Communication intervention for autism spectrum disorders in minimally verbal children (Protocol)

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**Communication intervention for autism spectrum disorders in minimally verbal children (Protocol)**

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Communication intervention for autism spectrum disorders in minimally verbal children

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ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To evaluate the effectiveness of communication interventions in children with ASD who are minimally verbal.
BACKGROUND

Description of the condition

Autism spectrum disorder (ASD) is one of the most common neurodevelopmental disabilities. Data from the Autism and Developmental Disabilities Monitoring (ADDM) Network, an active surveillance system in the USA, has reported an increase in prevalence of 6.7 per 1000 in the year 2000, to 14.7 per 1000 in 2010 (ADDM Network 2014). Similar increasing trends have also been observed worldwide (Crien 2002; Gillberg 1999; Lai 2014).

ASD is characterized by social communication difficulties and repetitive, restricted behaviours and routines. A clinical diagnosis of ASD is based on observed behavioural criteria, as defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM) (APA 2013). Although ASD has no known cause, it is understood that both the genes and the environment play a role (Chaste 2012).

Language difficulties have been removed as a core feature of ASD in the most recent edition of the DSM (APA 2013). However, a significant proportion of children with ASD experience difficulties acquiring spoken language. The severity of these difficulties varies considerably across individuals. Most children with ASD acquire language during the preschool years (Anderson 2007; Howlin 2009), typically by five years of age (Tager-Flusberg 2005). However, 25% to 30% of children with ASD fail to develop any functional spoken language, or remain minimally verbal (Anderson 2007; Norrelgen 2015; Tager-Flusberg 2013). Language difficulties in children with ASD can result in a number of adverse sequelae, including behavioural difficulties (Bott 1997; McClintock 2003; Sigaloo 2000), poor adaptive functioning and social skills (Anderson 2007; Hudry 2010), which result in reduced quality of life and opportunities to participate in the community. Up to 25% of minimally verbal children with ASD show an increase in aberrant behaviours such as social withdrawal during adolescence (Lord 2010).

There has been a lack of consensus in the literature regarding the definition of the term ‘minimally verbal’. For example, Tager-Flusberg 2013 proposed benchmark criteria to identify this group. The first stage is “pre-verbal” and the next stage is “first words” where the child is required to have an age equivalent of greater than 15 months for vocabulary and pragmatic abilities. Kasari 2013 defines minimally verbal children as those with “a very small repertoire of spoken words or fixed phrases that are used communicatively”. Other studies describe this group as children who use no words or single words (Thurm 2015). A number of studies have used definitions as provided by diagnostic tools. For example, the Autism Diagnostic Interview - Revised (ADI-R) describes Stage 1 as “no phrase speech and greater than or equal to three words but single words used on a daily basis” and Stage 2 as “no speech used on a daily basis and less than a 5 word vocabulary” (Rutter 2003). For the purposes of this review, we define minimally verbal as children who have fewer than 30 functional words or who are unable to use speech alone to communicate, or both, and who are at an age where one would expect them to use language (i.e. mental age of greater than two years). This interpretation accommodates a range of quantitative definitions across studies.

The reason children with ASD fail to develop verbal communication remains unknown. Further to the underlying genetic and environmental markers of ASD and language, which are poorly understood, researchers have applied structural and functional imaging or neurophysiological techniques to examine potential abnormalities in the brain structures of children with ASD to explain language outcomes (De Fossé 2004; Freitag 2009; Just 2004; Kumar 2010; Stanfield 2008). It remains unclear, however, as to how these structural and functional changes directly explain the language difficulties that occur in children with ASD.

