b> <b>G1:</b> 3/6 <b>G2:</b> 2/10 <b>G3:</b> 5/10 <b>G4:</b> 4/6</p>	<p><b>ERS score, time 4, mean ± SD:</b> Communication: <b>G1:</b> 4.10 ± 0.37 <b>G2:</b> 2.57 ± 0.58 <b>G3:</b> 2.74 ± 0.76 <b>G4:</b> 2.20 ± 0.72 <b>G1/G2/G3/G4:</b> <i>P</i> = 0.0003 <b>G1/G2:</b> <i>P</i> &lt; 0.05 <b>G1/G3:</b> <i>P</i> &lt; 0.05 <b>G1/G4:</b> <i>P</i> &lt; 0.05 <b>G1/BL:</b> <i>P</i> = 0.0003 Structure: <b>G1:</b> 4.14 ± 0.29 <b>G2:</b> 2.20 ± 0.57 <b>G3:</b> 2.69 ± 0.41 <b>G4:</b> 2.28 ± 0.10 <b>G1/G2/G3/G4:</b> <i>P</i> = 0.0001 <b>G1/G2:</b> <i>P</i> &lt; 0.05 <b>G1/G3:</b> <i>P</i> &lt; 0.05 <b>G1/G4:</b> <i>P</i> &lt; 0.05 <b>G1/BL:</b> <i>P</i> = 0.0002 Socialization: <b>G1:</b> 3.78 ± 0.53 <b>G2:</b> 2.40 ± 0.80 <b>G3:</b> 2.76 ± 0.69 <b>G4:</b> 2.33 ± 0.73 <b>G1/G2/G3/G4:</b> <i>P</i> = 0.0057 <b>G1/G2:</b> <i>P</i> &lt; 0.05 <b>G1/G3:</b> <i>P</i> &lt; 0.05 <b>G1/G4:</b> <i>P</i> &lt; 0.05 <b>G1/BL:</b> <i>P</i> = 0.0014 Developmental: <b>G1:</b> 4.12 ± 0.24 <b>G2:</b> 2.68 ± 0.84 <b>G3:</b> 3.20 ± 0.48 <b>G4:</b> 2.50 ± 0.33 <b>G1/G2/G3/G4:</b> <i>P</i> = 0.0025 <b>G1/G2:</b> <i>P</i> &lt; 0.05 <b>G1/G3:</b> <i>P</i> = NS <b>G1/G4:</b> <i>P</i> &lt; 0.05 <b>G1/BL:</b> <i>P</i> = 0.0006</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Van Bourgondien et al., 2003 (continued)	<p><b>Concomitant therapies:</b> Receiving at-least one medication for behavioral control, %: <b>Total: 53</b></p> <p>Behavior control medications, mean <math>\pm</math> SD: <b>G1: 1.5 <math>\pm</math> 1.4</b> <b>G2: 0.3 <math>\pm</math> 0.5</b> <b>G3: 1.4 <math>\pm</math> 2.0</b> <b>G4: 1.7 <math>\pm</math> 2.0</b></p> <p><b>N at enrollment:</b> <b>G1: 6</b> <b>G2: 10</b> <b>G3: 10</b> <b>G4: 6</b></p> <p><b>N at followup:</b> <b>G1: 6</b> <b>G2: 10</b> <b>G3: 10</b> <b>G4: 6</b></p>			<p>Behavior: <b>G1: 4.43 <math>\pm</math> 0.37</b> <b>G2: 2.29 <math>\pm</math> 0.76</b> <b>G3: 2.8 <math>\pm</math> 0.32</b> <b>G4: 2.71 <math>\pm</math> 0.38</b> <b>G1/G2/G3/G4: P = 0.0001</b> <b>G1/G2: P &lt; 0.05</b> <b>G1/G3: P &lt; 0.05</b> <b>G1/G4: P &lt; 0.05</b> <b>G1/BL: P = 0.0001</b></p> <p>Total: <b>G1: 4.11 <math>\pm</math> 0.31</b> <b>G2: 2.67 <math>\pm</math> 0.60</b> <b>G3: 3.04 <math>\pm</math> 0.34</b> <b>G4: 2.85 <math>\pm</math> 0.35</b> <b>G1/G2/G3/G4: P = 0.0001</b> <b>G1/G2: P &lt; 0.05</b> <b>G1/G3: P &lt; 0.05</b> <b>G1/G4: P &lt; 0.05</b> <b>G1/BL: P = 0.0001</b></p> <p><b>Global ratings, mean <math>\pm</math> SD:</b> Programming: <b>G1: 5.00 <math>\pm</math> 0.00</b> <b>G2: 2.25 <math>\pm</math> 0.89</b> <b>G3: 3.00 <math>\pm</math> 1.10</b> <b>G4: 2.60 <math>\pm</math> 0.89</b> <b>G1/G2/G3/G4: P = 0.0001</b> <b>G1/G2: P &lt; 0.05</b> <b>G1/G3: P &lt; 0.05</b> <b>G1/G4: P &lt; 0.05</b></p> <p>Desirability: <b>G1: 135.83 <math>\pm</math> 4.02</b> <b>G2: 69.13 <math>\pm</math> 25.89</b> <b>G3: 75.36 <math>\pm</math> 35.28</b> <b>G4: 33.6 <math>\pm</math> 24.2</b> <b>G1/G2/G3/G4: P = 0.0001</b> <b>G1/G2: P &lt; 0.05</b> <b>G1/G3: P &lt; 0.05</b> <b>G1/G4: P &lt; 0.05</b> <b>G2/G3: P = NS</b> <b>G2/G4: P &lt; 0.05</b> <b>G3/G4: P &lt; 0.05</b></p>

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Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)

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<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Van Bourgondien et al., 2003 (continued)				<p><b>Family satisfaction survey, community involvement, mean <math>\pm</math> SD:</b>  <b>G1:</b> 5.0 <math>\pm</math> 0.0 (n=5)  <b>G3:</b> 3.10 <math>\pm</math> 1.44 (n=3)  <b>G4:</b> 3.33 <math>\pm</math> 0.58 (n=10)  <b>G1/G3:</b> P &lt; 0.05  <b>G1/G4:</b> P = 0.13</p> <p><b>Skills index, mean <math>\pm</math> SD:</b>  <b>G1:</b> 3.5 <math>\pm</math> 1.5  <b>G2:</b> 3.3 <math>\pm</math> 2.1  <b>G3:</b> 3.1 <math>\pm</math> 2.1  <b>G4:</b> 2.6 <math>\pm</math> 1.8</p> <p><b>Index of negative behaviors, mean <math>\pm</math> SD:</b>  <b>G1:</b> 1.8 <math>\pm</math> 0.3  <b>G2:</b> 1.4 <math>\pm</math> 0.6  <b>G3:</b> 1.6 <math>\pm</math> 0.5  <b>G4:</b> 1.6 <math>\pm</math> 0.6  <b>G1/G2:</b> P = 0.05</p> <p><b>Negative behavior observations, mean <math>\pm</math> SD:</b>  <b>G1:</b> 16.8 <math>\pm</math> 6.8  <b>G2:</b> 20.4 <math>\pm</math> 11.7  <b>G3:</b> 16.0 <math>\pm</math> 12.8  <b>G4:</b> 24.2 <math>\pm</math> 12.5</p> <p><b>Negative behavior observations without stereotypes, mean <math>\pm</math> SD:</b>  <b>G1:</b> 0.7 <math>\pm</math> 0.6  <b>G2:</b> 4.2 <math>\pm</math> 5.8  <b>G3:</b> 2.0 <math>\pm</math> 2.3  <b>G4:</b> 6.5 <math>\pm</math> 9.0</p> <p><b>Harms:</b>  NR</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Garcia-Villamizar et al., 2000†, 2002*</p> <p><b>Country:</b> Spain, Germany</p> <p><b>Enrollment period:</b> 1996-2000†*</p> <p><b>Funding:</b> Horizon Program of European Union, Cosejería de Asuntos Sociales de la Comunidad Autónoma de Madrid (Spain)</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Nonrandomized controlled trial</p>	<p><b>Intervention:</b> Sheltered and supported community-based work environments*</p> <p><b>Intervention target:</b> To analyze the differential impact of two modalities of work on clinical symptom evolution between 1996 &amp; 1999†</p> <p><b>Groups:</b> <b>G1:</b> Sheltered work group (SHW)†* <b>G2:</b> Supported work group (SPW)†*</p> <p><b>Primary outcome:</b> NR</p> <p><b>Treatment duration:</b> Average length of community employment: 30 months for an average of 20 hours/week</p> <p><b>Frequency of contact during study:</b> Beginning and end of program</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment† 5 years from start of program*</p> <p><b>Measure of treatment fidelity/adherence reported:</b></p> <p><b>Co-interventions held stable during treatment:</b></p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1:</b> 26 <b>G2:</b> 25</p> <p><b>N at followup:</b> <b>G1:</b> 26 <b>G2:</b> 21</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Diagnosis of autism</li> <li>• Provision of informed consent</li> <li>• For G2, sheltered workshop enrollment prior to participation in supported work, no severe behavior problems, acceptable professional and vocational abilities</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• See inclusion</li> </ul> <p><b>Age, yrs, mean ± SD:</b> <b>G1:</b> 21.07 ± 4.18 <b>G2:</b> 21.64 ± 3.75</p> <p><b>IQ, Leiter (total score), mean ± SD:</b> <b>G1:</b> 55.52 ± 14.43 <b>G2:</b> 57.41 ± 15.01</p> <p><b>Gender, n:</b> Male: <b>G1:</b> 18 <b>G2:</b> 21</p> <p>Female: <b>G1:</b> 8 <b>G2:</b> 4</p> <p><b>DSM-based diagnostic approach reported:</b></p> <ul style="list-style-type: none"> <li>• Yes (DSM-IV &amp; CARS)</li> </ul>	<p><b>QoL QNR score, mean ± SD:*</b> Environmental control: <b>G1:</b> 10.00 ± 2.23 <b>G2:</b> 10.80 ± 2.50 <b>G1/G2:</b> <i>P</i> = NS</p> <p>Community involvement: <b>G1:</b> 11.88 ± 3.01 <b>G2:</b> 13.28 ± 3.22 <b>G1/G2:</b> <i>P</i> = NS</p> <p>Perception of personal change: <b>G1:</b> 7.50 ± 1.03 <b>G2:</b> 8.00 ± 0.93 <b>G1/G2:</b> <i>P</i> = NS</p> <p>Total Score: <b>G1:</b> 29.53 ± 5.26 <b>G2:</b> 31.40 ± 6.94 <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>CARS score, mean ± SD:†</b> <b>G1:</b> 35.26 ± 6.51 <b>G2:</b> 32.23 ± 8.59</p>	<p><b>QoL QNR score, mean ± SD:*</b> Environmental control: <b>G1:</b> 10.82 ± 2.26 <b>G2:</b> 13.04 ± 2.03 <b>G1/G2:</b> <i>P</i> &lt; 0.002 <b>G2/BL:</b> <i>P</i> &lt; 0.001</p> <p>Community Involvement : <b>G1:</b> 12.35 ± 3.01 <b>G2:</b> 14.04 ± 1.71 <b>G1/G2:</b> <i>P</i> &lt; 0.01 <b>G2/BL:</b> <i>P</i> = 0.187</p> <p>Perception of Personal Change: <b>G1:</b> 7.62 ± 1.62 <b>G2:</b> 8.95 ± 1.30 <b>G1/G2:</b> <i>P</i> &lt; 0.008 <b>G2/BL:</b> <i>P</i> &lt; 0.007</p> <p>Total score: <b>G1:</b> 30.76 ± 5.51 <b>G2:</b> 35.96 ± 3.43 <b>G1/G2:</b> <i>P</i> &lt; 0.0001 <b>G2/BL:</b> <i>P</i> &lt; 0.001</p> <p><b>CARS score, mean ± SD:†</b> <b>G1:</b> 38.26 ± 7.40 <b>G2:</b> 32.19 ± 7.26 <b>G1/BL:</b> <i>P</i> &lt; 0.006 <b>G2/BL:</b> <i>P</i> = 0.71</p> <p><b>Harms:</b> NR</p>

Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
<p><b>Author:</b> Remington et al., 2001</p> <p><b>Country:</b> Canada</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> Ontario Mental Health Foundation</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Double blind, placebo controlled randomized crossover design</p>	<p><b>Intervention:</b> Clomipramine: 25 mg at bedtime for 2 days, 25 mg 2 times/day for 2 days, 25 mg 3 times/day for 2 days, and 50 mg twice a day; doses then increased in 25 mg increments every 3-4 days as clinically indicated; planned treatment period: 7 weeks (actual mean 4.5 weeks)</p> <p>Haloperidol: 0.25 mg at bedtime for 2 days, 0.25 mg 2 times/day for 2 days, 0.25 mg 3 times/day for 2 days, and 0.5 mg twice a day; doses then increased in 0.5 mg increments every 3-4 days as clinically indicated; planned treatment period: 7 weeks (actual mean 5.8 weeks)</p> <p>Placebo: planned treatment period: 7 weeks (actual mean 5.4 weeks); placebo also administered for 1 week before first phase and between each treatment phase</p> <p><b>Intervention target:</b> Treatment of autistic disorder</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> <b>G1:</b> study participants <b>G1a:</b> clomipramine phase <b>G1b:</b> haloperidol phase <b>G1c:</b> placebo phase</p> <p><b>Treatment duration:</b> Each phase 7 weeks (total 21 weeks)</p> <p><b>Frequency of contact during study:</b> Every two weeks</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• DSM-IV diagnosis of autism confirmed independently by two investigators</li> <li>• A recommendation based on initial assessment of pharmacotherapy</li> <li>• Evidence haloperidol or clomipramine had not been used previously</li> <li>• If haloperidol or clomipramine had been used previously, an adequate therapeutic trial was not completed</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• See inclusion criteria</li> </ul> <p><b>Age, yrs, mean (range):</b> <b>G1:</b> 16.3 (10-36)</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, n (%):</b> Male: <b>G1:</b> 30 (83.3) Female: <b>G1:</b> 6 (16.7)</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>CARS score, mean ± SD:</b> <b>G1:</b> 41.8 ± 7.1</p> <p><b>DOTES score, mean ± SD:</b> <b>G1:</b> 0.6 ± 2.2</p> <p><b>ESRS score, mean ± SD:</b> <b>G1:</b> 6.6 ± 6.7</p> <p><b>ABC score, mean:</b> Irritability: <b>G1:</b> NR*</p> <p>Lethargy: <b>G1:</b> NR*</p> <p>Stereotypy: <b>G1:</b> NR*</p> <p>Hyperactivity: <b>G1:</b> NR*</p> <p>Inappropriate speech: <b>G1:</b> NR*</p>	<p><b>CARS score, mean ± SD:</b> <b>G1a:</b> 37.8 ± 8.7 <b>G1b:</b> 36.7 ± 6.1 <b>G1c:</b> 39.4 ± 7.0 <b>G1a/G1b/G1c:</b> <i>P</i> = 0.05</p> <p><b>G1a/BL:</b> <i>P</i> = NS <b>G1b/BL:</b> <i>P</i> &lt; 0.05 <b>G1c/BL:</b> <i>P</i> = NS</p> <p><b>DOTES score, mean ± SD:</b> <b>G1a:</b> 2.0 ± 2.9 <b>G1b:</b> 2.3 ± 3.3 <b>G1c:</b> 0.8 ± 1.7 <b>G1a/G1b/G1c:</b> <i>P</i> = NS</p> <p><b>ESRS score, mean ± SD:</b> <b>G1a:</b> 10.3 ± 7.3 <b>G1b:</b> 7.8 ± 5.8 <b>G1c:</b> 7.9 ± 7.1 <b>G1a/G1b/G1c:</b> <i>P</i> = NS</p> <p><b>ABC score, mean:</b> Irritability: <b>G1a:</b> NR* <b>G1b:</b> NR* <b>G1c:</b> NR* <b>G1a/G1b/G1c:</b> <i>P</i> = 0.03</p> <p><b>G1a/BL:</b> <i>P</i> = NS <b>G1b/BL:</b> <i>P</i> &lt; 0.05 <b>G1c/BL:</b> <i>P</i> = NS</p> <p>Lethargy: <b>G1a:</b> NR* <b>G1b:</b> NR* <b>G1c:</b> NR* <b>G1a/G1b/G1c:</b> <i>P</i> = NS</p> <p>Stereotypy: <b>G1a:</b> NR* <b>G1b:</b> NR* <b>G1c:</b> NR* <b>G1a/G1b/G1c:</b> <i>P</i> = NS</p>

Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Remington et al., 2001 (continued)	<p><b>Measure of treatment fidelity/adherence reported:</b> Yes</p> <p><b>Co-interventions held stable during treatment:</b> Yes</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1a:</b> 32 <b>G1b:</b> 33 <b>G1c:</b> 32</p> <p><b>N at followup:</b> <b>G1a:</b> 12 <b>G1b:</b> 23 <b>G1c:</b> 21</p> <p><b>G1a/G1b/G1c:</b> <math>P &lt; 0.001</math></p>			<p>Hyperactivity: <b>G1a:</b> NR* <b>G1b:</b> NR* <b>G1c:</b> NR* <b>G1a/G1b/G1c:</b> <math>P = 0.01</math> <b>G1a/BL:</b> <math>P = NS</math> <b>G1b/BL:</b> <math>P &lt; 0.05</math> <b>G1c/BL:</b> <math>P = NS</math></p> <p>Inappropriate speech: <b>G1a:</b> NR* <b>G1b:</b> NR* <b>G1c:</b> NR* <b>G1a/G1b/G1c:</b> <math>P = NS</math></p> <p><b>Harms:</b> Discontinued early due to behavioral problems only: <b>G1a:</b> 8 <b>G1b:</b> 3 <b>G1c:</b> 10</p> <p>Discontinued early due to physiologic effects and behavioral problems: <b>G1a:</b> 4 <b>G1b:</b> 1 <b>G1c:</b> 0</p> <p>Discontinued early due to physiologic effects only: <b>G1a:</b> 8 <b>G1b:</b> 6 <b>G1c:</b> 1</p> <p>Fatigue or lethargy: <b>G1a:</b> 4 <b>G1b:</b> 5 <b>G1c:</b> 0</p> <p>Tremors: <b>G1a:</b> 2 <b>G1b:</b> 0 <b>G1c:</b> 0</p> <p>Tachycardia: <b>G1a:</b> 1 <b>G1b:</b> 0 <b>G1c:</b> 0</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Remington et al., 2001 (continued)				<p>Insomnia:  <b>G1a: 1</b>  <b>G1b: 0</b>  <b>G1c: 0</b></p> <p>Diaphoresis:  <b>G1a: 1</b>  <b>G1b: 0</b>  <b>G1c: 0</b></p> <p>Nausea or vomiting:  <b>G1a: 1</b>  <b>G1b: 0</b>  <b>G1c: 0</b></p> <p>Decreased appetite:  <b>G1a: 1</b>  <b>G1b: 0</b>  <b>G1c: 0</b></p> <p>Preexisting right bundle branch block:  <b>G1a: 1</b>  <b>G1b: 0</b>  <b>G1c: 0</b></p> <p>Dystonia:  <b>G1a: 0</b>  <b>G1b: 1</b>  <b>G1c: 0</b></p> <p>Depression:  <b>G1a: 0</b>  <b>G1b: 1</b>  <b>G1c: 1</b></p> <p>Persistent nosebleeds:  <b>G1a: 0</b>  <b>G1b: 0</b>  <b>G1c: 1</b></p>



**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<b>Author:</b> Silver et al., 2001  <b>Country:</b> UK  <b>Enrollment period:</b> NR  <b>Funding:</b> NR  <b>Author industry relationship disclosures:</b> NA  <b>Design:</b> RCT	<b>Intervention:</b> School-based Emotion Trainer computer intervention, 10 daily half hour computer sessions (used mean 8.4 times, range 2-15 times)  <b>Intervention target:</b> Better recognition and prediction of emotional responses in others  <b>Primary outcome:</b> NR  <b>Groups:</b> <b>G1:</b> computer sessions and standard lessons <b>G2:</b> standard lessons only  <b>Treatment duration:</b> 2-3 weeks  <b>Frequency of contact during study:</b> Daily during school  <b>Last followup post-treatment:</b> End of treatment  <b>Measure of treatment fidelity/adherence reported:</b> Yes  <b>Co-interventions held stable during treatment:</b> NR  <b>Concomitant therapies:</b> NR  <b>N at enrollment:</b> <b>G1:</b> 12 <b>G2:</b> 12  <b>N at followup:</b> <b>G1:</b> 10 <b>G2:</b> 11	<b>Inclusion criteria:</b> Clear diagnosis of autistic spectrum disorder Age equivalent $\geq 7$ years on the British Picture Vocabulary Scale Chronological age 10-18  <b>Exclusion criteria:</b> See inclusion criteria  <b>Age, yrs, mean <math>\pm</math> SD:*</b> <b>G1:</b> 13.9 $\pm$ 0.9 <b>G2:</b> 14.75 $\pm$ 2.0  <b>Mental age, BPVS age equivalent, yrs, mean <math>\pm</math> SD:</b> <b>G1:</b> 10.67 $\pm$ 2.25 <b>G2:</b> 12.0 $\pm$ 3.33  <b>Gender:</b> NR  <b>DSM-based diagnostic approach reported:</b> No	<b>Facial Expression Photographs, total error score, mean <math>\pm</math> SD:</b> <b>G1:</b> 4.27 $\pm$ 1.85 <b>G2:</b> 4.45 $\pm$ 2.34  <b>Emotion Recognition Cartoons, total error score, mean <math>\pm</math> SD:</b> <b>G1:</b> 4.36 $\pm$ 3.35 <b>G2:</b> 3.27 $\pm$ 1.79  <b>Strange Stories, compound Likert score, mean <math>\pm</math> SD:</b> <b>G1:</b> 18.3 $\pm$ 16.4 <b>G2:</b> 20.8 $\pm$ 22.9	<b>Facial Expression Photographs, total error score, mean:</b> <b>G1:</b> NR** <b>G2:</b> NR** ANOVA: group X time $P = NS$ ; time $P = 0.029$  <b>Emotion Recognition Cartoons, total error score, mean:</b> <b>G1:</b> NR** <b>G2:</b> NR** ANOVA: group X time $P = 0.041$  <b>Strange Stories, compound Likert score, mean:</b> <b>G1:</b> NR** <b>G2:</b> NR** ANOVA: group X time $P = 0.016$  <b>Harms:</b> NR

**Comments:**

\* Chronological age means and SD converted from years/months to years

\*\* Values are only represented graphically.

The teaching tasks were computer based and the assessment tasks were paper based.

The number of times a child used the computer program significantly correlated with an improvement in score on the Emotion Recognition Cartoons and the Strange Stories but not with improvement on the Facial Expression Photographs.

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Mawhood et al., 1999</p> <p><b>Country:</b> UK</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> Nuffield Foundation, Department of Employment, National Autistic Society</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Prospective cohort study</p>	<p><b>Intervention:</b> Supported employment scheme: upon suitable job identification, full time support worker provided for 1<sup>st</sup> 2-4 weeks; support decreased to 1-2 times/week during the 2<sup>nd</sup> month; further reduction in support so by the 4<sup>th</sup> month, occasional planned meetings (a support worker could be contacted anytime during an emergency)</p> <p><b>Intervention target:</b> Employment</p> <p><b>Primary outcome:</b> Employment</p> <p><b>Groups:</b> <b>G1:</b> supported employment scheme <b>G2:</b> no employment support</p> <p><b>Treatment duration:</b> 2 years (mean <math>\pm</math> SD 17.03 <math>\pm</math> 6.64 months)</p> <p><b>Frequency of contact during study:</b> Daily for 2-4 weeks, then 1-2 times/week during 2<sup>nd</sup> month, then occasional meetings during 4<sup>th</sup> month</p> <p><b>Last followup post-treatment:</b> Immediately post treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p>	<p><b>Inclusion criteria:</b> Formal diagnosis of autism or Asperger syndrome IQ <math>\geq</math> 70 on either WAIS performance or verbal scale Actively seeking work Able to travel independently and prepared to work within the greater London area (<b>G1</b>) or outside greater London area (<b>G2</b>) Capable of eventually maintaining employment with minimal support No additional psychiatric or physical problems that would adversely affect employability</p> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>Age, yrs, mean <math>\pm</math> SD:</b> <b>G1:</b> 31.1 <math>\pm</math> 9.1 <b>G2:</b> 28.0 <math>\pm</math> 6.1</p> <p><b>Mental age, mean <math>\pm</math> SD:</b> WORD reading accuracy test: <b>G1:</b> 16.6 <math>\pm</math> 1.5 <b>G2:</b> NR</p> <p>WORD comprehension test: <b>G1:</b> 13.8 <math>\pm</math> 3.6 <b>G2:</b> NR</p> <p>WORD spelling test: <b>G1:</b> 16.2 <math>\pm</math> 2.1 <b>G2:</b> NR</p> <p>British Ability Scales Number subtest <b>G1:</b> 12.9 <math>\pm</math> 1.8 <b>G2:</b> NR</p> <p><b>IQ, mean <math>\pm</math> SD:</b> WAIS verbal IQ: <b>G1:</b> 104.1 <math>\pm</math> 17.3 <b>G2:</b> 101.6 <math>\pm</math> 0.50</p> <p>WAIS performance IQ: <b>G1:</b> 91.6 <math>\pm</math> 15.7 <b>G2:</b> 92.2 <math>\pm</math> 0.12</p>	<p><b>Employed, n:</b> <b>G1:</b> 8 <b>G2:</b> 3</p> <p><b>Time in work, % (range):</b> <b>G1:</b> 18.58 (0-100) <b>G2:</b> 10.79 (0-100) <b>G1/G2:</b> <math>P = 0.35</math></p> <p><b>Rosenberg Self-Esteem Inventory score, mean <math>\pm</math> SD:</b> <b>G1:</b> 21.79 <math>\pm</math> 4.78 <b>G2:</b> 21.50 <math>\pm</math> 4.43</p>	<p><b>Employed, n (%):</b> <b>G1:</b> 19 (63.3) <b>G2:</b> 5 (25) <b>G1/BL:</b> <math>P = 0.009</math> <b>G2/BL:</b> <math>P = 0.69</math> <b>G1+G2/BL:</b> <math>P = 0.01</math></p> <p><b>Employment, n:</b> Permanent jobs: <b>G1:</b> 9 <b>G2:</b> 3</p> <p>Temporary/seasonal jobs: <b>G1:</b> 10 <b>G2:</b> 2</p> <p><b>Time to find employment, months, mean (range):</b> <b>G1:</b> 8.7 (6-23) <b>G2:</b> 8.4 (3-16)</p> <p><b>Hours worked/week, mean (range):</b> <b>G1:</b> 31.3 (16-38.75) <b>G2:</b> 36.5 (35-40) <b>G1/G2:</b> <math>P = 0.506</math></p> <p><b>Wages/hour, £, mean (range):</b> <b>G1:</b> 5.71 (3.71-9.49) <b>G2:</b> 4.14 (3.83-4.5) <b>G1/G2:</b> <math>P = 0.024</math></p> <p><b>Type of jobs found, n:</b> Administrative/clerical: <b>G1:</b> 16 <b>G2:</b> 1</p> <p>Computing: <b>G1:</b> 2 <b>G2:</b> 0</p> <p>Photography laboratory: <b>G1:</b> 1 <b>G2:</b> 0</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Mawhood et al., 1999 (continued)	<p><b>N at enrollment:</b>  <b>G1:</b> 30  <b>G2:</b> 20</p> <p><b>N at followup:</b>  <b>G1:</b> 30  <b>G2:</b> 17</p>	<p>WAIS full-scale IQ:  <b>G1:</b> 98.8 ± 16.3  <b>G2:</b> 97.7 ± 0.22</p> <p>BPVS:  <b>G1:</b> 94.7 ± 21.2  <b>G2:</b> 91.8 ± 0.46</p> <p>EOWPVT:  <b>G1:</b> 99.3 ± 19.1  <b>G2:</b> 98.6 ± 0.13</p> <p><b>Gender, n:</b>  Male:  <b>G1:</b> 27  <b>G2:</b> 20  Female:  <b>G1:</b> 3  <b>G2:</b> 0</p> <p><b>DSM-based diagnostic approach reported:</b>  No</p>		<p>Sales support:  <b>G1:</b> 1  <b>G2:</b> 0</p> <p>Warehouse/factory:  <b>G1:</b> 2  <b>G2:</b> 1</p> <p>Postman/messenger/outdoor:  <b>G1:</b> 0  <b>G2:</b> 3</p> <p><b>Time in work, % (range):</b>  <b>G1:</b> 26.81 (0-87.5) (n=26)  <b>G2:</b> 7.61 (0-82.3) (n=17)  <b>G1/BL:</b> <i>P</i> = 0.22  <b>G2/BL:</b> <i>P</i> = 0.91  <b>G1+G2/BL:</b> <i>P</i> = 0.02</p> <p><b>Rosenberg Self-Esteem Inventory score, mean ± SD:</b>  <b>G1:</b> 22.08 ± 4.00  <b>G2:</b> 22.25 ± 5.12</p> <p><b>Harms:</b>  NR</p>

