

## *Comparative Effectiveness Research Review Disposition of Comments Report*

**Research Review Title:** Interventions for Adolescents and Young Adults with Autism Spectrum Disorders

Draft review available for public comment from November 29, 2011 to December 27, 2011.

**Research Review Citation:** Lounds Taylor J, Dove D, Veenstra-VanderWeele J, Sathe NA, McPheeters ML, Jerome RN, Warren Z. Interventions for Adolescents and Young Adults with Autism Spectrum Disorders. Comparative Effectiveness Review No. 65. (Prepared by the Vanderbilt Evidence-based Practice Center under Contract No. 290-2007-10065-I.) AHRQ Publication No. 12-EHC063-EF. Rockville, MD: Agency for Healthcare Research and Quality. August 2012. Available at: [www.effectivehealthcare.ahrq.gov/reports/final.cfm](http://www.effectivehealthcare.ahrq.gov/reports/final.cfm).

### **Comments to Research Review**

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The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

Commentator & Affiliation	Section	Comment	Response
<b>TEP #1</b>	Clarity and Usability	The same sentence appears on ES 1 and ES2 (beginning with "In addition to impairments...")	We have deleted the recurrence.
<b>TEP #1</b>	Clarity and Usability	The executive summary is very concise and nicely done. This may be particularly useful to clinicians, researchers, and policy makers who are not able to read the full report. Therefore, it would be helpful to include a brief paragraph at the end of each topic section that outlines the primary problems with the existing studies in those areas (i.e., why were the studies rated as poor?) I know this information is presented in the full report, but even a couple sentences generally stating what the main problems were and why almost all the studies were poor would help give people a sense of what needs to be tackled in future studies in those topic areas.	We have added this information to a summary table in the discussion section of the executive summary.
<b>TEP #2</b>	Clarity and usability	Need to highlight main point and to use language less tied to the jargon of this specific field (e.g. harms needs to be clarified for the readers of this report), such as to highlight absence of evidence as opposed to negative evidence.	We have been careful to emphasize that there is a lack of current research in a new and growing field, rather than evidence that interventions are not effective.
<b>TEP #4</b>	Clarity and usability	Well done	Thank you for your comments.
<b>Peer reviewer #5</b>	Clarity and Usability	As noted in the report, the state of evidence is inadequate. There are very few studies that provide guidance to policy makers, clinicians and families.	We hope that the review makes a contribution toward more research in this area.
<b>Peer reviewer #5</b>	Clarity and Usability	The clear policy recommendations are more emphasis on research in this population.	We agree and have noted this in the future research section of the report.
<b>Peer reviewer #5</b>	Clarity and Usability	The need for more research and the need for better outcome measures deserves greater emphasis.	We have emphasized this point in the future research section.
<b>Peer Reviewer #3</b>	Clarity and usability	The report is well-written. Tables and figures are appropriately formatted. Navigation through the document is straightforward.	Thank you for your comments.
<b>Peer Reviewer #3</b>	Clarity and usability	The material is presented at a level that is appropriate for readers with a scientific background in medicine, behavioral interventions, or education, though it is probably too technical for a lay audience.	Thank you for your comments. The AHRQ may develop a consumer guide from this review that is more specifically targeted at the lay audience.
<b>TEP #5</b>	Clarity and Usability	well it is pretty long. but yes the conclusions can be used to guide future research though not clinical practice and the quality of the evidence is so poor.	Thank you for your comments.
<b>TEP #5</b>	Clarity and Usability	most of these clinical decisions will have to depend on discussion between client and practitioner. the key issue is "finding the right intervention for the right type of ASD person at the right time for the right outcome" that is a significant endeavor.	We agree and hope the report will be helpful for noting research that exists and where further research is needed to inform such decisions.

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<b>TEP #5</b>	Discussion/ Conclusions	2) the importance of replication from two independent groups using two independent samples. are there examples of this you could highlight? to me, that is persuasive evidence of efficacy even in the absence of methodologic rigor.	Neither replication nor methodologic rigor was present in many of the interventions examined in this review. This is noted more clearly in our assessments of the strength of evidence.
<b>TEP #5</b>	Discussion/ Conclusions	1) you say the ABC is the "best" outcome measure in terms of reliability and validity. not sure i agree and there is no reference for this statement.	We have modified this statement to clarify that the ABC is widely used, easily repeatable, and highly sensitive instrument.
<b>TEP #1</b>	Discussion/ Conclusion	The methodological approach section will be particularly useful to researchers.	Thank you for your comments.
<b>TEP #1</b>	Discussion/ Conclusion	My concern with the statement about outcome measures is that although 28 of 31 studies may have employed "valid outcome measures," questions remain about the appropriateness of some measures to really measuring meaningful outcomes in adolescents and adults. It would be good to include a paragraph about the need to develop and validate appropriate and meaningful outcome measures for use in this population to make sure that we are actually measuring what needs to be measured with respect to the targets of each intervention.	We have emphasized this point in the future research section.
<b>TEP #3</b>	Discussion/ Conclusions	Implications are clearly stated and limitations of the research in this area are only too evident.	Thank you for your comments.
<b>Peer Reviewer #1</b>	Discussion/ Conclusions	No major literature is omitted	Thank you for your comments.
<b>TEP #3</b>	Discussion/ Conclusions	Future Research section is rather too general. Bullet points indicating essential methodological strategies that need to be incorporated in future research would be more helpful	We have added additional detail to the future research section but elected to keep it in paragraph form.
<b>TEP #4</b>	Discussion/ Conclusions	Reasonably clear - with recognition of the suggestions above re what future research should include.	Thank you for your comments.
<b>Public reviewer (anonymous)</b>	Discussion/ Conclusions	The comment "Although RCTs are often considered the gold standard for assessing intervention effectiveness ..... observational designs can be rich sources of information". If RCTs are gold standards, then they are the gold standard. Do not allow wiggle room for the social scientist to use poorly designed observational studies to provide "guidance" about therapy.	We agree that well done RCTs are subject to less risk of bias than observational studies. However, well conducted observational studies can also be sources of important information, despite the challenge in these studies of establishing causality. We outline areas for methodologic improvement in the future research section of the report.
<b>Public reviewer (anonymous)</b>	Discussion/ Conclusions	Using a waiting list as a control to a group in an intervention should be viewed with great skepticism. I think that it is impossible to separate the placebo effect from the intervention effect in this design. In fairness, you did report the study as only "fair".	We agree that the study is methodologically flawed and thus was rated only as fair using our quality assessment system.