Further to the neural underpinnings of language and ASD, some researchers have focused on cognitive and neural mechanisms impacting verbal development in these children. Cognitive ability (intelligence quotient (IQ)) and difficulties with social communication skills seem to be influential contributors (Norrelgen 2015). For example, one study found non-verbal cognitive ability, gestures and imitation to be the strongest predictors of later expressive language ability in children with ASD (Luyster 2008). Joint attention skills have also been suggested to impact the development of language in children with ASD. Joint attention has been defined as the ability to respond to social interaction bids from others, and the ability to initiate social interaction with others, as well as the co-ordination of these two skills (Alessandri 2005; Mundy 2007). A number of studies have found joint attention to be predictive of later language abilities in both children with ASD and typically developing children (e.g. Charman 2003; Mundy 1999; Mundy 2007). Consequently, joint attention has been included in a number of intervention programmes (Dawson 2010; Kasari 2012; Lawton 2012).

Another study found that vocal and motor imitation, along with joint attention, were more impaired in children with ASD who had not developed language by five years of age (Luyster 2008; Thurm 2007). It has been proposed that childhood apraxia of speech may cause some children with ASD to fail to develop verbal communication, however, to date, there has been limited evidence to support this hypothesis (Pickett 2009; Schoen 2011; Shriberg 2011).

Whilst aetiological mechanisms are poorly understood, arguably more work has been conducted as regards prognostication of outcomes in these children. Studies suggest that early acquisition of speech and language (by five years of age) is predictive of more favourable outcomes, such as adaptive and social functioning, in later years (Anderson 2007). There is some evidence that communication interventions are less effective if applied after five years of age (Pickett 2009). Some children develop spoken language during adolescence (12 years of age and above) (Wodka 2013), although the chance of this happening is less likely than at younger ages (Tager-Flusberg 2013). These differential responses to intervention based on a child’s age warrants further research stratified by different age groups of children (preschool age or school age).

Description of the intervention

To date, there is no consensus regarding the most appropriate and effective communication intervention for children with ASD who are minimally verbal. This Cochrane review will focus on interventions that target the acquisition and development of communication skills delivered directly during social-communicative interactions between the child with ASD and another person (usually a therapist). As such, the review will not include pharmaceutical interventions, dietary interventions or interventions delivered to children through other means without another person facilitating this intervention (e.g. through
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Verbally-based communication interventions

Verbally-based interventions are those that use verbal strategies to target the ability to use sounds, words and sentences to express oneself. They range from naturalistic, child-centred and developmental-pragmatic approaches (e.g. Gutstein 2002), to structured and more didactic methods (e.g. Lovaas 1987) (see Paul 2008 and Prizant 1998 for an overview). Discrete Trial Training (DTT) (Lovaas 1987), for example, is a structured approach, which involves simplifying a skill into a series of steps and teaching the child those steps one at a time (this is known as ‘discrete trials’). Although this approach has been shown to improve expressive and receptive language skills (Delprete 2001; Reichow 2009), some argue it fails to promote spontaneous communication and to generalize newly learned skills beyond the training setting (Owens 2009). Prelinguistic/Milieu Communication Training (P/MCT) is an approach that uses modelling of communicative behaviour and correction of child responses, time delay (waiting for the child to initiate/respond) and incidental teaching in natural environments. This approach capitalizes on the child’s natural interests (Yoder 2006). Some novel approaches are also being evaluated to see if these may address the specific difficulties experienced by children with ASD who are minimally verbal (e.g. Rapid Motor Imitation Antecedent (RMIA), a programme that has been adapted from the DTT model) (Paul 2013).

Augmentative and alternative communication (AAC) interventions

Augmentative and alternative communication (AAC) interventions refer to a variety of non-verbal communication methods to help minimally verbal children with ASD acquire and develop speech and language skills (Ganz 2004; Kasari 2014; Merinda 2009). AAC also provides children with an alternative means of communicating if they are unable to do so verbally. There are two main types of AAC: aided and unaided. Aided systems use supplementary materials, including graphic symbols such as picture books, texture-based systems such as Braille, and speech-generating devices (SGD) that produce digitalized speech. Unaided systems use manual signs and graphic gestures; these may be formal such as sign language and key word signs, or informal such as idiosyncratic movements. Some AAC interventions incorporate structured and hierarchical behavioural approaches. The Picture Exchange Communication System (PECS) (Bondy 1998), for example, includes six phases of teaching; the child moves up the hierarchy as they make progress. In the first phase the child is physically prompted to make specific requests for items they want using pictures, and in the final phase (the most advanced phase) the child uses the pictures to communicate independently. In recent years, the use of new technologies, such as smartphones, iPads and tablets, has burgeoned. A systematic review of tablet computers and portable media devices that had been adapted to serve as SGDs found that the devices usually facilitated verbal ability and that language acquisition was faster for individuals using SGDs compared to manual signs or low technology AAC (Lorah 2015).