**Comments:**

More individuals in the control group (10% vs. 3%) had attended special needs courses (*P* = NS).

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes**</b>
<p><b>Author:</b> McDougle et al., 1998</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> June 1994 to February 1997</p> <p><b>Funding:</b> Public Health Service, National Alliance for Research in Schizophrenia and Depression, Theodore and Vada Stanley Foundation, Connecticut Department of Mental Health and Addiction Services, Research Unit on Pediatric Psychopharmacology (RUPP), NIMH</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> RCT, double blind; subsequent open label trial</p>	<p><b>Intervention:</b> Risperidone starting at 1 mg/day, gradually increasing by 1 mg daily every 3-4 days to a maximum dosage of 10 mg/day, twice daily as tolerated for at least 7 weeks. Those treated with placebo subsequently given a 12 week open label trial of risperidone.</p> <p><b>Intervention target:</b> CGI global Improvement, repetitive behavior, aggression, sensory motor behaviors, social relationship to people, affectual reactions, sensory responses, language, overall behavioral symptoms of autism and mood states</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> <b>G1:</b> risperidone <b>G2:</b> placebo <b>G2a:</b> open label trial of risperidone</p> <p><b>Daily dose, mean ± SD:</b> <b>G1:</b> 2.9 ± 1.4 <b>G2:</b> 3.9 ± 1.5</p> <p><b>Treatment duration:</b> 12 weeks</p> <p><b>Frequency of contact during study:</b> Baseline, end of weeks 4, 8, and 12</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> NA</p> <p><b>Co-interventions held stable during treatment:</b> Yes</p>	<p><b>Inclusion criteria:</b> Diagnosis of autism or PDD-NOS Moderate CGI scores Y-BOCS compulsion (repetitive behavior) subscale score &gt; 10 SIB-Q score ≥ 25 Ritvo-Freeman Real-life Rating Scale overall score ≥ 0.20</p> <p><b>Exclusion criteria:</b> Met DSM-IV criteria for schizophrenia or had psychotic symptoms Significant acute medical condition</p> <p><b>Age, yrs, mean ± SD:</b> <b>G1:</b> 26.0 ± 6.7 <b>G2:</b> 29.7 ± 7.8</p> <p><b>Mental age, full scale IQ, mean ± SD:</b> <b>G1:</b> 55.5 ± 26.8 <b>G2:</b> 52.9 ± 22.1</p> <p><b>Gender, n:</b> Male: <b>G1:</b> 13 <b>G2:</b> 9 Female: <b>G1:</b> 2 <b>G2:</b> 7</p> <p><b>DSM-based diagnostic approach reported:</b> Yes (DSM-IV, ADOS, ADI)</p>	<p><b>CGI scale score, mean (SE):</b> <b>G1:</b> 4 (0) <b>G2:</b> 4 (0) <b>G2a:</b> 4 (0)</p> <p><b>Modified Y-BOCS score, mean (SE):</b> <b>G1:</b> 16.15 (3.58) <b>G2:</b> 14.29 (3.50) <b>G2a:</b> 14.27 (2.92)</p> <p><b>SIB-Q total score, mean (SE):</b> <b>G1:</b> 47.8 (19.5) <b>G2:</b> 37.7 (11.9) <b>G2a:</b> 32.43 (15.89)</p> <p><b>Ritvo-Freeman subscale score, mean (SE):</b> Sensory motor behaviors: <b>G1:</b> 0.79 (0.65) <b>G2:</b> 0.71 (0.58) <b>G2a:</b> 0.68 (0.48)</p> <p>Social relationship to people: <b>G1:</b> NR <b>G2:</b> NR <b>G2a:</b> NR</p> <p>Affectual reactions: <b>G1:</b> 1.02 (0.39) <b>G2:</b> 0.78 (0.49) <b>G2a:</b> 0.75 (0.53)</p> <p>Sensory responses: <b>G1:</b> NR <b>G2:</b> NR <b>G2a:</b> 0.70 (0.38)</p> <p>Language: <b>G1:</b> NR <b>G2:</b> NR <b>G2a:</b> NR</p> <p><b>Ritvo-Freeman overall behavioral symptom score, mean (SE):</b> <b>G1:</b> 0.60 (0.44) <b>G2:</b> 0.53 (0.41) <b>G2a:</b> 0.50 (0.38)</p>	<p><b>CGI scale score, 12 weeks, mean (SE):</b> <b>G1:</b> 2.54 (1.27) <b>G2:</b> 4 (0.79) <b>G2a:</b> 2.47 (1.06) <b>G1/G2:</b> <i>P</i> &lt; 0.001 <b>G2a/BL:</b> <i>P</i> &lt; 0.001</p> <p><b>Responders (CGI much improved or very much improved), n (%):</b> <b>G1:</b> 8/14 (57) <b>G2:</b> 0 <b>G2a:</b> 9/15 (60)</p> <p><b>Modified Y-BOCS score, 12 weeks, mean (SE):</b> <b>G1:</b> 12.77 (3.63) <b>G2:</b> 14.35 (3.02) <b>G2a:</b> 11.47 (3.64) <b>G1/G2:</b> <i>P</i> &lt; 0.02 <b>G2a/BL:</b> <i>P</i> &lt; 0.03</p> <p><b>SIB-Q total score, 12 weeks, mean (SE):</b> <b>G1:</b> 24.2 (9.5) <b>G2:</b> 32.8 (15.0) <b>G2a:</b> 23.07 (13.45) <b>G1/G2:</b> <i>P</i> &lt; 0.01 <b>G2a/BL:</b> <i>P</i> &lt; 0.05</p> <p><b>Ritvo-Freeman subscale score, 12 weeks, mean (SE):</b> Sensory motor behaviors: <b>G1:</b> 0.38 (0.38) <b>G2:</b> 0.64 (0.49) <b>G2a:</b> 0.44 (0.31) <b>G1/G2:</b> <i>P</i> &lt; 0.007 <b>G2a/BL:</b> <i>P</i> &lt; 0.04</p> <p>Social relationship to people: <b>G1:</b> NR <b>G2:</b> NR <b>G2a:</b> NR <b>G1/G2:</b> <i>P</i> = NS <b>G2a/BL:</b> <i>P</i> = NS</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes**</b>
McDougle et al., 1998 (continued)	<p><b>Concomitant therapies, n:</b> Chloral hydrate (2 g/day) for agitation: NR</p> <p><b>N at enrollment:</b> G1: 15 G2: 16 G2a: 16</p> <p><b>N at followup:*</b> G1: 12 G2: 12 G2a: 15</p>		<p><b>VAS mood scores, clinician rated, mean (SE):</b> Anxious or nervous: G1: 70.4 (16.4) G2: 66.6 (22.1) G2a: 62.67 (26.04)</p> <p>Depressed: G1: 23.8 (17.6) G2: 23.1 (28.1) G2a: NR</p> <p>Irritable: G1: 51.8 (23.2) G2: 31.5 (24.4) G2a: 27.33 (23.75)</p> <p>Calm: G1: NR G2: NR G2a: 26.67 (22.25)</p> <p>Restless: G1: NR G2: NR G2a: 54.67 (28.25)</p>	<p>Affectual reactions: G1: 0.35 (0.37) G2: 0.82 (0.57) G2a: 0.33 (0.28) G1/G2: <i>P</i> &lt; 0.003 G2a/BL: <i>P</i> &lt; 0.007</p> <p>Sensory responses: G1: NR G2: NR G2a: 0.44 (0.36) G1/G2: <i>P</i> = NS (<i>P</i> &lt; 0.02; n=24) G2a/BL: <i>P</i> &lt; 0.004</p> <p>Language: G1: NR G2: NR G2a: NR G1/G2: <i>P</i> = NS G2a/BL: <i>P</i> = NS</p> <p><b>Ritvo-Freeman overall behavioral symptom score, 12 months, mean (SE):</b> G1: 0.32 (0.27) G2: 0.45 (0.41) G2a: 0.27 (0.33) G1/G2: <i>P</i> &lt; 0.05 G2a/BL: <i>P</i> &lt; 0.003</p> <p><b>VAS mood scores, 12 months, clinician rated, mean (SE).***</b> Anxious or nervous: G1: 42.3 (28.0) G2: 60.0 (28.5) G1/G2: <i>P</i> &lt; 0.02 (<i>P</i> &lt; 0.03; n=24) G2a: 37.93 (29.95) G2a/BL: <i>P</i> &lt; 0.02</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes**
McDougle et al., 1998 (continued)				<p>Depressed:  <b>G1:</b> 8.5 (11.4)  <b>G2:</b> 19.4 (25.4)  <b>G2a:</b> NR  <b>G1/G2:</b> <math>P &lt; 0.03</math>  (<math>P &lt; 0.08</math>; <math>n=24</math>)  <b>G2a/BL:</b> <math>P = NS</math></p> <p>Irritable:  <b>G1:</b> 21.8 (20.4)  <b>G2:</b> 22.3 (24.9)  <b>G1/G2:</b> <math>P &lt; 0.01</math>  <b>G2a:</b> 14.13  (16.27)  <b>G2a/BL:</b> <math>P &lt; 0.05</math></p> <p>Calm:  <b>G1:</b> NR  <b>G2:</b> NR  <b>G2a:</b> 46.60  (24.01)  <b>G1/G2:</b> <math>P = NS</math>  <b>G2a/BL:</b> <math>P &lt; 0.01</math></p> <p>Restless:  <b>G1:</b> NR  <b>G2:</b> NR  <b>G2a:</b> 27.00  (22.82)  <b>G1/G2:</b> <math>P = NS</math>  <b>G2a/BL:</b> <math>P &lt; 0.03</math></p> <p><b>Harms:</b>  At least one adverse event, n (%):  <b>G1:</b> 13/15 (87)  <b>G2:</b> 5/16 (31)</p> <p>Sedation:  <b>G1:</b> 9  <b>G2:</b> 0</p> <p>Agitation:  <b>G1:</b> 2  <b>G2:</b> 5</p> <p>Enuresis:  <b>G1:</b> 2  <b>G2:</b> 0</p> <p>Weight gain:  <b>G1:</b> 2  <b>G2:</b> 0</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes**</b>
McDougle et al., 1998 (continued)				Dyspepsia, diarrhea, constipation: <b>G1: 1</b> <b>G2: 0</b>  Abnormal gait, <b>G1: 1</b> <b>G2: 0</b>

**Comments:**

\* 24/31 completed the entire 12 week study; of these 14/24 were 13-30 years old (**G1: 8; G2: 6**). 7/31 completed only 1-4 weeks of treatment; of these 5/7 were 13-30 years old (**G1: 2; G2: 3**).