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<b>Public reviewer (anonymous)</b>	Discussion/ Conclusions	Future research: "dearth of evidence" is true for all developmental disorders. Perhaps looking at areas of commonality would be more appropriate. For example, does are present secondary education system prepare anyone for a job? I realize that this might be a politically charged statement, but I would like to make the point that we need to look at places where research can actually give us usable data.	This is a very good point. This scope of this particular review is on autism, but certainly there are commonalities across developmental disorders that might provide information of use to policy makers in particular.
<b>Public reviewer (anonymous)</b>	Discussion/ Conclusions	Overall, I think that this research was well designed, well carried out, and well reported. Thank you for the effort and for the opportunity to add my 2 cents.	Thank you for your review of the report and comments.
<b>Peer reviewer #5</b>	Discussion/ Conclusions	The future research section calls for more study in all areas - including combined treatment (e.g., medication + psychosocial or educational) .	Thank you for your comments. We will also be conducting a future research needs project in this area to generate and prioritize research gaps and needs related to interventions for this population.
<b>Peer reviewer #5</b>	Discussion/ Conclusions	It must be said that this is not just a matter of more funding. The general research community may not be ready to carry out sophisticated studies. For example, there is only one randomized trial in children with ASDs that combined medication and behavioral treatment. The group that completed this combined treatment trial had previously accomplished two multisite, placebo-controlled, randomized trials before taking the combined treatment trials. This suggests that treatment networks are needed to build this sophistication.	We have emphasized this point in the future research section.
<b>Peer reviewer #5</b>	Discussion/ Conclusions	The report mentions that medication trials have relied on currently available drugs - which is accurate and worth pointing out.	Thank you for your comments.
<b>Peer reviewer #5</b>	Discussion/ Conclusions	A comment that pharmaceutical/academic partnerships are needed to evaluate compounds not yet on the marketplace might be useful.	We have added such a statement to the future research section of the report.
<b>Peer reviewer #5</b>	Discussion/ Conclusions	The clear message is that evidence is inadequate. In many ways, this was "already known," but this carefully done review leaves no doubt.	Thank you for your comments.
<b>Peer reviewer #5</b>	Discussion/ Conclusions	The clear implications are the need for more intervention research. This point is made. The manuscript makes in clear that research is needed in all spheres (educational, vocational, recreational, adaptive skills, and medications).	Thank you for your comments. We will also be conducting a future research needs project in this area to generate and prioritize research gaps and needs related to interventions for this population.

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<b>Peer Reviewer #3</b>	Discussion/conclusions	Discussion accurately summarizes the findings and offers valuable suggestions for future research. However, several suggestions could be discussed in more detail. The review notes that most studies with random assignment did not use correct random assignment procedures (p. 64). This is largely a reporting issue. For example, the articles by McDougle, Laugeson, and Garcia-Villamizar (cited above) gave little or no description of the randomization procedures. Thus, a recommendation for greater transparency in reporting would be advantageous.	We have emphasized this point in the future research section.
<b>Peer Reviewer #3</b>	Discussion/conclusions	[Additional detail for discussion section] Another barrier may be the lack of standards for appropriate procedures; a reference to a more specific standard than the one presented in Appendix E (e.g., the Cochrane Handbook, which presents methods for concealed allocation) would be beneficial.	We have emphasized this point in the future research section.
<b>Peer Reviewer #3 (Smith)</b>	Discussion/conclusions	[Additional detail for discussion section] The review notes the absence of fidelity measures in most studies (p. 64). Again, this is largely a reporting issue, as several articles refer to procedures for monitoring fidelity but do not present data.	We have emphasized this point in the future research section.
<b>Peer Reviewer #3</b>	Discussion/conclusions	[Additional detail for discussion section] A more fundamental impediment is that many of the studies are retrospective program evaluations rather than prospective trials. As a rule, manuals on which to base fidelity measures are not available for these programs. Thus, manual development is a priority.	We have added this point in the future research section.
<b>Peer Reviewer #3</b>	Discussion/conclusions	[Additional detail for discussion section] It might also be worthwhile to identify types of programs that may be appropriate candidates for manuals (e.g., model programs such as TEACCH, programs that combine intervention procedures tested in studies with single-subject experimental designs, programs that adapt efficacious treatments for other clinical populations).	We have added this point to the future research section.
<b>Peer Reviewer #3</b>	Discussion/conclusions	[Additional detail for discussion section] While 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.	We agree and have added this point to the future research section.