Combined communication interventions (verbally-based intervention plus AAC)

Combined programmes, sometimes referred to as ‘total communication’ interventions, use components from both verbally-based communication interventions and AAC interventions. The Hanen® More than Words programme (Sussman 2001), for example, is a parent training programme that teaches parents to use strategies (e.g. comment on the child’s interests, use AAC, use cues to encourage turn-taking) in their everyday routines to help their child to communicate. The Means, Opportunities, Reasons and Expectations (MORE) programme is another approach that uses both verbally-based communication interventions and AAC interventions (Emerson 2013).

Comprehensive interventions with a communication focus

A broad range of comprehensive programmes for ASD have been developed. These target a range of developmental skills such as cognition, behaviour, play, emotional regulation and social skills, in addition to communication. Pivotal Response Training (PRT) is an example of a naturalistic behavioural intervention, derived from the principles of Applied Behaviour Analysis (ABA), which facilitates stimulus and response generalization, increases spontaneity, reduces prompt dependency and increases motivation (Koegel 2006). Other examples include the Denver Model (and Early Start Denver Model) (Rogers 2000; Rogers 2009), the Relationship Development Intervention (Gutstein 2002), the Learning Experience and Alternative Program (LEAP) (Strain 1998), the Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH) programme (Mesibov 2005), and the Social Communication, Emotional Regulation Transactional Support (SCERTS) model (Prizant 2006).

Comprehensive programmes, most of which have not been adapted for use in children who are minimally verbal, go beyond the scope of the current review. We will only include such programmes if they have been adapted so that the focus is on communication, and the primary aim of the study is to improve communication skills, such as the recently published trial by Kasari 2014. This trial combined a Joint Attention and Symbolic Play Engagement and Regulation (JASPER) intervention with Prelinguistic Milieu Training (PMT) to improve communicative spoken language in minimally verbal children. Similarly, we will only include parent-mediated interventions, such as the Parent-Mediated Communication Focused Treatment (PACT) (Green 2010) and the Hanen® More than Words programme (Sussman 2001), if the intervention targets communication and the aims of the study are communication specific.

Each of the above approaches use different mechanisms to improve speech acquisition and development in minimally verbal children (see How the intervention might work). Consequently, we will conduct separate subgroup analyses to further explore these different types of interventions (classified in the manner stated above, or even more precisely, depending on the number of studies that we can include in each subgroup).

How the intervention might work

Verbally-based communication interventions

The underlying theory behind many verbally-based interventions is that the lack of verbal communication originates from other
inherent areas of difficulty in ASD, including reduced levels of social motivation, reduced attention to child-directed speech, immaturity of speech motor development and generally poor imitation skills. It is thought that limitations in all of these domains, if serious enough, leads to severe language impairment. If this theory is correct, an intervention that focuses specifically on speech production together with more intensive and orientated guidance from caregivers, may be enough to trigger the speech learning process. Similarly, efforts that seek out approaches for reciprocal interaction mediated by word exchanges might also work through 'turning on' or 'turning up' the expressive language system (Schoen 2011; Shriberg 2011).