\*\* Where available, P-values reported for drug X time interaction are from ANCOVAs using baseline and 12-week values; P-values reported for VAS are from 2-way ANOVAs with repeated measures for all patients that completed at least 4 weeks (n=30; ITT analysis) and for completers (n=24). The latter value was also included if only one of the tests was significant. P-values reported for the open label trial from 1-way ANOVA with repeated measures.

\*\*\* No other significant difference over time reported for any of the other mood measures.

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> McDougle et al., 1998</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> Pfizer, NIH, National Alliance for Research on Schizophrenia and Depression, Theodore and Vada Stanley Research Foundation, Connecticut Department of Mental Health and Addiction Services</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Prospective case series</p>	<p><b>Intervention:</b> Sertraline, started at 50 mg/day with further increases of 50 mg/day every week (maximum 200 mg/day as tolerated, attained within 3 weeks). Actual dose, mg, mean <math>\pm</math> SD (range): 122.0 <math>\pm</math> 60.5 (50-200)</p> <p><b>Intervention target:</b> Reduced repetitive thoughts/behavior and aggression; enhancement of social relatedness</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> <b>G1:</b> sertraline <b>Ga:</b> autistic disorder <b>Gb:</b> Asperger's disorder <b>Gc:</b> PPD NOS</p> <p><b>Treatment duration:</b> 12 weeks</p> <p><b>Frequency of contact during study:</b> 0, 4, 8 and 12 weeks</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies, n:*</b> 1000-3000 mg chloral hydrate: 4</p> <p><b>N at enrollment:</b> <b>G1:</b> 42 <b>G1a:</b> 22 <b>G1b:</b> 6 <b>G1c:</b> 14</p> <p><b>N at followup:</b> <b>G1:</b> 37</p>	<p><b>Inclusion criteria:</b> DSM-IV diagnosis of ASD Y-BOCS score &gt; 15 (verbal patients) or &gt; 7 (nonverbal patients) S-IBQ score <math>\geq</math> 25 Ritvo-Freeman Real-Life rating scale overall score <math>\geq</math> 0.20 or VABS Maladaptive Behavior subscale part 1 score <math>\geq</math> 14 or VABS Maladaptive Behavior subscale part 2 score <math>\geq</math> 5 Psychotropic drug-free for <math>\geq</math> 4 weeks before start of trial</p> <p><b>Exclusion criteria:</b> DSM-IV diagnosis of psychotic or bipolar disorder Significant medical problem (e.g., seizure)</p> <p><b>Age, yrs, mean <math>\pm</math> SD:</b> <b>G1:</b> 26.1 <math>\pm</math> 5.8</p> <p><b>Mental age:</b> NR</p> <p><b>IQ, mean <math>\pm</math> SD:</b> <b>G1:</b> 60.5 <math>\pm</math> 22.7</p> <p><b>Gender, n (%):</b> Male: <b>G1:</b> 27 (64) Female: <b>G1:</b> 15 (36)</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>CGI scale score, mean <math>\pm</math> SD:</b> <b>G1a:</b> NA <b>G1b:</b> NA <b>G1c:</b> NA</p> <p><b>Y-BOCS score, mean <math>\pm</math> SD:</b> Total: <b>G1a:</b> 16.5 <math>\pm</math> 6.7 <b>G1b:</b> 25.7 <math>\pm</math> 41.1 <b>G1c:</b> 18.2 <math>\pm</math> 4.8</p> <p>Obsession subscale: <b>G1a:</b> 2.6 <math>\pm</math> 5.1 <b>G1b:</b> 12.5 <math>\pm</math> 2.7 <b>G1c:</b> 4.2 <math>\pm</math> 5.7</p> <p>Compulsion subscale: <b>G1a:</b> 13.9 <math>\pm</math> 4.1 <b>G1b:</b> 13.2 <math>\pm</math> 2.7 <b>G1c:</b> 14.0 <math>\pm</math> 3.6</p> <p><b>SIB-Q total score, mean <math>\pm</math> SD:</b> <b>G1a:</b> 32.7 <math>\pm</math> 16.5 <b>G1b:</b> 17.5 <math>\pm</math> 7.7 <b>G1c:</b> 36.2 <math>\pm</math> 16.4</p> <p><b>Ritvo-Freeman behavioral symptom score, mean <math>\pm</math> SD:</b> Overall: <b>G1a:</b> 0.48 <math>\pm</math> 0.49 <b>G1b:</b> 0.26 <math>\pm</math> 0.38 <b>G1c:</b> 0.77 <math>\pm</math> 0.53</p> <p>Subscale I: <b>G1a:</b> 0.71 <math>\pm</math> 0.59 <b>G1b:</b> 0.33 <math>\pm</math> 0.20 <b>G1c:</b> 0.71 <math>\pm</math> 0.52</p> <p>Subscale II: <b>G1a:</b> 0.21 <math>\pm</math> 0.72 <b>G1b:</b> -0.17 <math>\pm</math> 0.45 <b>G1c:</b> 0.42 <math>\pm</math> 0.57</p> <p>Subscale III: <b>G1a:</b> 0.81 <math>\pm</math> 0.52 <b>G1b:</b> 0.40 <math>\pm</math> 0.28 <b>G1c:</b> 1.12 <math>\pm</math> 0.56</p> <p>Subscale IV: <b>G1a:</b> 0.71 <math>\pm</math> 0.52 <b>G1b:</b> 0.66 <math>\pm</math> 0.59 <b>G1c:</b> 0.88 <math>\pm</math> 0.53</p>	<p><b>CGI scale score, 12 weeks, mean <math>\pm</math> SD:</b> <b>G1a:</b> 2.1 <math>\pm</math> 1.0 <b>G1b:</b> 4.0 <math>\pm</math> 0.0 <b>G1c:</b> 2.3 <math>\pm</math> 0.9 <b>G1/BL:</b> <i>P</i> = 0.0001</p> <p><b>Responders (CGI much improved or very much improved), n (%):</b> <b>G1:</b> 24 (57) <b>G1a:</b> 15 (68) <b>G1b:</b> 0 <b>G1c:</b> 9 (64)</p> <p><b>Y-BOCS score, 12 weeks, mean <math>\pm</math> SD:</b> Total: <b>G1a:</b> 11.5 <math>\pm</math> 5.8 <b>G1b:</b> 27.8 <math>\pm</math> 5.3 <b>G1c:</b> 14.8 <math>\pm</math> 5.7 <b>G1/BL:</b> <i>P</i> = 0.0005</p> <p>Obsession subscale: <b>G1a:</b> 2.2 <math>\pm</math> 4.2 <b>G1b:</b> 13.8 <math>\pm</math> 3.0 <b>G1c:</b> 3.8 <math>\pm</math> 5.2 <b>G1/BL:</b> <i>P</i> = NS</p> <p>Compulsion subscale: <b>G1a:</b> 9.3 <math>\pm</math> 3.8 <b>G1b:</b> 14.0 <math>\pm</math> 3.6 <b>G1c:</b> 11.0 <math>\pm</math> 3.3 <b>G1/BL:</b> <i>P</i> = 0.0001</p> <p><b>SIB-Q total score, 12 weeks, mean <math>\pm</math> SD:</b> <b>G1a:</b> 15.5 <math>\pm</math> 9.5 <b>G1b:</b> 18.8 <math>\pm</math> 7.7 <b>G1c:</b> 20.2 <math>\pm</math> 12.8 <b>G1/BL:</b> <i>P</i> = 0.0001</p>



**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
McDougle et al., 1998 (continued)			Subscale V: <b>G1a:</b> $-0.02 \pm 0.53$ <b>G1b:</b> $-0.50 \pm 0.30$ <b>G1c:</b> $0.15 \pm 0.51$  <b>VABS Maladaptive Behavior subscales score, mean <math>\pm</math> SD:</b> <b>G1a:</b> $27.0 \pm 9.4$ <b>G1b:</b> $19.8 \pm 8.6$ <b>G1c:</b> $28.3 \pm 10.8$	<b>Ritvo-Freeman behavioral symptom score, 12 weeks, mean <math>\pm</math> SD:</b> Overall: <b>G1a:</b> $0.17 \pm 0.29$ <b>G1b:</b> $0.29 \pm 0.36$ <b>G1c:</b> $0.33 \pm 0.33$ <b>G1/BL:</b> $P = 0.0001$  Subscale I: <b>G1a:</b> $0.40 \pm 0.33$ <b>G1b:</b> $0.33 \pm 0.20$ <b>G1c:</b> $0.37 \pm 0.33$ <b>G1/BL:</b> $P = 0.001$  Subscale II: <b>G1a:</b> $-0.10 \pm 0.53$ <b>G1b:</b> $0.02 \pm 0.26$ <b>G1c:</b> $0.15 \pm 0.49$ <b>G1/BL:</b> $P = NS$  Subscale III: <b>G1a:</b> $0.38 \pm 0.25$ <b>G1b:</b> $0.37 \pm 0.32$ <b>G1c:</b> $0.61 \pm 0.49$ <b>G1/BL:</b> $P = 0.001$  Subscale IV: <b>G1a:</b> $0.32 \pm 0.36$ <b>G1b:</b> $0.57 \pm 0.54$ <b>G1c:</b> $0.46 \pm 0.47$ <b>G1/BL:</b> $P = 0.0001$  Subscale V: <b>G1a:</b> $-0.11 \pm 0.45$ <b>G1b:</b> $-0.42 \pm 0.23$ <b>G1c:</b> $-0.09 \pm 0.46$ <b>G1/BL:</b> $P = NS$  <b>VABS Maladaptive Behavior subscales score, 12 weeks, mean <math>\pm</math> SD:</b> <b>G1a:</b> $13.8 \pm 6.0$ <b>G1b:</b> $20.2 \pm 8.2$ <b>G1c:</b> $19.5 \pm 9.1$ <b>G1/BL:</b> $P = 0.000$

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
McDougle et al., 1998 (continued)				<p><b>Harms:</b>            Withdrew due to persistent agitation despite chloral hydrate: 3</p> <p>Adverse effects, completers, n:            Anorexia:  <b>G1: 1</b>            Headache:  <b>G1: 1</b>            Tinnitus:  <b>G1: 1</b>            Alopecia:  <b>G1: 1</b>            Weight gain:  <b>G1: 3</b>            Sedation:  <b>G1: 1</b>            Anxiety/agitation:  <b>G1: 2</b></p>

**Comments:**

\* Chloral hydrate 500 to 1000 mg could be administered to any patient up to four times in 24 hours for agitation, as needed. No other psychotropic drugs were administered to the patients during the study.

CGI was assigned by the research nurse with input from the patient (when possible) and the patient's treatment team.

No adverse cardiovascular, extrapyramidal, or proconvulsant effects were identified.

Statistical analyses: ANOVA of time effects; ANOVA by ASD subtype also available in Table 1 for all scales and subscales