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<b>Peer Reviewer #3</b>	Discussion/conclusions	[Additional detail for discussion section] In the discussion of interventions for individuals with ASD across the life span, it would be fruitful to mention the dearth of information not only on developmental trajectories of ASD symptoms (as indicated on p. 64), but also on the effects of aging on health, cognitive skills, and other domains of functioning.	We have emphasized this point in the future research section in terms of the trajectory from childhood through adolescence and into adulthood. The report did not address the issues of aging.
<b>TEP #2</b>	Executive summary	ES-15, line 39 - comment about effectiveness inferred from from studies of young children implies that the children were < 8 and implies that those studies didn't include adolescents	We have noted that these studies involved mostly younger children.
<b>TEP #2</b>	Executive summary	ES-12, line 54 - the statement that there was little consistency across studies of SRIs is not warranted - two fair studies, one positive (why was this fluvoxamine study of fair quality ?) and one negative (and underpowered) and the case series positive (but poor quality) - sounds like not enough fair or higher evidence but not lacking consistency, in contrast to the literature with younger children	We have revised the text note that consistency was limited across studies of SRIs as a whole.
<b>TEP #2</b>	Executive summary	ES-14, line 39 - problem is that the statement implies children independent of adolescents which are part of this study population - revise to clarify,	We have noted that these studies included mostly younger children.
<b>TEP #2</b>	Executive summary	ES-14, line 42 - "Population studies may be helpful to empirically group ASD patients by age in a way that fosters more effective studies of treatments." - specific design should be presented - is this going to be a poor, fair or good quality study and who will pay for it ?	The identification of specific study designs is beyond the scope of the future research section of the CER; however, it is a component of a separate activity of the AHRQ Effective Healthcare program by which EPCs develop documents specifically focused on future research needs after the publication of a CER.
<b>TEP #2</b>	Executive Summary	ES-1, line 39 - instead of "often pediatricians or other behavioral providers" change to "often pediatricians or behavioral providers, child neurologists, child psychiatrists, or psychologists	We have changed the text as noted.
<b>TEP #3</b>	Executive Summary	Key questions are highly relevant & made explicit in both the Executive summary and the main text (p 34-35)	Thank you for your comments.
<b>Public reviewer (anonymous)</b>	Executive summary	As a pediatrician with 30 years of experience, I have grave concerns about what is now called "autism". Until we have a better way to clearly diagnose this, I think we must accept that this group under study is extremely heterogeneous and that finding common variables, meaningful outcomes, and realistic solutions will be elusive.	We agree that ASDs are heterogeneous and have highlighted that heterogeneity in the Introduction and Discussion sections of the report.
<b>TEP #1</b>	General	Overall, this is a very nicely done report. It is important in indicating significant gaps in the existing literature and the clear need for much more research.	Thank you for your comments.

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<b>TEP #2</b>	General	Target population and audience are well-defined. Key questions are appropriate and explicitly stated.	Thank you for your comments.
<b>TEP #2</b>	General	The abstract should emphasize the need for evidence and lack of funding for developing evidence - needs to emphasize further absence of evidence generally- for those reading these reports not used to the format, the implication is the studies have been done and were negative.	We note in the abstract that "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."
<b>TEP #2</b>	General	It would be useful to highlight more in a concluding sentence that only five studies of fair quality have been done concerning this large and important topic.	We have noted that there were only 5 fair quality studies in the Conclusion section.
<b>TEP #2</b>	General	need to comment on how spanning the adolescent and adult group may have biased the presentation - how would this report look if the adolescents were combined with the children and adults separated - are there studies that made neither report because of this awkward age grouping (e.g. with subjects before and after the age of full consent to participate)	We re-examined studies excluded because of the age of participants and determined that including them would not have changed our conclusions about effects in adolescents and young adults with ASD.
<b>TEP #3</b>	General	This is a very depressing report to read although the conclusions are not unexpected - viz: there are relatively few intervention studies with a focus on older children/adults and those that do exist are of generally low quality.	We agree that research on this population is greatly lacking.
<b>TEP #3</b>	General	The report is of high significance for all those involved either in research or provision of services for young people with ASD and highlights the need for major improvements in both the quantity and quality of research in this area.	Thank you for your comments.
<b>TEP #3</b>	General	Report is very well structured and organised and easy to follow.	Thank you for your comments.
<b>TEP #3</b>	General	Main points are highlighted both in conclusions to the report and in Executive Summary	Thank you for your comments.
<b>TEP #3</b>	General	Conclusions re poor quality of almost all work in this are highly significant	Thank you for your comments.
<b>Peer reviewer #7</b>	General	Yes, the report is meaningful, if only to demonstrate how little is known about ASD treatments. The populations and interventions are clear and the key questions well stated.	Thank you for your comments; we agree that little research on this population exists.
<b>Peer reviewer #7</b>	General	As a member of the AHRQ EHC Stakeholder workgroup, I was able to share with the EPC directors a bit about communicating uncertainty in Nov 2011, but those suggestions were made after this report had been written. Something to consider in future reports.	Thank you for your comments.

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Peer reviewer #6	General	The introduction states that the target audience for this report is clinicians, employers, policymakers, and others who must make informed decisions about the provision of health care services for adolescents and adults with Autism Spectrum Disorders (ASD). If this is really the case then the biggest problem with this report is that it will be of little use to these groups.	We have revised this section to focus on researchers as consumers of the review, given the current lack of data.
Peer reviewer #6	General	My suggestion is to start with a review of the current papers discussing alternative ways to determine Evidence Based Practice (Kazdin would be a good starting point) and then to focus much more on what we have learned about serving adolescents and adults with ASD, rather than how well studies fit rigorous criteria for EBP.	The methods used in this review are those of the Evidence-based Practice Centers of AHRQ's Effective Healthcare Program. The methods are published and accessible at <a href="http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayProduct&amp;productID=318">http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayProduct&amp;productID=318</a> .
Peer reviewer #6	General	More should be said about information that can be applied to this clinical population immediately.	It is not the role of the EPC to provide clinical guidance; as noted in the report, this is not a guideline, but a review of the science.
Peer reviewer #6	General	One example is that a lot more could be said about vocational and residential possibilities than simply that the studies were poorly done from the point of view of a RCT. Many of the vocational studies cited here point to certain jobs that people with ASD seem to do well and models for training them to work to do those jobs. We might not have conclusive evidence on which jobs tend to work out best for people with ASD or which training or support models lead to the longest job retention but at this point the field would benefit from any ideas about possible jobs and training models.	As noted in the report and in the EPC methods guidance, we do not require that included studies be RCTs and we assess quality of studies by study design. The report provides a report on data that exist, while noting that additional research is necessary.
Peer reviewer #6	General	We also have learned about different kinds of residential models like farms or apartments or boarding houses or individually owned homes and etc.	Studies of this type did not meet our criteria for inclusion in this review.
Peer reviewer #6	General	More discussion on what the studies have done, what models they have used, and what they can teach us would provide a lot more of value to the target audience than the current report does.	We feel that there is adequate detail about the studies in the results section of the report to fit within the requirements of the CER.
Peer reviewer #6	General	The problem is that the RCT model of evaluating evidence-based practices comes from the evaluation of pharmacological interventions and this model does not work well with psychological and educational services.	We agree and have not limited the review to any specific study designs except for excluding single case reports.