Augmentative and alternative communication (AAC) interventions

There are a number of theories as to why AAC systems may facilitate vocal production. First, based on the principle of automatic reinforcement, AAC interventions may form an interactive reinforcement system that increases the effectiveness of speech production (Millar 2006). Essentially, it is thought that if the spoken word and its symbol are presented simultaneously along with a reinforcer, minimally verbal children will begin to produce approximations of the word. Second, for those children with deficits in motor skills or cognitive function, mastering other skills for establishing basic communication may help them to conquer the difficulties encountered during vocal production (Romski 1996). Third, it has been proposed that AAC interventions may reduce the pressure for children to communicate verbally, and in doing so, reduce demands on auditory-vocal channels and indirectly increase the chances of spontaneous vocal production (Kasari 2014).

Comprehensive interventions with a communication focus

Some comprehensive programmes have been adapted to specifically target communication. For instance, Pivotal Response Therapy (PRT) was designed to target ‘pivotal’ areas of a child’s development (including motivation, response to multiple cues, self-management, and the initiation of social interactions) (Koegel 2006). Pivotal behaviours are central to a broad range of areas of a child’s functioning and, when promoted, may lead to improvements in verbal communication. In addition, parent-mediated communication interventions aim to enhance parent-child interactions by increasing parental sensitivity and responsiveness to the child’s communication needs. Through a range of interaction strategies, such as routines and familiar repetitive language and pauses, the child’s prelinguistic and early language skills may be improved (Green 2010; Sussman 2001). Finally, joint attention symbolic play and emotion regulation intervention may help develop the child’s verbal skills by promoting the child’s play skills and attention to social interaction (Kasari 2013).

Why it is important to do this review

The ability to communicate is an essential life skill. Communication is key to forming and maintaining relationships, academic performance and in enabling an individual to participate and function in his/her community. Difficulties communicating can also have an impact on family quality of life and stress. The evidence suggests that up to 25% to 30% of children with ASD will remain minimally verbal when they reach school age (Anderson 2007; Tager-Flusberg 2013). Historically, most studies that have investigated communication interventions for children with ASD have focused on the language development of verbal children. Little attention has been given to children who are minimally verbal (Kasari 2013; Paul 2013; Tager-Flusberg 2013), with the exception of a workshop on the topic of minimally verbal children with ASD organized by the National Institutes of Health (NIH) in 2010, signalling the critical need for greater research focus in this area (NIH 2010). At present there is no consensus on what may be the most effective intervention approach for children with ASD who are minimally verbal. We cannot assume that interventions that work for verbal children will also work for children who are minimally verbal and, therefore, a systematic review to evaluate the existing evidence on interventions for this population is needed.

A number of reviews have been conducted that have investigated communication interventions for children with ASD (e.g. Goldstein 2002; Kim 2009; Thunberg 2013). None of these reviews have focused specifically on children with ASD who are minimally verbal. The existing reviews have not systematically reviewed the quality of included studies so that risk of bias for each included study can be judged. This Cochrane review will use a more comprehensive range of databases to search the literature, will use different inclusion criteria compared to the previous reviews and it will provide the most up-to-date information on the available evidence on interventions for minimally verbal children with ASD.

In this review, we aim to address two main questions. First, are communication interventions beneficial for minimally verbal children with ASD and, if so, which type of intervention is the most effective? Second, do the outcomes of preschool and school-age children with ASD differ when such interventions are applied? This review will provide a summary of the available evidence on interventions for children with ASD who are minimally verbal. This will assist decision-making around the types and amount of intervention for this group of children as well as inform the planning of resources to support them. This information is highly relevant for clinicians, service-providers, families and policymakers.

OBJECTIVES

To evaluate the effectiveness of communication interventions in children with ASD who are minimally verbal.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs).

Types of participants

We will include participants in the review if they meet the following three criteria.