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Brodkin et al., 1997</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> National Alliance for Research on Schizophrenia and Depression, Connecticut Department of Mental Health and Addiction Services, NIH, CoCensys Pharmaceuticals</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Case series (open label)</p>	<p><b>Intervention:</b> Open label treatment with Clomipramine. Initial dose 50 mg daily, increased by 50 mg every 3 or 4 days to a maximum dosage of 250 mg daily, as tolerated, if maximal clinical response was not obtained. The maximum dosage of clomipramine was attained within 3 weeks, and patients received this dose for a minimum of 9 weeks.</p> <p>Average daily dose (mg): 139.4 ± 50.4</p> <p><b>Intervention target:</b> Total repetitive thoughts and behavior, aggression, aspects of social relatedness, such as eye contact and verbal responsiveness, change in these specific symptom clusters over time, autistic behavior, full-scale IQ, CGI, and adverse effects</p> <p><b>Primary outcome:</b> CGI</p> <p><b>Groups:</b> <b>G1:</b> clomipramine <b>Ga:</b> responders (CGI scores of 1 = "very much improved" or 2 = "much improved" at the end of week 12) <b>Gb:</b> nonresponders</p> <p><b>Treatment duration:</b> 12 weeks</p> <p><b>Frequency of contact during study:</b> Every 4 weeks</p> <p><b>Last followup post-treatment:</b> End of 12 weeks</p> <p><b>Measure of treatment fidelity/adherence reported:</b> Yes</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Principal diagnosis of PDD</li> <li>Did not meet criteria for any other DSM-IV Axis I or Axis II disorder other than mental retardation</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>DSM-IV criteria for a psychotic disorder</li> <li>Abused illicit substances within the previous 6 months</li> <li>Serum pregnancy test positive (females)</li> <li>Significant acute medical condition</li> </ul> <p><b>Age, yrs, mean ± SD:</b> <b>G1:</b> 30.2 ± 7.0 (n=35) <b>G1a:</b> 30.7 ± 7.0 <b>G1b:</b> 29.6 ± 6.4</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, n :</b> Male: <b>G1:</b> 24 Female: <b>G1:</b> 11</p> <p><b>DSM-based diagnostic approach reported:</b> Yes (DSM-IV, ADI, ADOS)</p>	<p><b>IQ (full scale), mean ± SD:</b> <b>G1:</b> 64.6 ± 27.2 <b>G1a:</b> 62.7 ± 28.4 <b>G1b:</b> 67.0 ± 26.5 <b>G1a/G1b:</b> <i>P</i> = NS**</p> <p><b>ABC score, mean ± SD:</b> <b>G1:</b> 101.4 ± 17.5 <b>G1a:</b> 107.3 ± 17.2 <b>G1b:</b> 94.2 ± 15.4 <b>G1a/G1b:</b> <i>P</i> = NS**</p> <p><b>Y-BOCS score, mean ± SD:</b> Total: <b>G1a:</b> 18.7 ± 6.8 <b>G1b:</b> 17.9 ± 6.2</p> <p>Obsession subscale, verbal patients (n=18): <b>G1a:</b> 10 ± 6.8 <b>G1b:</b> 6.7 ± 6.2</p> <p>Compulsion subscale: <b>G1a:</b> 13.7 ± 3.3 <b>G1b:</b> 13.9 ± 2.5</p> <p><b>Brown Aggression scale total score, mean ± SD:</b> <b>G1a:</b> 10.6 ± 7.4 <b>G1b:</b> 6.5 ± 4.1</p> <p><b>Ritvo-Freeman Real-life rating overall score, mean ± SD:</b> <b>G1a:</b> 0.72 ± 0.54 <b>G1b:</b> 0.45 ± 0.43</p>	<p><b>CGI score, mean ± SD:</b> <b>G1a:</b> 1.89 ± 0.32 <b>G1b:</b> 3.8 ± 0.86 <b>G1/BL:</b> <i>P</i> &lt; 0.001 <b>G1a/G1b:</b> <i>P</i> &lt; 0.001</p> <p><b>Y-BOCS score, mean ± SD:</b> Total: <b>G1a:</b> 9.1 ± 3 <b>G1b:</b> 17.3 ± 7.8 <b>G1/BL:</b> <i>P</i> &lt; 0.001 <b>G1a/G1b:</b> <i>P</i> &lt; 0.001</p> <p>Obsession subscale, verbal patients (n=18): <b>G1a:</b> 4.4 ± 2.8 <b>G1b:</b> 8 ± 6.6 <b>G1/BL:</b> <i>P</i> = NS <b>G1a/G1b:</b> <i>P</i> &lt; 0.001</p> <p>Compulsion subscale: <b>G1a:</b> 6.9 ± 2.1 <b>G1b:</b> 12.5 ± 3.3 <b>G1/BL:</b> <i>P</i> &lt; 0.001 <b>G1a/G1b:</b> <i>P</i> &lt; 0.001</p> <p><b>Brown Aggression scale total score, mean ± SD:</b> <b>G1a:</b> 3.7 ± 3.6 <b>G1b:</b> 6.4 ± 4.6 <b>G1/BL:</b> <i>P</i> &lt; 0.001 <b>G1a/G1b:</b> <i>P</i> &lt; 0.001</p> <p><b>Ritvo-Freeman Real-life rating overall score, mean ± SD:</b> <b>G1a:</b> 0.18 ± 0.24 <b>G1b:</b> 0.44 ± 0.40 <b>G1/BL:</b> <i>P</i> &lt; 0.001 <b>G1a/G1b:</b> <i>P</i> &lt; 0.001</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Brodkin et al., 1997 (continued)	<p><b>Co-interventions held stable during treatment:</b> Yes</p> <p><b>Concomitant therapies, n:*</b> Carbamazepine (800mg): <b>G1:</b> 2 Phenobarbitol: <b>G1:</b> 1</p> <p><b>N at enrollment:</b> <b>G1:</b> 35</p> <p><b>N at followup:</b> <b>G1:</b> 33 <b>G1a:</b> 18 <b>G1b:</b> 15</p>			<p><b>Harms, n:</b> Clinically significant side effects: <b>G1:</b> 13/33</p> <p>Dropped out due to AE (agitation and cramping, respectively): <b>G1:</b> 2</p> <p>Weight gain: <b>G1a:</b> 3 <b>G1b:</b> 0</p> <p>Constipation: <b>G1a:</b> 2 <b>G1b:</b> 1</p> <p>Seizure:*** <b>G1a:</b> 1 <b>G1b:</b> 2</p> <p>Sedation: <b>G1a:</b> 1 <b>G1b:</b> 1</p> <p>Agitation: <b>G1a:</b> 0 <b>G1b:</b> 1</p> <p>Anorgasmia: <b>G1a:</b> 1 <b>G1b:</b> 0</p>

**Comments:**

\* Chloral hydrate (500-1000 mg) could be administered up to 4 times a day for agitation, as needed.

\*\* No significant relationship between treatment response (**G1a** vs. **G1b**) as defined by either ABC score (<78 vs. ≥78) or IQ (≤70 vs. >70)

\*\*\* Two patients had a prior history of seizures.

Results by disease diagnosis type not included here, as there were no significant differences among diagnostic subtypes in the change any outcomes over the course of treatment.

No significant difference in clomipramine dosage between **G1a** (131 ± 53 mg daily) and **G1b** (150 ± 47 mg daily).

Significant improvement over time was identified for each subscale of the Ritvo-Freeman Real-Life Rating Scale (n=33), including Sensory Motor Behaviors (*P* < 0.001), Social Relationship to People (*P* < 0.001), Affectual Reactions (*P* < 0.01), Sensory Responses (*P* < 0.001), and Language (*P* < 0.02).

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Bebko et al., 1996</p> <p><b>Country:</b> Canada</p> <p><b>Enrollment period:</b> 1993</p> <p><b>Funding:</b> Sharp Canada</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Prospective case series</p>	<p><b>Intervention:</b> Facilitated communication (FC) using multiple methods for 6 weeks with up to 7 months of follow up data</p> <p><b>Intervention target:</b> Communication</p> <p><b>Primary outcome:</b> Percentage of correct responses on three designs: setwork (visual stimulus with picture cards and words), headphones (audio stimulus with separate audio channels for student and facilitator), and receptive vocabulary (tasks from PPVT-R). The experimental conditions for the setwork design were combinations of intervention with FC vs. no FC and facilitators that were informed vs. not informed. The experimental conditions for the headphones design were the facilitator receiving the same word as the student, a different word, or a neutral word.</p> <p><b>Groups:</b> <b>G1:</b> All participants all receiving facilitated communication <b>G2:</b> All participants none receiving facilitated communication <b>Ga:</b> facilitator informed <b>Gb:</b> facilitator not informed</p> <p><b>Treatment duration:</b> 6 weeks; follow up 5 to 7 months (with additional FC use)</p> <p><b>Frequency of contact during study:</b> NR</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>From one of four classrooms of a regional program specializing in autism</li> <li>Consent obtained</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>See inclusion criteria</li> </ul> <p><b>Age, yrs, mean (range):</b> <b>G1&amp;G2:</b> 13 (6-21)</p> <p><b>Mental age, range:</b> <b>G1:</b> 1 year 3 months to 4 years 0 months</p> <p><b>Gender, n (%):</b> Male: <b>G1&amp;G2:</b> 15 (75) Female: <b>G1&amp;G2:</b> 5 (25)</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>Setwork design, % correct responses:</b> <b>G1a:</b> 56.86 <b>G1b:</b> 30.00 <b>G2a:</b> 36.71 <b>G2b:</b> 35.71 <b>G1a/G1b/G2a/G2b:</b> <i>P</i> = 0.0138</p> <p><b>Headphones design, % correct responses:*</b> <b>G1a:</b> NR <b>G1b:</b> NR <b>G2a:</b> NR <b>G2b:</b> NR <b>G1a/G1b/G2a/G2b:</b> <i>P</i> = NS</p> <p><b>Receptive vocabulary design, % correct responses:*</b> <b>G1a:</b> NR <b>G1b:</b> NR <b>G2a:</b> NR <b>G2b:</b> NR <b>G1a/G1b/G2a/G2b:</b> <i>P</i> = NS</p>	<p><b>Setwork design, follow up, % correct responses:</b> <b>G1a:</b> 75.00 <b>G1b:</b> 25.57 <b>G2a:</b> 53.57 <b>G2b:</b> 32.57 <b>G1a/BL:</b> <i>P</i> = 0.345 <b>Ga/Gb:</b> <i>P</i> &lt; 0.01 <b>Ga/BL:</b> <i>P</i> &lt; 0.03</p> <p><b>Headphones design, % correct responses:</b> <b>G1a:</b> NR <b>G1b:</b> NR <b>G2a:</b> NR <b>G2b:</b> NR <b>G1/BL:</b> <i>P</i> &gt; 0.30</p> <p><b>Harms:</b> NR</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
Bebko et al., 1996 (continued)	<p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1&amp;G2: 20</b></p> <p><b>N at 5-7 month followup:</b> <b>G1&amp;G2: 7</b></p>			

**Comments:**

\* Data reported graphically

Baseline results taken over initial 6 weeks

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> McDougle et al., 1996</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NIH, Connecticut Dept. of Mental Health and Addiction Services, Korczak Foundation for Autism and Related Disorders</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Double-blind, placebo-controlled randomized crossover trial</p>	<p><b>Intervention:</b> Acute tryptophan depletion. 24 hours of a low tryptophan diet followed by tryptophan-free amino acid drink or sham (amino acid drink with tryptophan added). Behavior measurements were taken at baseline, 180, 300, and 420 minutes after the amino acid drink. Patients resumed normal diet until crossover experiment occurred 7 days later.</p> <p><b>Intervention target:</b> Autistic behaviors</p> <p><b>Primary outcome:</b> Biochemical measures (plasma free and total tryptophan) and behavioral measures including change in global severity, symptoms of autism (RFRLRS), repetitive thoughts and behaviors, and 18 other behavioral parameters scored by VAS.</p> <p><b>Groups:</b> <b>G1:</b> acute tryptophan depletion <b>G2:</b> sham</p> <p><b>Treatment duration:</b> 2 days; 7 days between treatment and sham</p> <p><b>Frequency of contact during study:</b> 1 week</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> NR</p> <p><b>Co-interventions held stable during treatment:</b> NR</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Adults with autistic disorder</li> <li>• No psychotropic drugs for at least 5 weeks</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Identifiable cause of autism</li> <li>• Seizures</li> <li>• Positive pregnancy test</li> </ul> <p><b>Age, yrs, mean ± SD (range):</b> <b>G1+G2:</b> 30.5 ± 8.5 (20-53)</p> <p><b>Mental age (WAIS-R IQ) mean ± SD:</b> <b>G1+G2:</b> 90.8 ± 23.5</p> <p><b>Gender, n (%):</b> Male: <b>G1+G2:</b> 16 (80) Female: <b>G1+G2:</b> 4 (20)</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>Plasma tryptophan, micromol/L, mean ± SD:</b> Free: <b>G1:</b> 16.0 ± 2.1 <b>G2:</b> 18.2 ± 10.7 Total: <b>G1:</b> 105.1 ± 43.7 <b>G2:</b> 115 ± 29.9</p> <p><b>RFRLRS subscale 1-5 scores:</b> <b>G1:</b> NR <b>G2:</b> NR <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Repetitive thoughts severity scale score:</b> <b>G1:</b> NR <b>G2:</b> NR <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Repetitive behaviors severity scale score:</b> <b>G1:</b> NR <b>G2:</b> NR <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Behavioral VAS scores:</b> <b>G1:</b> NR <b>G2:</b> NR <b>G1/G2:</b> <i>P</i> = NS</p>	<p><b>Plasma tryptophan, micromol/L, mean ± SD:</b> Free: <b>G1:</b> 5.0 ± 4.4 <b>G2:</b> 33.6 ± 7.0 <b>G1/BL:</b> <i>P</i> &lt; 0.001 <b>G2/BL:</b> <i>P</i> &lt; 0.003</p> <p>Total: <b>G1:</b> 14.7 ± 4.5 <b>G2:</b> 199.0 ± 53.5 <b>G1/BL:</b> <i>P</i> &lt; 0.001 <b>G2/BL:</b> <i>P</i> &lt; 0.001</p> <p><b>Significant global worsening of behavior symptoms, n (%):</b> <b>G1:</b> 11/17 (65) <b>G2:</b> 0/17 (0) <b>G1/G2:</b> <i>P</i> = 0.001</p> <p><b>RFRLRS sensory motor behaviors subscale score:**</b> <b>G1:</b> NR <b>G2:</b> NR <b>G1/G2:</b> <i>P</i> &lt; 0.05</p> <p><b>RFRLRS subscale 2-5 scores:</b> <b>G1:</b> NR <b>G2:</b> NR <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Repetitive thoughts severity scale score:**</b> <b>G1:</b> NR <b>G2:</b> NR <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Repetitive behaviors severity scale score:**</b> <b>G1:</b> NR <b>G2:</b> NR <b>G1/G2:</b> <i>P</i> = NS</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
McDougle et al., 1996 (continued)	<p><b>Concomitant therapies:</b> NR*</p> <p><b>N at enrollment:</b> <b>G1=G2: 20</b></p> <p><b>N at followup:</b> <b>G1=G2: 17</b></p>			<p><b>Behavioral VAS scores:</b></p> <p>Calm: <b>G1: NR</b> <b>G2: NR</b> <b>G1/G2: <math>P &lt; 0.01</math></b></p> <p>Happy: <b>G1: NR</b> <b>G2: NR</b> <b>G1/G2: <math>P &lt; 0.03</math></b></p> <p>Other behaviors: <b>G1: NR</b> <b>G2: NR</b> <b>G1/G2: <math>P = NS</math></b></p> <p><b>Harms:</b> Nausea and vomiting: <b>G1: 1</b> <b>G2: 2</b></p>