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<b>Peer reviewer #6</b>	General	<p>Dr. Alan Kazdin, one of the foremost clinical psychological researchers of our time and one, who has done as many randomized controlled studies as anyone in the field and was recently recognized by the American Psychological Association for distinguished scientific applications of Psychology, has written about this mismatch in 2 separate articles. First, in a 2008 article in the American Psychologist he says that the our RCT model is of limited in its use for psychological research because it is not the effectiveness of the treatment per se that we need to determine but rather how the treatment can be used in many different situations to help many different people, which is really what psychological and educational interventions are all about.</p> <p>Therefore the RCT model that is so effective for evaluating drug treatments will need to be supplemented by other kinds of empirical studies and clinical judgments to know if a treatment is effective for helping different people in different situations.</p>	<p>As noted above, we accepted all study designs and did not limit the report to RCTs. We do this in this particular review because we recognize the importance and value of data provided by a range of types of studies. Nonetheless, research should be designed in such a way to minimize bias.</p>
<b>Peer reviewer #6</b>	General	<p>As Dr. Kazdin wrote in his paper, a RCT says that there is evidence for specific interventions in the highly controlled contexts in which they were studied but not yet much evidence for EBP in the clinical contexts where judgments and decisions are made by individual clinicians informed by evidence, expert judgments, and patient considerations. In his more recent paper accepting his award (2011) Kazdin argues that the current research agenda based only on RCT's has raised the bar with more stringent and fixed methodological criteria for conducting and reporting research. Realistically those designs can never meet the demand of the many clinical research questions the field wants to ask so we need to look at a wider variety of designs including single-case models, smaller and less rigorous clinical trials, and qualitative studies to name a few, and do more to explore the many possible models for delivering effective treatment.</p>	<p>See the response above. Studies of any design should be conducted to minimize bias, including by inclusion of an appropriate comparator.</p>
<b>Peer reviewer #6</b>	General	<p>If we wait until the standard of research that is being proposed in this review is achieved, Kazdin argues that most adolescents and adults who are alive today will not be around to benefit from any of those results. Moreover, given the rising cost of implementing these designs and the economic realities of our society it is probable that most of what this review would consider being acceptable studies will never be done at all.</p>	<p>See response above.</p>

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<b>Peer reviewer #6</b>	General	This is not to see that RCT's do not play a role. As mentioned earlier Kazdin himself has probably done more RCT studies than anyone in the field of Clinical Psychology. Rather it is saying that this should only be one of many strategies that can help the field advance.	We agree and have not limited the review to any specific study designs. The only excluded study design was the single case report.
<b>Peer reviewer #6</b>	General	Therefore, a more realistic way of looking at what we have learned and how this might help today's adolescents and adults with ASD is essential and this paper falls far short of that. To read this paper one would think that science has nothing to contribute to our understanding of how to help adolescents and adults with autism. I think that is more a reflection of the rigid criteria and standard that this review has adopted and that a more flexible and creative way of looking at the field would contribute a lot more to the target audience and the field in general.	Non RCTs could have been assessed as good quality in our assessment, per EPC methods.
<b>Peer reviewer #6</b>	General	I do not mean to be overly harsh and to minimize the incredible amount of work that was put into this review and how thorough and detailed it is. I also recognize that what the authors did is what most of us were trained to do and they did it very well.	We appreciate your recognition of the effort necessary to conduct a review of this scope.
<b>Peer reviewer #6</b>	General	On the other hand there is a growing movement and literature on how RCT's are not the only away to evaluate large clinical programs like the ones that are the topic of this review and this literature has been totally ignored.	As noted above, this is a review within the AHRQ EPC program and, as such, we have used the methods published for the EPC program. These methods do not limit reviews to RCTs, nor do they assume that only RCTs can be of good quality.
<b>Peer Reviewer #2</b>	General	Very good and thorough review in an area with very limited research and publication.	Thank you for your comments.
<b>TEP #4</b>	General	The one area or key question that seems not addressed has to do with non-psychiatric or non-neurologic co-morbid conditions among adolescents and young adults with ASD - e.g., GI disorders, abnormal nutrition, immune function disorders, endocrine disorders. Undoubtedly, any systematic review here too will find little or no reviewable data re treatment, but would help to acknowledge that these are areas of concern and thus to lay the ground for future research. So, initial questions are whether adolescents and young adults have different rates or especially manifestations of these kinds of conditions - and then whether there have been any studies of interventions for these co-morbid conditions in this population.	We included a key question specifically addressing medical comorbidities (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.)), but no relevant studies met our inclusion criteria. We have noted this as an area for additional research in the future research section of the report.