1. They have received a diagnosis of autism spectrum disorder (ASD), autism, autistic disorder, Asperger’s syndrome, pervasive developmental disorder (PDD) and PDD - not otherwise specified (PDD-NOS). The diagnosis must be made using standard diagnostic criteria such as the Childhood Autism Rating Scale (CARS) (Schopler 1986), Gilliam Autism Rating Scale (GARS) (Gilliam 1995), Autism Diagnostic Interview - Revised (ADI-R) (Lord 1994), Autism Diagnostic Observation
Types of interventions

Language-focused interventions that primarily aim to improve spoken communication (expressive language or speech, or both) or use of non-verbal communication (e.g. augmentative and alternative communication (AAC)), compared with no treatment, wait-list control or treatment as usual. We will exclude studies that have other treatment controls (i.e. one treatment is directly compared to another in the RCT) due to the limited methodology to support multiple treatment comparisons through meta-analyses. Eligible interventions include the following.

1. Verbally-based communication interventions (such as Prelinguistic Milieu Teaching (PMT) (Yoder 2006), Discrete Trial Training (DTT) (Lovas 1987), Prompts for Restructuring Oral Muscular Phonetic Targets (PROMPT) (Chumpelik 1984)).

2. AAC interventions (such as Picture Exchange Communication System (PECS) (Bondy 1998), SGDs, sign language).

3. Combined communication interventions (verbally-based communication and AAC interventions).

4. Comprehensive (multi-modal) interventions that aim to improve spoken communication or AAC ability, or both.

We will exclude studies that use comprehensive interventions for ASD that target a range of developmental skills (such as fine motor) unless the aims of the study specifically focus on spoken communication or the use of AAC, or both. Equally, we will only include parent training programmes if they have a specific focus on spoken communication or use of AAC, or both.

We will exclude interventions that focus on improving social skills as a primary aim, although social communication may be a secondary outcome. We will exclude interventions that require physical support from a third party for the child to communicate; for example, Facilitated Communication (Biklen 1990) and Rapid Prompting Method (HALO 2016). We will only include interventions that involve the child independently communicating.

Types of outcome measures

Primary outcomes

1. Spoken communication (expressive language or speech, or both). This may be in the form of sounds, words and phrases/sentences. Spoken communication may be used in a variety of ways (e.g. to request, comment). Outcomes will be measured using formal standardized assessments, standardized parent-report checklists and tools, novel instruments (newly-designed scales specific to a study), language samples and vocabulary counts.

2. Non-verbal communication/augmentative communication (as measured by, for example, the phase of PECS (Bondy 1998)). Vocabulary used on a device, or the number of key word signs a child uses.

3. Adverse events. This may include increased stress in parents or increased anxiety in the child in response to completing a particular intervention.

Secondary outcomes

1. Social communication and pragmatic language skills.

2. Other communication skills such as adaptive communication (Vineland Adaptive Behavior Scales, Second Edition (VABS-II) (Sparrow 2005)).

3. Quality of life for the individual or their family (parent stress) and parent satisfaction as measured by either standardized instruments, such as Parenting Stress Index (Abidin 1995), quality of life scales, tools such as Focus on the Outcomes of Communication Under Six (Thomas-Stonell 2013), or novel instruments invented by the designers of the study.

4. Non-core aspects of behaviour and function, for example, nonverbal cognition, challenging behaviours, self-mutilation and aggression, as measured by either standardized instruments or novel instruments invented by study designers.

We will synthesise results for the following time points: at the end of intervention, one year after the end of intervention and more than one year of follow-up. We will include dose of intervention in the subgroup analysis.

We will create a ‘Summary of findings’ table for each main comparison using the software developed by the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) working group: GRADE profiler Guideline Development Tool (GRADEpro GDT) (GRADEpro GDT). We will include all primary and secondary outcomes in the ‘Summary of findings’ table.

Search methods for identification of studies

Electronic searches

We will search the electronic databases and trials registers listed below and will not use any date or language restrictions. We will seek to translations of non-English language papers and assess them for potential inclusion in the review as necessary.

1. The Cochrane Central Register of Controlled Trials (CENTRAL, current issue, part of the Cochrane Library), and which includes the Cochrane Developmental, Psychosocial and Learning Problems Group Specialized Register.