**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> McDougle et al., 1996</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> September 1990 to December 1993</p> <p><b>Funding:</b> NIH, Connecticut Dept. of Mental Health and Addiction Services, Korczak Foundation for Autism and Related Disorders, Solvay Pharmaceuticals</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Double-blind placebo-controlled RCT</p>	<p><b>Intervention:</b> Fluvoxamine maleate, 12 weeks, started at 50 mg daily and titrated up by 50 mg every 3-4 days to a maximum of 300 mg/day, in the inpatient and outpatient settings.</p> <p><b>Intervention target:</b> Symptoms of autism</p> <p><b>Primary outcome:</b> Repetitive thoughts and behaviors (Y-BOCS), maladaptive behavior (VMBS), aggression (BAS), global improvement (CGI), symptoms of autism (RFRLRS)</p> <p><b>Groups:</b> G1: fluvoxamine G2: placebo</p> <p><b>Treatment duration:</b> 12 weeks</p> <p><b>Frequency of contact during study:</b> 4 weeks</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR*</p> <p><b>N at enrollment:</b> G1: 15 G2: 15</p> <p><b>N at followup:</b> G1: 15 G2: 15</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Adults with autistic disorder</li> <li>• No psychotropic drugs for at least 6 weeks</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Met criteria for schizophrenia or had psychotic symptoms</li> <li>• Substance abuse in the last 6 months</li> <li>• Notable medical illness including seizures</li> <li>• Pregnancy test positive</li> </ul> <p><b>Age, yrs, mean ± SD:</b> G1: 30.1 ± 7.1 G2: 30.1 ± 8.4</p> <p><b>Mental age (IQ), mean ± SD:</b> G1: 82.5 ± 26.8 G2: 77.3 ± 33.1</p> <p><b>Gender, n:</b> Male: G1: 13 G2: 14 Female: G1: 2 G2: 1</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>Y-BOCS score, mean ± SD:</b> G1: 21.4 ± 7.3 G2: 21.5 ± 6.8</p> <p><b>VMBS score, mean ± SD:</b> G1: 19.5 ± 6.8 G2: 22.3 ± 8.1</p> <p><b>BAS score, mean ± SD:</b> G1: 9.3 ± 10.8 G2: 12.3 ± 12.3</p> <p><b>CGI score:**</b> G1+G2: moderate severity</p> <p><b>RFRLRS overall score, mean ± SD:</b> G1: NR G2: NR</p>	<p><b>Y-BOCS score, 12 weeks, mean ± SD:</b> G1: 13.7 ± 9.1 G2: 21.9 ± 6.7 G1/BL: <i>P</i> &lt; 0.003 G2/BL: <i>P</i> = NS G1/G2: <i>P</i> &lt; 0.001</p> <p><b>VMBS score, 12 weeks, mean ± SD:</b> G1: NR G2: NR G1/G2: <i>P</i> &lt; 0.001</p> <p><b>BAS score, 12 weeks, mean ± SD:**</b> G1: NR G2: NR G1/G2: <i>P</i> &lt; 0.001</p> <p><b>CGI score, 12 weeks, mean ± SD:**</b> G1: NR G2: NR G1/G2: <i>P</i> &lt; 0.001</p> <p><b>Responders, CGI much improved or very much improved, n (%):</b> G1: 8/15 (53) G2: 0/15 (0) G1/G2: <i>P</i> = 0.001</p> <p><b>RFRLRS overall score, mean ± SD:**</b> G1: NR G2: NR G1/G2: <i>P</i> &lt; 0.03</p> <p><b>Harms:</b> Mild sedation: G1: 2 G2: 1</p> <p>Nausea: G1: 3 G2: 1</p>

Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
<p><b>Author:</b> Willemssen-Swinkels et al., 1995</p> <p><b>Country:</b> Netherlands</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> Janusz Korczak Foundation, DuPont Pharma</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Placebo controlled crossover study</p>	<p><b>Intervention:</b> 2 week single blind placebo period; 3rd week, 1 dose of naltrexone-hydrochloride (100 mg) or placebo followed by 6 days placebo;* 4 weeks naltrexone or placebo; 4 week wash out; then crossover to alternate treatment</p> <p>1 dose 100 mg (1.61 ± 0.24 mg/kg), then: 1st cohort: 50 mg daily (0.80 ± 0.13 mg/kg) 2nd cohort: 150 mg daily (2.45 ± 0.33 mg/kg)</p> <p><b>Intervention target:</b> Self-injurious behavior</p> <p><b>Primary outcome:</b> Self-injurious behavior</p> <p><b>Groups:</b> <b>G1:</b> 1st cohort, 50 mg naltrexone hydrochloride <b>G2:</b> 2nd cohort, 150 mg naltrexone hydrochloride <b>G3:</b> 1st cohort, placebo <b>G4:</b> 2<sup>nd</sup> cohort, placebo <b>Ga:</b> autism</p> <p><b>Treatment duration:</b> 4 weeks</p> <p><b>Frequency of contact during study:</b> Daily</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> Yes</p> <p><b>Concomitant therapies, n:</b> Antiepileptics: 5; Neuroleptics: 11</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Two clinicians agreed that the subject had fulfilled the set of DSM-III-R criteria for autistic disorder as a child and still fulfilled when current behavior was considered</li> <li>Social impairment had to be more serious than could be expected on the basis of the level of mental retardation only</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>See inclusion criteria</li> </ul> <p><b>Age, yrs, mean ± SD:</b> <b>Total:</b> 29 ± 6.0</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, n (%):</b> Male: <b>Total:</b> 27 Female: <b>Total:</b> 6</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p> <p>Diagnosis, n: ASD: 24 SIB: 26 Down syndrome: 1 Hunter's syndrome: 1 Congenital anomalies of unknown origin: 6 Congenital hydrocephalus: 1</p>	<p><b>ABC stereotypy factor, mean ± SD:</b> <b>G1a+G2a:</b> 9.7 ± 4.7 <b>G3a+G4a:</b> 8.3 ± 5.2</p>	<p><b>ABC stereotypy factor, mean ± SD:</b> 2 weeks: <b>G1a+G2a:</b> 10.2 ± 4.6 <b>G3a+G4a:</b> 8.8 ± 5.0 4 weeks: <b>G1a+G2a:</b> 10.0 ± 4.7 <b>G3a+G4a:</b> 9.0 ± 4.8 <b>G1+G2/G3+G4:</b> <i>P</i> = 0.018 <b>G1+G3/G2+G4:</b> <i>P</i> = NS <b>CGIS rating score, mean ± SD:</b> 4 weeks: <b>G1:</b> NR** <b>G2:</b> NR** <b>G3:</b> NR** <b>G4:</b> NR** <b>G1+G2/G3+G4:</b> <i>P</i> = 0.03 <b>G1+G3/G2+G4:</b> <i>P</i> = NS <b>Harms, n:</b> Withdrew due to adverse effect: <b>G1:</b> 1 <b>G2:</b> 0 Sedation: <b>G1:</b> 0 <b>G2:</b> 3 Increase in SIB and acting out behavior: <b>G1:</b> 1 <b>G2:</b> 0 Nausea and tiredness: <b>G1:</b> 1 <b>G2:</b> 0</p>

Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)

Study Description	Intervention	Inclusion/Exclusion Criteria/Population	Baseline Measures	Outcomes
Willemsen-Swinkels et al., 1995 (continued)	<p><b>N at enrollment:</b>  <b>G1=G3:</b> 19  <b>G2=G4:</b> 14  <b>G1a:</b> 13  <b>G2a:</b> 11</p> <p><b>N at followup:</b>  <b>G1=G3:</b> 18  <b>G2=G4:</b> 14  <b>G1a:</b> 12  <b>G2a:</b> 11</p>			

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria / Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Eberlin et al., 1993</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NR</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Prospective case series</p>	<p><b>Intervention:</b> Facilitated communication</p> <p><b>Intervention target:</b> Communication</p> <p><b>Primary outcome:</b> Number of correct answers with screened facilitation (the facilitator is blind to what the subject sees). Questions were vocabulary (Stanford-Binet: Fourth Edition) and knowledge of personal information (Personal Interview Questionnaire).</p> <p><b>Groups:</b> G1: facilitated communication</p> <p><b>Treatment duration:</b> 20 hours total (40 half-hour sessions, 1-2 sessions per day, 3-5 days/week)</p> <p><b>Frequency of contact during study:</b> 3-5 days/week over course of study</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> G1: 21</p> <p><b>N at followup:</b> G1: 21</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Diagnosis of autism</li> <li>• Subjective impression by a speech therapist that FC may be successful</li> <li>• No history of property destruction</li> <li>• Available to participate</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• See inclusion criteria</li> </ul> <p><b>Age, yrs, mean (range):</b> G1: 15.5 (11.3-20.2)</p> <p><b>Mental age, years, range:</b> Social-communicative skills: G1: 0.3-3.2 Adaptive skills composite score: G1: 1.5-5.8 Receptive language: G1: 1.4-5.3 Expressive language: G1: 0.7-6.3 Verbal language development scale: G1: 1.6-5.1</p> <p>Mild to moderate mental retardation: G1: 2</p> <p>Moderate to severe mental retardation G1: 11</p> <p>Severe to profound mental retardation: G1: 8</p> <p><b>Gender, n (%):</b> Male: G1: 20 (95) Female: G1: 1 (5)</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>Stanford-Binet vocabulary, no facilitation, correct answers, median (range):</b> G1: 7 (0-14)</p> <p><b>Stanford-Binet vocabulary, initial screened facilitation, correct answers, median (range):</b> G1: 0 (0-14)</p> <p><b>Personal interview, no facilitation, correct answers, median (range):</b> G1: 1 (0-13)</p> <p><b>Personal interview, initial screened facilitation, correct answers, median (range):</b> G1: 0 (0-2)</p> <p><b>Combined score, no facilitation, correct answers, median:</b> G1: 8</p> <p><b>Combined score, no facilitation, correct answers:</b> 0: G1: 5 1: G1: 2 2 or more: G1: 14</p> <p><b>Combined Score, initial screened facilitation, correct answers, median:</b> G1: 0</p> <p><b>Combined score, no facilitation, correct answers:</b> 0: G1: 19 1: G1: 0 2 or more: G1: 2</p>	<p><b>Stanford-Binet vocabulary, screened facilitation, correct answers, median (range):</b> G1: 0 (0-14)</p> <p><b>Stanford-Binet vocabulary, unscreened facilitation, correct answers, median (range):</b> G1: NR</p> <p><b>Personal Interview, screened facilitation, correct answers, median (range):</b> G1: 0 (0-10)</p> <p><b>Personal Interview, unscreened facilitation, correct answers, median (range):</b> G1: NR</p> <p><b>Combined Score, screened facilitation, correct answers, median:</b> G1: 0</p> <p><b>Combined score, screened facilitation, correct answers:</b> 0: G1: 15 1: G1: 4 2 or more: G1: 2</p> <p><b>Answered more questions correctly with screened FC than with pre-FC communication skills:</b> G1: 1</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Eberlin et al., 1993 (continued)			<p><b>Answered more questions correctly with screened FC than with pre-FC communication skills:</b></p> <p><b>G1: 0</b></p>	<p><b>Combined Score, unscreened facilitation, correct answers, median:</b></p> <p><b>G1: 1</b></p> <p><b>Combined score, screened facilitation, correct answers:</b></p> <p>0: <b>G1: 10</b></p> <p>1: <b>G1: 9</b></p> <p>2 or more: <b>G1: 2</b></p> <p><b>Answered more questions correctly with unscreened FC than with pre-FC communication skills:</b></p> <p><b>G1: 2</b></p> <p><b>Harms:</b></p> <p>NR</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Cook et al., 1992</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> 1988 to 1990</p> <p><b>Funding:</b> Harris Center for Developmental Studies, NIH, Adolescent Mental Health Academic Award, Autism Society of America in Indiana and Illinois</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Retrospective case series</p>	<p><b>Intervention:</b> Fluoxetine administered to treat perseverative behavior; dose range: 20 mg every other day - 80 mg daily</p> <p><b>Intervention target:</b> Improvement of Clinical Global Impression ratings</p> <p><b>Primary outcome:</b> CGI</p> <p><b>Groups:</b> G1: fluoxetine</p> <p><b>Treatment duration:</b> Actual days taking drug: mean days <math>\pm</math> SD (range): 189 <math>\pm</math> 153 (11-426)</p> <p><b>Frequency of contact during study:</b> Monthly clinic visit</p> <p><b>Last followup post-treatment:</b> Immediately post-treatment</p> <p><b>Measure of treatment fidelity/adherence reported:</b> No</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies, n (%):</b> Neuroleptics: G1: 8 (35) Carbamazepine: G1: 1 (4) Lithium carbonate: G1: 2 (9) Clonidine and alprazolam: G1: 1 (4) Methylphenidate: G1: 1 (4)</p> <p><b>N at enrollment:</b> G1: 23</p> <p><b>N at followup:</b> G1: 23</p>	<p><b>Inclusion criteria:</b> ASD Clinician assessment and diagnosis of perseverative behavior ranging from self-injurious behavior to complex rituals</p> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>Age, yrs, mean <math>\pm</math> SD:</b> G1: 15.9 <math>\pm</math> 6.2</p> <p><b>Mental age:</b> NR</p> <p><b>Gender, n (%):</b> Male: G1: 18 (78) Female: G1: 5 (22)</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>CGI, overall clinical severity, mean <math>\pm</math> SD:</b> G1: 5.7 <math>\pm</math> 0.8</p> <p><b>CGI, severity of perseverative or compulsive behavior, mean <math>\pm</math> SD:</b> G1: 5.5 <math>\pm</math> 1.5</p>	<p><b>CGI, overall clinical severity, mean <math>\pm</math> SD:</b> G1: 4.9 <math>\pm</math> 1.1 G1/BL: <math>P &lt; 0.002</math></p> <p><b>CGI, overall clinical severity, improvement, n:</b> G1: 15/23</p> <p><b>CGI, severity of perseverative or compulsive behavior, mean <math>\pm</math> SD:</b> G1: 4.7 <math>\pm</math> 1.6 G1/BL: <math>P &lt; 0.005</math></p> <p><b>Harms, n (%):</b> Hyperactivity/restlessness/agitation: G1: 5 (22)</p> <p>Insomnia: G1: 4 (17)</p> <p>Elated affect: G1: 4 (17)</p> <p>Decreased appetite: G1: 4 (17)</p> <p>Increased rate of screaming: G1: 2 (9)</p> <p>Increased socially inappropriate behavior: G1: 1 (4)</p> <p>Crying spells: G1: 1 (4)</p> <p>Yawning: G1: 1 (4)</p> <p>Maculopapular rash: G1: 1 (4)</p> <p><b>CGI side effects, n (%):</b> None: G1: 10 (43)</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Cook et al., 1992 (continued)				Do not significantly interfere with functioning: <b>G1: 8 (35)</b>  Significantly interferes with functioning: <b>G1: 4 (17)</b>  Outweighs therapeutic effect: <b>G1: 1 (4)</b>