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<b>Public reviewer (APTA)</b>	General	Recent advances in autism research focus on associated motor impairments that are not currently part of the diagnostic criteria for ASD. Evidence exists that motor behaviors are qualitatively and quantitatively different in individuals with ASD. Significant impairments in motor coordination, postural control, imitation, and praxis are present. <sup>1</sup>	Thank you for your comments. We have noted that motor impairments may be associated with ASD.
<b>Public reviewer (APTA)</b>	General	Understanding the limitations in the planning and coordination of movement and posture is fundamental to a comprehensive understanding of the qualitative social impairment in ASDs. <sup>1</sup> There is emerging empirical support for a developmentally important linkage between motor and social communication impairments in autism.	Thank you for your comments.
<b>Public reviewer (APTA)</b>	General	APTA recommends that physical therapy be included as an additional intervention. Physical therapists play an integral role in the treatment of this patient population. As discussed above, the motor impairments commonly observed in individuals with ASD may impact function and development at a very basic level, limiting participation in school, home, and community activities.	We included studies of any intervention. No studies of physical therapy-related interventions met all of our criteria.
<b>Public reviewer (APTA)</b>	General	APTA would also like to note that facilitated communication and music therapy are not typically provided by physical therapists. For the individual with ASD, the physical therapist acts as an integrative, collaborative, and supportive member of the life span care team, meeting the dynamic and complex needs of the individual and the family. In addition to expertise in assessing and analyzing movement and motor performance as part of a comprehensive functional assessment, physical therapists also serve as health care providers by promoting health and wellness; implementing a wide variety of supports throughout the lifespan; and developing collaborative professional partnerships with families and caregivers, medical specialty teams (developmental and rehabilitation), educational teams, and community members.	Thank you for your comments. The report groups interventions including facilitated communication under the broad category of “allied health” interventions. We have clarified that such interventions are not provided by physical therapists. (DONE-NS)
<b>Public reviewer (APTA)</b>	General	APTA would encourage the report to acknowledge that effective interventions are needed across the lifespan for this patient population.	The report notes the need for lifelong management in the “Importance of this Review” section, but we have also added a comment to the Discussion.
<b>Public reviewer (APTA)</b>	General	Physical therapists play a role in improving participation and engagement in physical fitness and recreational activities for individuals with ASD.	Thank you for your comments; the report notes that physical therapists engage in such activities.
<b>Public reviewer (APTA)</b>	General	Quality of life cannot be overlooked in individuals with ASD.	We agree and noted the need to study outcomes related to quality of life in the future research section of the report.

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<b>Public reviewer (APTA)</b>	General	APTA recognizes that there is a need for additional research for this patient population by physical therapists. The lack of evidence on how motor interventions affect the future motor and social communication functions of individuals with ASD is a significant research gap. <sup>1</sup>	We have added a point about better understanding the effects of motor impairments to the future research section.
<b>Public reviewer (APTA)</b>	General	However, research suggests that decreased levels of physical activity <sup>5</sup> , decreased participation in community-based sports and recreation programs <sup>6</sup> , and increased risk for activity-related health and wellness impairments <sup>7</sup> will impact independent living skills for individuals with ASD.	We have noted a need for more research into factors fostering independent living skills in the future research section of the report.
<b>Public reviewer (APTA)</b>	General	APTA would like the report to reflect the importance of motor performance impairments which are inherent in ASD but are not widely recognized. <sup>123</sup> Individuals with ASD may have basic fine and gross motor impairments or more complex limitation and planning impairments. These impairments have potential neurological and clinical importance for interventions and eventual outcomes and warrant focused assessment through physical therapy evaluation and intervention decision making. <sup>4</sup>	We have noted that individuals with ASD may have impaired motor impairments in the report's introduction.
<b>Peer reviewer #5</b>	General	The report is clinically meaningful (though the state of evidence is inadequate). The key questions are clear and relevant. The key questions were developed via internal discussion, focus groups of consumers and other "stakeholders." This was followed by an Expert Panel review.	Thank you for your comments.
<b>Peer Reviewer #3</b>	General	This report presents a systematic review of research on therapies for adolescents and young adults with autism spectrum disorders (ASD), age 13-30 years, including behavioral treatments, educational interventions, vocational training, life skills program, medications, and allied health services. Thirty-one studies met eligibility criteria for inclusion in the review. Twenty-six of these studies were rated as having poor quality; 5 were rated as fair (4 randomized clinical trials [RCTs] of medications and 1 RCT of a life skills program); and none were rated as good. Given the absence of good studies and scarcity of fair studies, the report concludes that the available research offers little guidance to guide therapy.	Thank you for your comments.
<b>Peer Reviewer #3</b>	General	Although this conclusion is disappointing, it accurately conveys the current state of the science and as such can usefully inform the ASD community, as well as practitioners, researchers, and policy makers.	Thank you for your comments.

Commentator & Affiliation	Section	Comment	Response
<b>Peer Reviewer #3</b>	General	The review is based on a thorough search of the literature and accurate summaries of individual studies. Key questions are well-chosen. Review criteria are appropriate and generally clearer than in a previous review by this group. The conclusions are consistent with the findings.	Thank you for your comments.
<b>Peer Reviewer #3</b>	General	However, there are some aspects of the report that are confusing, including contradictions between the abstract and the main text, inconsistencies in how interventions are categorized, incompletely explained eligibility criteria for studies, and quality ratings that are difficult to replicate from the coding definitions. In addition, it would be helpful to expand on some of the comments in "Future Research."	See responses to specific comments. We have also revised the abstract.
<b>TEP #5</b>	General	An excellent review from both a content and a methodological point of view. i have no major comments that would substantially change the review. a job well done. this paper will be an important source of information for parents, policy makers and researchers and clinicians for years to come.	Thank you for your comments.
<b>TEP #1</b>	Introduction	It may be worth mentioning the policy implications of research to understand the effectiveness of various interventions for adolescents and adults with ASD. There are currently several state programs that provide intensive intervention (almost always ABA) to young children with ASD--if certain types of interventions were found to be beneficial for adolescents and/or adults with ASD, then there would be more of a justification for state programs to designed to serve these individuals. Currently, with such a lack of high quality research in this area, it is difficult to make the argument that large scale intervention efforts (as opposed to just supportive care) should be put in place or continued once children with ASD reach school age or adolescence.	We have made this point in the section on future research.

Commentator & Affiliation	Section	Comment	Response
<b>TEP #1</b>	Introduction	As far as the types of interventions reviewed, the categories seem to make good sense. My only question is whether communication interventions should be considered in "allied health interventions" along with sensory integration, music therapy, etc. Especially for nonverbal individuals or those with limited language, augmentative communication interventions play a very central role in potentially increasing independence. Therefore, specific communication interventions may be better served as their own category--and "facilitated" communication should be mentioned separately from augmentative communication.	<p>We recognize that there are multiple ways to categorize intervention approaches. We considered different approaches, but none worked as well for organizing the studies meeting our review criteria in a logical and meaningful manner.</p> <p>We note that the approach selected for this report did not have an impact on our conclusions or the overall strength of evidence. Further, the only communication-focused studies meeting our criteria addressed facilitated communication, which is better situated in the allied health category.</p>
<b>TEP #1</b>	Introduction	Additionally, with the move to consider social and communication symptoms together, one option might be to include certain communication interventions in behavioral interventions and leave others (e.g., facilitated communication) in allied health interventions.	<p>We recognize that there are multiple ways to categorize intervention approaches. We considered different approaches, but none worked as well for organizing the studies meeting our review criteria in a logical and meaningful manner.</p> <p>We note that the approach selected for this report did not have an impact on our conclusions or the overall strength of evidence. Further, the only communication-focused studies meeting our criteria addressed facilitated communication, which is better situated in the allied health category.</p>
<b>TEP #2</b>	Introduction	Introduction is generally sound.	Thank you for your comments.
<b>TEP #3</b>	Introduction	Heterogeneity of the condition is highlighted appropriately.	Thank you for your comments.
<b>TEP #3</b>	Introduction	Background and rationale to the review are stated clearly. Introduction is brief but concise and comprehensive, giving background to ASD and the types of intervention reported for young people with these disorders.	Thank you for your comments.
<b>TEP #3</b>	Introduction	Brief summaries of the different intervention modalities used are helpful	Thank you for your comments.
<b>Peer reviewer #7</b>	Introduction	Nice overview; good balance between background and focus of report.	Thank you for your comments.
<b>TEP #4</b>	Introduction	Helpful in setting the basis.	Thank you for your comments.

Commentator & Affiliation	Section	Comment	Response
<b>Public reviewer (anonymous)</b>	Introduction	Introduction reflects current literature, but my very basic underlying question is "what exactly are we calling autism?"	We recognize that ASDs are heterogeneous disorders and have noted that heterogeneity in the Introduction and Discussion sections of the review. Further, we note how each study diagnosed/operationalized ASD in results text and tables.
<b>Peer reviewer #5</b>	Introduction	Report presents significant disability associated with autism spectrum disorders. Also notes the relative lack of attention to older adolescents and adults with ASDs.	Thank you for your comments.
<b>Peer Reviewer #3</b>	Introduction	The Introduction provides a succinct overview of ASD in adolescence and young adulthood, and it clearly states the rationale, scope, and significance of the review. However, the categorization of interventions is a bit muddled because some categories refer to treatment modality (e.g., behavioral approaches, medications) whereas others refer to content (e.g., vocational, life skills). My suggestion is to categorize into two modalities (behavioral/educational interventions and medications) and then have sub-categories by content (behavioral/educational intervention for social skills, academics, job readiness, etc.).	We recognize that there are multiple ways to categorize intervention approaches and appreciate these suggestions. We considered different approaches, but none worked as well for organizing the studies meeting our review criteria in a logical and meaningful manner.  We note that the approach selected for this report did not have an impact on our conclusions or the overall strength of evidence.
<b>TEP #5</b>	Introduction	all the elements of a systematic review are addressed	Thank you for your comments.
<b>TEP #5</b>	Introduction	the question is clearly formulated (though i think the difference between q 3 and 4 could be more clearly articulated. took me a while to see how they were different).	Question 4 is intended to focus on the transition process. We have italicized that portion of the question to make the focus more clear.
<b>TEP #5</b>	Introduction	the study population is clearly defined	Thank you for your comments.
<b>TEP #5</b>	Introduction	the criteria for study inclusion are also defined; though i think you will get come argument from some quarters about why you did not include single case designs that are multiple base-line.	We did not exclude any study designs except single case reports. We selected our inclusion criteria in consultation with our content and technical experts as a minimum threshold for comparing interventions. We recognize that setting a minimum of 20 participants for studies to be included effectively excluded much of the literature on behavioral interventions using single-subject designs. Because there is no separate comparison group in these studies they would be considered case reports (if only one individual included) or case series (multiple individuals) under the rubric of the EPC study designs. Case reports and case series can have rigorous evaluation of pre- and post- measures, as well as strong characterization of the study participants, and case series that included at least 20 individuals with ASD in our

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Commentator & Affiliation	Section	Comment	Response
			<p>age range were included in the review. Single-subject design studies can be helpful in assessing response to treatment in very short timeframes and under very tightly controlled circumstances, but they typically do not provide information on longer term or functional outcomes, nor are they ideal for external validity without multiple replications. In addition, noncomparative designs such as case reports or case series do not provide direct evidence of comparative effectiveness, nor do single-subject designs permit inference about effects at a population level. Comparative effectiveness reviews are intended to seek population-level conclusions about comparative effectiveness.</p> <p>Single-subject designs are useful in serving as demonstration projects, yielding initial evidence that an intervention merits further study, and, in the clinical environment, they can be useful in identifying whether a particular approach to treatment is likely to be helpful for a specific child. Our goal was to identify and review the best evidence for assessing the efficacy and effectiveness of therapies for adolescents and young adults with ASD, with an eye toward utility in the treatment setting. With the assistance of our content and 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.</p>
<b>TEP #1</b>	Methods	This all looks good.	Thank you for your comments.
<b>TEP #2</b>	Methods	Inclusion and exclusion criteria, search strategies are appropriate.	Thank you for your comments.