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**Comments:**

Data on 16 additional patients with mental retardation available in paper.

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Elliott et al., 1991</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> NR</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Nonrandomized trial with crossover design</p>	<p><b>Intervention:</b> Analog language teaching sessions: conducted individually in clinical setting, three 15-minute sessions/week</p> <p>Natural language teaching sessions: 3 participants in different training settings (garden, kitchen, shower room); three 45-minute sessions/week</p> <p><b>Intervention target:</b> Language</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> <b>G1:</b> analog language teaching phase <b>G2:</b> natural language teaching phase</p> <p><b>Treatment duration:</b> 1 month each phase</p> <p><b>Frequency of contact during study:</b> Weekly</p> <p><b>Last followup post-treatment:</b> 8 weeks post-intervention</p> <p><b>Measure of treatment fidelity/adherence reported:</b> Yes</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p> <p><b>N at enrollment:</b> <b>G1:</b> 23 <b>G2:</b> 23</p> <p><b>N at followup:</b> <b>G1:</b> 23 <b>G2:</b> 23</p>	<p><b>Inclusion criteria:</b> DSM-III-R criteria for autism; severe mental retardation Residential treatment program</p> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>Age, yrs, mean (range):</b> <b>G1=G2:</b> 26 (17-37)</p> <p><b>Mental age (Slosson Intelligence test and/or Bayley Scales of Infant Development), yrs, mean (range):</b> <b>G1=G2:</b> 3.2 (1.7-5.1)</p> <p><b>Gender, n (%):</b> Male: <b>G1=G2:</b> 19 (83) Female: <b>G1=G2:</b> 4 (17)</p> <p><b>DSM-based diagnostic approach reported:</b> Yes</p>	<p><b>Three dimensional objects identified, n:</b> <b>G1:</b> NR <b>G2:</b> NR</p> <p><b>Two dimensional representations identified, n:</b> <b>G1:</b> NR <b>G2:</b> NR</p>	<p><b>Nouns generalized, post training, mean:</b> <b>G1:</b> 15.7 <b>G2:</b> 12.8 <b>G1/G2:</b> <i>P</i> = NS</p> <p><b>Items retrained, 8 weeks, mean %:</b> <b>G1=G2:</b> 92.2</p> <p><b>Harms:</b> NR</p>

**Comments:**

The natural language teachings were longer than the analogue language teaching in recognition of a natural advantage of group versus individual instruction.

Paper also includes analysis of possible effect modification by sequence of training, intellectual level, and communicative modality.



**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
<p><b>Author:</b> Nelson et al., 1980</p> <p><b>Country:</b> US</p> <p><b>Enrollment period:</b> NR</p> <p><b>Funding:</b> Boston Univ.</p> <p><b>Author industry relationship disclosures:</b> NR</p> <p><b>Design:</b> Randomized crossover trial, unspecified randomization method</p>	<p><b>Intervention:</b> Four-step procedure to teach the shoe-lacing task in a clinical setting. Crossover between two treatment conditions (color-coded shoelace/eyelet prompt and no prompt).</p> <p>Followup experiment: assessment of preference for color-coded prompt versus position cues.</p> <p>Initial training phase (10 trials) followed by a color-reversal phase (10 trials) that required a binary choice between color or position cues.</p> <p><b>Intervention target:</b> Acquisition of an adaptive skill (a shoe lacing task).</p> <p><b>Primary outcome:</b> NR</p> <p><b>Groups:</b> <b>G1:</b> extra prompt first <b>G2:</b> no extra prompt first</p> <p><b>Treatment duration:</b> Until completion of the task (approximately 30 trials/session, one session/day)</p> <p><b>Frequency of contact during study:</b> NA</p> <p><b>Last followup post-treatment:</b> One followup session post-treatment but timing not specified</p> <p><b>Measure of treatment fidelity/adherence reported:</b> NR</p> <p><b>Co-interventions held stable during treatment:</b> NR</p> <p><b>Concomitant therapies:</b> NR</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Autism diagnosis</li> <li>Onset prior to 30 months of age</li> <li>Five behavioral disturbances “characteristic of autism” (disturbances of perception, developmental rate, relating, speech and language, and mobility)</li> <li>Inability to lace shoes</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>See inclusion criteria</li> </ul> <p><b>Age, yrs, mean ± SD:</b> <b>G1:</b> 11.5 ± 3.0 <b>G2:</b> 13.1 ± 4.1</p> <p><b>Mental age, mean ± SD:</b> <b>G1:</b> 3.0 ± 4.1 <b>G2:</b> 3.1 ± 0.9</p> <p><b>Gender, n:</b> Male: <b>Total:</b> 13 Female: <b>Total:</b> 7</p> <p><b>DSM-based diagnostic approach reported:</b> NR (study pre-dates DSM-III)</p>	<p><b>Number of trials to complete task, initial treatment condition, mean ± SD:</b> <b>G1:</b> 108.7 ± 87.1 <b>G2:</b> 137.2 ± 110.7 <b>G1/G2:</b> <i>P</i> = NS</p>	<p><b>Number of trials to complete task, cross-over treatment condition, mean ± SD:</b> <b>G1:</b> 81.6 ± 80.7 <b>G2:</b> 15.9 ± 9.9 <b>G1/G2:</b> <i>P</i> &lt; 0.05 ANOVA: intervention order effect (<i>P</i> &lt; 0.01).</p> <p><b>Harms:</b> NR</p>

**Interventions for Adolescents and Young Adults with Autism Evidence Table (continued)**

<b>Study Description</b>	<b>Intervention</b>	<b>Inclusion/Exclusion Criteria/Population</b>	<b>Baseline Measures</b>	<b>Outcomes</b>
Nelson et al., 1980 (continued)	<b>N at enrollment:</b> <b>G1: 10</b> <b>G2: 10</b>  <b>N at followup:</b> <b>G1: 10</b> <b>G2: 10</b>			

## Abbreviations

ABC	Aberrant Behavior Checklist
ADI	Autism Diagnostic Interview
ADOS	Autism Diagnostic Observation Schedule
AQ	Autism Spectrum Quotient
AS	Asperger syndrome
ASD	Autism Spectrum Disorders
BAS	Brown Aggression Scale
BL	Baseline
BPVS	British Picture Vocabulary Scale
CAM	Cambridge Mindreading
CARS	Childhood Autism Rating Scale
CGI	Clinical Global Improvement
COPM	Canadian Occupational Performance Measure
DISCUS	Dyskinesia Identification System Condensed User Scale
DSM	Diagnostic and Statistical Manual of Mental Disorders
EOWVPT	Expressive One Word Picture Vocabulary Test
ERS	Environmental Rating Scale
ES	Effect size
FATCAT	Functional Assessment Tool for Cognitive Assistive Technology
FC	Facilitated communication
FQS	Friendship Quality Scale
G	Group
HFA	High functioning autism
IEP	Individualized Education Plan
IQ	Intelligence quotient
mg	milligrams
N, n	Number
NA	Not applicable
N-CBRF	Nisonger Child Behavior Rating Form
NIH	National Institutes of Health
NR	Not reported
NS	Not significant
NSEC	Neuroleptic Side Effects Checklist
PPVT-R	Peabody Picture Vocabulary Test – Revised
QPQ	quality of play questionnaire
RFRLRS	Ritvo-Freeman Real-Life Rating Scale
SD	Standard deviation
SE	Standard error
SHW	Sheltered workgroup
SIB	Self-injurious Behavior
SIB-Q	Self-injurious Behavior Questionnaire
SPW	Supported workgroup
SRS	Social Responsiveness Scale
SSRS	Social Skills Rating Scale
TASSK	Test of Adolescent Social Skills Knowledge
VABS	Vineland Adaptive Behavior Scales
VAS	Visual analog scale
VMBS	Vineland Maladaptive Behavior Subscales
Y-BOCS	Yale-Brown Obsessive Compulsive Scale
Yrs	Years

# Appendix E. Quality Assessment Form

## Study Design

1. Did the study employ a group design?

Group designs may include randomized controlled trials, prospective or retrospective cohorts, case-control studies.

**NOTE: Assess studies that include 2 groups but which we will report on as case series as group design studies.**

+ = **yes**

- = **no**

2. Were the groups randomly assigned?

+ = **yes**

- = **no**

3. Was there an appropriate comparison group?

The comparison group should accurately represent the characteristics of the intervention group in the absence of the intervention. Specifically, factors that are likely to be associated with the intervention selected and with outcomes observed should be evenly distributed between groups, if possible. These factors may include, for example, age, IQ, severity, etc.

+ = **yes**

- = **no or not reported (NR)**

**NA**

4. If an RCT, was randomization done correctly?

+ = **yes**

- = **no or not reported (NR)**

**NA for all non-RCTs**

### Considerations:

Was the approach to randomization described? Were random techniques like computer-generated, sequentially numbered opaque envelope used?

Were technically nonrandom techniques, like alternate days of the week used?

## Participant Ascertainment/Inclusion

1. Was a systematic diagnostic confirmation approach used within the study?

+ = **yes**

- = **no or not reported (NR)**

**Considerations:** Does the study indicate confirmation of an ASD diagnosis (e.g. reports diagnosis within study [not necessary to indicate specific tool used], review of medical records to confirm diagnosis, etc.)

2. Was the sample clearly characterized (e.g., information provided to characterize participants in terms of impairments associated with their ASD, including cognitive or language levels)?

+ = **yes**

- = **no or not reported (NR)**

### Considerations:

Study must report at minimum a measure of language, cognition, or intellectual disability.

How reproducible is the study in terms of the sample participants? Do the authors provide enough information that you could recreate the study population in a new study?

3. Were inclusion and exclusion criteria clearly stated?

+ = **yes**

- = **no or not reported (NR)**

**Considerations:**

Did the authors report this information?

4. Do the authors report attrition?

+ = **yes**

- = **no**

**NA**

**Considerations:**

Do they report loss to follow-up and/or drop-out?

**Intervention**

1. Was the intervention fully described?

+ = **yes**

- = **no or not reported (NR)**

**Considerations:**

Is there sufficient detail to allow replication of the intervention?

Does the study describe the dosage, formulation, timing, duration, intensity, etc. of the intervention?

2. For behavioral studies, was treatment fidelity monitored in a systematic way?

+ = **yes**

- = **no or not reported (NR)**

**NA**

3. Did the authors measure and report adherence to the intended treatment process?

+ = **yes**

- = **no or not reported (NR)**

**NA**

**Considerations:**

Does the study report number of hours of treatment or treatment sessions or time period receiving therapy (planned vs. actually received)? Do they provide pill count data for pharmacologic interventions?