Commentator & Affiliation	Section	Comment	Response
<b>TEP #2</b>	Methods	Weakness is definition of poor, fair, good quality is not sufficient or the criteria for good are so high as to not be useful.	We used standard descriptions of good, fair, and poor quality and adapted the quality grading approach used successfully in a prior review of therapies for children with ASD. We note in the report abstract and Discussion section that the lower quality of the evidence likely reflects the recency of research of the field and recommend areas for improvement.
<b>TEP #3</b>	Methods	Some might argue that setting minimum n of 20 is too harsh and excludes too many studies, but in my view this is an acceptable minimum to set.	We agree that the N of 20 strikes a balance that allows us to account for typically smaller study sizes in ASD research while including studies with sample sizes large enough to suggest effects of interventions.
<b>TEP #3</b>	Methods	Inclusion/exclusion criteria are explicit and relevant.	Thank you for your comments.
<b>TEP #3</b>	Methods	Study size should indicate that criterion of n= 20+ refers to total sample (thus studies of 10 in each arm would be included ).	We have clarified this statement in the Methods section. (done-ns)
<b>TEP #3</b>	Methods	Search strategy is clearly documents (p 39 on)	Thank you for your comments.
<b>TEP #3</b>	Methods	No diagnostic criteria are set - many studies do not use formal diagnostic measures to ascertain diagnostic status hence authors have accepted clinical labels for inclusion in review. Although quality of diagnosis is used in the general rating of each study it was not necessary for papers to give details of specific diagnostic instruments used. In my view this information should have been deemed necessary (cf Appendix E)	We did require that diagnoses be DSM-based and conducted within the study for studies to be assessed as greater than poor quality. We added notes to each results summary table to provide more information about each study's quality scoring.
<b>TEP #3</b>	Methods	Target population is explicitly defined (p 41-42) but perhaps intended audience needs clearer definition	We have clarified the uses of the report section.
<b>Peer reviewer #7</b>	Methods	Yes. The only issue I was left wondering about was how "20" was determined. The report states that it is a number to allow for sufficient effect size, but is that a statistical determination? Drawn from research or clinical studies experience?	We did not use statistical methods to determine the N of 20. We attempted to balance the realities of typical research in ASD (small study sizes) with the need to include enough participants to demonstrate an effect.
<b>TEP #4</b>	Methods	Inclusion and exclusion nicely stated - as noted above, would have considered other kinds of co-morbid conditions in the inclusion criteria (although expect no useful literature to be identified).	Thank you for your comments. We considered both medical and mental health related comorbidities as noted in Key Question 3.

Commentator & Affiliation	Section	Comment	Response
<b>TEP #4</b>	Methods	Re outcome measures, there is a tremendous need for any chronic condition affecting adolescents and young adults to include measures of functioning in developmentally appropriate ways. The World Health Organization Intl Classification of Functioning provides a framework for such outcome assessment - but the goals of much treatment (for many of the interventions included in this review) are mainly in areas of educational attainment, role performance (personal, social, employment, etc.), and participation in family/community affairs. It will help to assess these kinds of outcomes - and to call for them in expectations for future research.	We reported on the outcomes that were addressed in the studies meeting our criteria but agree that evidence about a wealth of outcomes is needed. We have emphasized this point in the future research section.
<b>Public reviewer (Jennifer Ganz)</b>	Methods	This work excluded over 700 studies with fewer than 20 participants, which means all single-case research was excluded. It is likely that most of the evidence for this low incidence population involves single-case research, which is an accepted research design in special education and behavioral psychology. By excluding this work, much of which includes rigorous single-case designs, it appears that most of the applicable research was ignored.	We selected our inclusion criteria in consultation with our content and technical experts as a minimum threshold for comparing interventions. We recognize that setting a minimum of 20 participants for studies to be included effectively excluded much of the literature on behavioral interventions using single-subject designs. Because there is no separate comparison group in these studies they would be considered case reports (if only one individual included) or case series (multiple individuals) under the rubric of the EPC study designs. Case reports and case series can have rigorous evaluation of pre- and post-measures, as well as strong characterization of the study participants, and case series that included at least 20 individuals with ASD in our age range were included in the review. Single-subject design studies can be helpful in assessing response to treatment in very short timeframes and under very tightly controlled circumstances, but they typically do not provide information on longer term or functional outcomes, nor are they ideal for external validity without multiple replications. In addition, noncomparative designs such as case reports or case series do not provide direct evidence of comparative effectiveness, nor do single-subject designs permit inference about effects at a population level. Comparative effectiveness reviews are intended to seek population-level conclusions about comparative effectiveness.

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Commentator & Affiliation	Section	Comment	Response
			<p>Single-subject designs are useful in serving as demonstration projects, yielding initial evidence that an intervention merits further study, and, in the clinical environment, they can be useful in identifying whether a particular approach to treatment is likely to be helpful for a specific child. Our goal was to identify and review the best evidence for assessing the efficacy and effectiveness of therapies for adolescents and young adults with ASD, with an eye toward utility in the treatment setting. With the assistance of our content and 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.</p>
<b>Public reviewer (anonymous)</b>	Methods	Methods were clearly stated and appropriate for the question of this study. Adjudication was appropriate.	Thank you for your comments.
<b>Public reviewer (anonymous)</b>	Methods	What is the relationship of the quality assessment (good, fair, poor) to the grading system of the USPSTF?	<p>We developed the quality grading system specifically for a prior review on therapies for children with ASD and adapted it for use in the current review. While the ratings of good, fair, and poor are broadly similar to USPSTF grading (e.g., good evidence comes from well-designed, representative studies), we note that the current review does not offer specific recommendations about treatments.</p>
<b>Peer reviewer #5</b>	Methods	<p>Search strategies were clearly described and were appropriate. Clear tracking of how articles were selected and reviewed. Some 4,500 articles were initially selected; 3,500 abstracts were reviewed; full text reviewed of 918 papers. Of these, 887 were excluded and 31 trials were examined for quality. These 31 reports were mapped to the key questions.</p>	Thank you for your comments.
<b>Peer Reviewer #3</b>	Methods	<p>Methods: For the most part, the methods are systematic and rigorous. The search procedures are explained well. Procedures for extracting data and rating the quality of the research design are appropriate. The elucidation of criteria for rating the studies as good, fair, or poor (as well as for rating the overall strength of evidence for an intervention on this scale ) are a substantial advance over the previous AHRQ autism review (pp. 15-17).</p>	Thank you for your comments.

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<b>Peer Reviewer #3</b>	Methods	The main concerns in the current review pertain to the inclusion/exclusion criteria. The review states, "The upper age of 30 accounted for potential developmental delays in individuals" (p. 12), but this statement is opaque. A 13-year-old individual with ASD may have a higher developmental level than a 30-year-old with ASD accompanied by intellectual disability. In any case, this is not a reason for excluding studies of older individuals with ASD. It seems simpler to note the importance of transition into adulthood as a justification for focusing on the period before, during, and after this transition.	We have clarified that our focus on this review is on the transitional period.
<b>Peer Reviewer #3</b>	Methods	Also, although the review gives a concise rationale for focusing on studies with $N > 20$ , it would be useful to acknowledge that this is a revision from the previous AHRQ review and offer a short explanation (e.g., because of the limited impact of including studies with $10 < N < 20$ on the findings in the previous review).	This review is distinct from our prior work, so as you have noted, we set new criteria for inclusion.
<b>TEP #5</b>	Methods	i would say up front that you checked the clinical trials registry.	We do not typically search clinical trials registries as EPC reviews do not address unpublished data.
<b>TEP #5</b>	Methods	there is no comment on calculation of effect sizes or number needed to treat. why is that?	We have presented the data that were available in the published literature. At this time, that does not include quantitative assessments of effect. Under the EPC methods, whether or not to calculate effect sizes or whether to use measures such as NNT depends on the particular review and topic.
<b>TEP #1</b>	Results	The level of detail is good.	Thank you for your comments.
<b>TEP #2</b>	Results	Detail is more than sufficiently presented, including the tables that detail very well the 31 studies with a very useful grid -	Thank you for your comments.
<b>TEP #2</b>	Results	problem is that even the executive summary reads more like a data dump than a synthesis of key messages useful for the field.	We have revised the Executive Summary to provide more synthesis.
<b>TEP #2</b>	Results	For example, ES-14, line 29 and throughout - why is this risperidone study of fair quality and not good ? Looking at the table (page 324 of 385 reveals concern with measurement of adherence but that should not be a concern if the comparator is placebo and outcomes are coded blindly in a double-blind study by definition or more detail needs to be provided, p 361 of 385 - says NR for primary outcome and NA for treatment adherence/fidelity (not consistent with table having a - suggesting a deficiency	We have reviewed the quality scoring and noted that the study did use masked assessors. The overall quality rating (fair) did not change, however. This is due, in part, to the lack of information on assessment of adherence.
<b>TEP #3</b>	Results	Quality of studies identified is generally so poor that complex statistical analysis/ meta analyses etc were not possible.	Thank you for your comments.

Commentator & Affiliation	Section	Comment	Response
<b>TEP #3</b>	Results	Results are clearly reported. There are summary paragraphs, in the form of Key Points, at the start of each intervention section which are very helpful.	Thank you for your comments.
<b>TEP #3</b>	Results	Characteristics of studies are clear although I think a very brief indication of why studies were rated as poor (ie, what were main flaws) would be helpful in summary tables. Almost all studies, with exception of drug trials are rated as poor and presumably within this category some are much poorer than others. More information on what criteria were not met would be very useful.	We have added such information to the tables summarizing studies.
<b>Peer reviewer #7</b>	Results	The tables are good.	Thank you for your comments.
<b>TEP #4</b>	Results	Generally fine.	Thank you for your comments.
<b>Peer reviewer #5</b>	Results	Amount of detail is sufficient.	Thank you for your comments.
<b>Peer reviewer #5</b>	Results	The basis for "good" fair and poor rating are generally clear. I might dicker with the rating of "fair" for the study by Remington et al (clomipramine, haloperidol and placebo in a three change crossover). In my view this is a poor quality study. The results offer very little information. The crossover design was a mistake, the treatment target was not clear.	We acknowledge the limitations of the study; however, we reviewed the quality scoring, and the paper remains fair quality.
<b>Peer reviewer #5</b>	Results	Similarly, the trial by Willemsen-Swinkels et al. does not meet a rating of "fair" - even though it was a placebo-controlled trial.	We acknowledge the limitations of the study; however, we reviewed the quality scoring, and the paper remains fair quality.
<b>Peer reviewer #5</b>	Results	Nonetheless, this did not leave me with concern that other studies were inadequately assessed.	Thank you for your comments.
<b>Peer Reviewer #3</b>	Results	Results: The summaries of studies appear to be highly accurate, and this writer was able to replicate almost all quality ratings by inspecting individual articles. However, there were some exceptions, especially related to blind coders.	Thank you for your comments. See specific responses to quality scoring issues noted.
<b>Peer Reviewer #3</b>	Results	[quality scoring issues] For example, the studies by McDougle (1986, 1988) incorporated a double-blind design but were rated as not having blind coders.	We have reviewed and corrected the quality scoring for these studies.
<b>Peer Reviewer #3</b>	Results	[quality scoring issues] The study by Laugeson (2009) included ratings from blind teachers but was rated as not having blind coders.	We have reviewed and corrected the quality scoring for this study.
<b>Peer Reviewer #3</b>	Results	[quality scoring issues] However, the study by Garcia-Villamizar (2010) is coded as having blind coding, even though the article refers merely to a "therapist blind to study objectives"(insufficient unless the therapist was also blind to group assignment).	We have reviewed and corrected the quality scoring for this study.

Commentator & Affiliation	Section	Comment	Response
<b>Peer Reviewer #3</b>	Results	A somewhat peripheral but important issue is that the intervention program led by Israel (1993) has repeatedly been charged with abuse and obstruction of justice over a period of many years. The director recently agreed to step down as part of a plea bargain agreement with the state of Massachusetts ( <a href="http://articles.boston.com/2011-05-25/lifestyle/29582413_1_shock-case-criminal-case-face-criminal-charges">http://articles.boston.com/2011-05-25/lifestyle/29582413_1_shock-case-criminal-case-face-criminal-charges</a> ). The charges of abuse stemmed from extensive use of aversive procedures linked to injuries and even a few deaths, almost universally condemned by colleagues, policy-makers, and consumer advocates. These procedures are euphemistically described as “crisis management” (p. 30) in the review. The concerns about procedures and potential adverse events deserve a brief mention in the review.	We appreciate your pointing this out. We re-examined the study and elected to remove it as the intervention is not replicable.
<b>TEP #5</b>	Results	no comment. all well done. no studies were overlooked.	Thank you for your comments.