4. Did the authors report differences in OR hold steady all concomitant interventions?

+ = **yes**

- = **no or not reported (NR)**

**Outcome Measurement**

1. Did outcome measures demonstrate adequate reliability and validity (including interobserver reliability for behavior observation coding)?

+ = **yes**

- = **no or not reported (NR)**

**Considerations:**

If the study used an established measure, has validity been established previously and do the authors provide a reference?

If the study used a new measure, was validity established?

For interobserver coding, was reliability and /or validity tested?

2. Were the primary & secondary outcomes clearly specified a priori?

+ = **yes**

- = **no or not reported (NR)**

**Considerations:**

Was there a “called shot?”

3. Were outcome data collected from sources appropriate to the target outcome (e.g. parent report, teacher report, direct behavior observation)?

+ = **yes**

- = **no or not reported (NR)**

**Considerations:**

Ex: Parent report for home-focused outcomes, teacher report for academic/school-focused, etc.

4. Were outcomes coded by individuals blinded to the intervention status of the participants?

+ = **yes**

- = **no or not reported (NR)**

**Analysis**

1. Was an appropriate statistical analysis used?

+ = **yes**

- = **no**

1a. For RCT’s, was there an intent-to treat analysis?

+ = **yes**

- = **no**

**NA**

**Considerations:**

Does the study report ITT analyses or last observation carried forward or note that all subjects were included in the final analyses?

1b. Did the study correct for multiple testing?

+ = **yes**

- = **no**

**NA**

1c. For observational studies, were potential confounders and effect measure modifiers captured?

+ = **yes**

- = **no**

**NA**

1d. For observational studies, were potential confounders and effect measure modifiers handled appropriately?

+ = **appropriate analysis**

- = **inappropriate analysis**

**NA**

**Considerations:**

Confounders are variables that are associated both with the intervention and the outcome and that change the relationship of the intervention to the outcome. These are variables that we would control for in analysis.

Effect measure modifiers are variables that we think of as stratifying, in that the relationship between the intervention and outcome is fundamentally different in different strata of the effect modifier. Observational research should include an assessment of potential confounders and modifiers, and if they are observed, analysis should control for or stratify on them.

Was the candidate variable selection discussed/noted? Was the model-building approach described?

Were any variables unrelated to the studied variables that could have altered the outcome handled appropriately?

Were any variables not under study that affected the causal factors handled appropriately?

## Appendix F. Excluded Studies

### Reasons for exclusion

**X-1** Ineligible population

**X-2** Not original research

**X-3** Ineligible study size

**X-4** Does not address key questions/Not an intervention study

**X-5** Not published in English

**X-6** Does not contain extractable data

**X-7** Unable to obtain full text

1. What is a reasonable cost of appropriate education? J Autism Dev Disord. 1980 Dec;10(4):459-72. PMID: 6821494. X-1, X-2, X-3, X-4
2. Sex education and sexual awareness building for autistic children and youth: some viewpoints and considerations. J Autism Dev Disord. 1985 Jun;15(2):213-27. PMID: 3997748. X-, X-2, X-3, X-4
3. Treatment of destructive behaviors in persons with developmental disabilities. J Autism Dev Disord. 1990 Sep;20(3):403-29. X-2, X-3
4. Community care: suffering acts of omission. Nurs Stand. 1992 Jun 17-23;6(39):50-1. PMID: 1642990. X-4
5. Position of the American Dietetic Association: nutrition in comprehensive program planning for persons with developmental disabilities. J Am Diet Assoc. 1992 May;92(5):613-5. PMID: 1374088. X-1, X-2, X-3, X-4
6. Three perspectives of facilitated communication: unexpected literacy, clever Hans, or enigma? Top Lang Disord. 1992 Aug;12(4):60-8. X-1, X-2, X-3, X-4
7. Auditory integration training. ASHA. 1994 Nov;36(11):55-8. PMID: 7529024. X-1, X-2, X-3, X-4
8. Auditory integration training and facilitated communication for autism. American Academy of Pediatrics. Committee on Children with Disabilities. Pediatrics. 1998 Aug;102(2 Pt 1):431-3. PMID: 9685446. X-2, X-4
9. MMR vaccine coverage shows signs of recovery. Commun Dis Rep CDR Wkly. 1999 Sep 24;9(39):345. PMID: 10510563. X-2, X-4
10. Significant achievement award. A comprehensive program for treating profoundly autistic children--Center for Autistic Children, Philadelphia. Psychiatr Serv. 2000 Nov;51(11):1439-40. PMID: 11058194. X-2
11. American Academy of Pediatrics: counseling families who choose complementary and alternative medicine for their child with chronic illness or disability. Committee on Children With Disabilities. Pediatrics. 2001 Mar;107(3):598-601. PMID: 11230608. X-2, X-4
12. Autism and Lovaas treatment: a systematic review of effectiveness evidence. Int J Technol Assess Health Care. 2001 Spring;17(2):252. PMID: 11446138. X-2, X-4
13. JAMA patient page. Autistic disorder. JAMA. 2001 Apr 4;285(13):1798. PMID: 11302153. X-2
14. Technical report: the pediatrician's role in the diagnosis and management of autistic spectrum disorder in children. Pediatrics. 2001 May;107(5):E85. PMID: 11331735. X-2, X-4
15. Science finds no link between MMR vaccine and autism. Mich Med. 2002 Sep-Oct;101(5):37. PMID: 12645252. X-2, X-4
16. Autism: neural basis and treatment possibilities. Symposium proceedings. London, United Kingdom, 18-20 June 2002. Novartis Found Symp. 2003;251:1-310. PMID: 14986681. X-2, X-4
17. MMR vaccine--how effective and how safe? Drug Ther Bull. 2003 Apr;41(4):25-9. PMID: 12724845. X-2, X-4
18. Ziprasidone may help treat behavior problems associated with autism. Brown University Child Adolesc Psychopharmacology Update. 2003;5(1):1. X-1, X-3, X-4
19. This is slow advocacy—not like the advocacy where our partners are able to tell us what they want. Ment Health Today. 2004 Dec-2005 Jan;22. PMID: 15657999. X-1, X-3, X-4
20. Global Advisory Committee on Vaccine Safety, 2-3 December 2004. Wkly Epidemiol Rec. 2005 Jan 7;80(1):3-7. PMID: 15673064. X-2, X-4



21. Randomized, controlled, crossover trial of methylphenidate in pervasive developmental disorders with hyperactivity. *Arch Gen Psychiatry*. 2005 Nov;62(11):1266-74. PMID: 16275814. X-1, X-3
22. Risperidone treatment of autistic disorder: longer-term benefits and blinded discontinuation after 6 months. *Am J Psychiatry*. 2005 Jul;162(7):1361-9. PMID: 15994720. X-1, X-3
23. Background and methodological approach. *Monographs of the Society for Research in Child Development*. 2006;71(2):29-47. X-1, X-2, X-3, X-4
24. Parent interviews. *Monogr Soc Res Child Dev*. 2006;71(2):48-74. X-1, X-2, X-3, X-4
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26. Risperidone: new indication. Behavioural disorders in children with autism or mental disabilities: no progress. *Prescrire Int*. 2006 Apr;15(82):43-5. PMID: 16602211. X-2, X-4
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30. Bibliography. Current world literature. *Developmental disorders*. *Curr Opin Neurol*. 2008 Apr;21(2):202-13. PMID: 18317281. X-2, X-4
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32. Inter-agency working. Unlock the full spectrum of care. *Health Serv J*. 2009 Feb 5;119(6142):24-5. PMID: 19326517. X-2
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## Appendix G. Quality of the Literature

**Table G-1. Quality of the literature**

<b>Author Year</b>	<b>Group Design</b>	<b>Random Assignment</b>	<b>Appropriate Comparison Group</b>	<b>Correct Randomization</b>	<b>Systematic Diagnostic Approach</b>	<b>Clear Sample Characterization</b>	<b>Clear Inclusion/Exclusion Criteria</b>	<b>Attrition Reported</b>	<b>Intervention Fully Described</b>	<b>Treatment Fidelity Monitored</b>	<b>Adherence Measured/ Reported</b>	<b>Concomitant Interventions Held Steady/ Reported</b>	<b>Outcome Measures Reliable and Valid</b>	<b>Outcome Data Collected From Appropriate Sources</b>	<b>Outcomes Coded Blindly</b>	<b>Appropriate Statistical Analysis</b>	<b>Rating</b>
Laugeson 2011 <sup>1</sup>	+	-	+	-	-	+	+	-	+	+	-	-	+	+	-	+	P
Verhoven 2011 <sup>2</sup>	-	NA	NA	NA	+	+	+	NA	-	-	NA	-	+	+	-	+	P
Garcia-Villamisar 2010 <sup>3</sup>	+	+	+	-	+	+	+	-	+	-	NA	-	+	+	+	+	F
Gentry 2010 <sup>4</sup>	-	NA	NA	NA	-	-	+	+	+	+	+	-	+	+	-	+	P
Greher 2010 <sup>5</sup>	-	NA	NA	NA	-	-	+	NA	+	-	-	-	-	+	-	-	P
Valenti 2010 <sup>6</sup>	-	NA	NA	NA	+	+	+	NA	+	-	NA	-	+	+	-	+	P
Laugeson 2009 <sup>7</sup>	+	+	+	-	-	+	+	+	+	+	NA	+	+	+	-	+	P
Lawer 2009 <sup>8</sup>	-	NA	NA	NA	-	-	+	NA	-	-	NA	-	+	+	-	+	P
Garcia-Villamisar 2007 <sup>9</sup>	+	-	+	NA	+	+	+	-	-	-	NA	-	+	+	-	+	P
Jewell 2007 <sup>10</sup>	-	NA	NA	NA	-	-	+	-	+	NA	NA	-	+	+	-	+	P
Tse 2007 <sup>11</sup>	-	NA	NA	NA	-	-	+	+	+	-	NA	-	+	+	-	+	P
Golan 2006-1 <sup>12</sup>	+	-	+	NA	-	+	+	+	+	-	+	+	+	+	+	+	P
Golan 2006-2 <sup>12</sup>	+	-	+	NA	-	+	-	+	+	-	+	-	+	+	+	+	P
Hellings 2006 <sup>13</sup>	+	+	-	+	+	+	+	+	+	NA	-	+	+	+	+	+	P
Kaplan 2005 <sup>14</sup>	-	NA	NA	NA	-	-	+	-	-	-	NA	-	-	+	-	+	P
Howlin 2005 <sup>15</sup>	-	NA	NA	NA	+	+	+	-	+	+	NA	-	+	+	-	+	P

Author Year	Group Design	Random Assignment	Appropriate Comparison Group	Correct Randomization	Systematic Diagnostic Approach	Clear Sample Characterization	Clear Inclusion/Exclusion Criteria	Attrition Reported	Intervention Fully Described	Treatment Fidelity Monitored	Adherence Measured/ Reported	Concomitant Interventions Held Steady/ Reported	Outcome Measures Reliable and Valid	Outcome Data Collected From Appropriate Sources	Outcomes Coded Blindly	Appropriate Statistical Analysis	Rating
O'Connor 2004 <sup>16</sup>	+	+	+	-	+	+	+	NA	+	NA	NA	-	+	+	-	+	P
Van Bourgondien 2003 <sup>17</sup>	+	-	+	NA	-	+	-	-	-	-	NA	-	-	+	-	-	P
Garcia-Villamizar 2002 <sup>18, 19</sup>	+	-	+	NA	+	+	-	-	-	-	NA	-	+	+	-	-	P
Remington 2001 <sup>20</sup>	+	+	+	+	+	-	+	+	+	NA	-	+	+	+	-	+	F
Silver 2001 <sup>21</sup>	+	+	+	-	-	+	+	+	+	+	+	-	+	-	+	-	P
Mawhood 1999 <sup>22</sup>	+	-	+	NA	-	+	+	+	+	+	+	-	+	+	-	-	P
McDougle 1998 <sup>23</sup>	-	NA	NA	NA	+	+	+	+	+	NA	-	+	+	+	-	+	P
McDougle 1998 <sup>24</sup>	+	+	+	+	+	+	+	+	+	NA	-	+	+	+	+	+	F
Brodkin 1997 <sup>25</sup>	-	NA	NA	NA	+	+	+	+	+	NA	-	+	+	+	-	+	P
Bebko 1996 <sup>26</sup>	-	NA	NA	NA	+	+	-	+	+	-	NA	-	+	+	-	+	P
McDougle 1996 <sup>27</sup>	+	+	+	-	+	+	+	+	+	NA	-	+	+	+	+	+	F
Willemsen-Swinkels 1995 <sup>28</sup>	+	+	+	-	+	-	+	+	+	NA	-	-	+	+	+	+	F
Eberlin 1993 <sup>29</sup>	-	NA	NA	NA	+	+	+	+	+	+	NA	-	+	+	-	-	P
Cook 1992 <sup>30</sup>	-	NA	NA	NA	+	+	-	+	+	NA	-	-	+	+	-	+	P
Elliott 1991 <sup>31</sup>	+	-	+	NA	+	+	-	-	+	+	NA	-	+	+	-	+	P
Nelson 1980 <sup>32</sup>	+	+	+	-	-	+	+	-	+	-	NA	-	+	+	-	+	P

F=fair; NA=not applicable; P=poor

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