2. Ovid MEDLINE (1946 to current).

1. Methods: study design, total duration, number of study centres and location, study setting, withdrawals, date of study.

2. Participants: number (N), mean age, age range, gender, severity of condition, diagnostic criteria, inclusion criteria, exclusion criteria.

3. Interventions: intervention, comparison, concomitant treatment, excluded treatments.

4. Outcomes: primary and secondary outcomes specified and collected, time points reported.

5. Notes: funding for trial, or any notable conflicts of interest of trial authors.

Two review authors (HS, CS) will independently extract outcome data from the included studies and record it in the ‘Characteristics of included studies’ table. We will resolve disagreements by consensus or by involving a third person (DL).

One review author (HS) will manually input the data from the data collection form into Review Manager (RevMan) (RevMan 2014). A second review author (DL) will spot check study characteristics for accuracy against the trial report. Once complete, HS and DL will double check that the review authors have entered data correctly by comparing the study reports with how the data are presented in the systematic review.

Assessment of risk of bias in included studies

Two review authors (HS, DL) will independently assess the risk of bias for each included study using the criteria outlined in Chapter 8 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011a). We will consult a third assessor (JZ) if there are any differences of opinion. We will assess the risk of bias for each included study across the following seven domains.

1. Random sequence generation
   - Low risk of bias: the sequence generation process was truly random, for example, a random number table or computer random number generator was used.
   - High risk of bias: the sequence generation process was non-random, for example, allocation by judgement of the clinician or preference of the participant.
   - Unclear risk of bias: there was insufficient information about the sequence generation process to permit a judgement of low or high risk of bias.

2. Allocation concealment
   - Low risk of bias: allocation of participants was done using central allocation or sequentially numbered, opaque, sealed envelopes.
   - High risk of bias: the allocation sequence was known to the investigators or participants.
   - Unclear risk of bias: the trial was described as randomized, but the method used to conceal the allocation was not described.

3. Blinding of participants and personnel
   - Low risk of bias: blinding of participants and key study personnel were ensured. It was unlikely that blinding was broken or unlikely a lack of blinding would influence the outcome, or both.
   - High risk of bias: blinding of participants and key study personnel was not done or was broken, and outcomes were likely to be influenced by the lack of blinding.
   - Unclear risk of bias: the term 'blinding' was mentioned but no details were given for who was blinded and how the blinding was ensured to permit a judgement of low or high risk.

4. Blinding of outcome assessment
   - Low risk of bias: if the outcome assessors were blinded to the intervention received by the participants, or if the outcome was unlikely to be influenced by lack of blinding.

Searching other resources

We will check the reference lists of all included studies and relevant reviews for additional references. In addition, we will ask experts in the field to provide details of ongoing clinical trials and any relevant unpublished material. We will also contact authors of identified trials to ask if they know of any other published or unpublished studies, or both, that have not been identified by our search strategy.

Data collection and analysis

Selection of studies

Two review authors (HS, JZ) will independently screen titles and abstracts identified by the literature search for potentially relevant studies. Of those deemed potentially relevant, the same review authors will obtain and independently assess the full text against the inclusion criteria. We will resolve any disagreement through discussion or, if required, we will consult a third review author (DL).

We will identify and exclude duplicates and collate multiple reports of the same study so that each study, rather than each report, is the unit of interest in the review. We will list all excluded studies and the reasons for exclusion in a ‘Characteristics of excluded studies’ table.

We will record the selection process in sufficient detail to produce a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram (Liberati 2009).

Data extraction and management

We will extract the following data from each included study.

1. Methods: study design, total duration, number of study centres and location, study setting, withdrawals, date of study.

2. Participants: number (N), mean age, age range, gender, severity of condition, diagnostic criteria, inclusion criteria, exclusion criteria.

3. Interventions: intervention, comparison, concomitant treatment, excluded treatments.

4. Outcomes: primary and secondary outcomes specified and collected, time points reported.
• High risk of bias: if no blinding of outcome assessment was mentioned but measurement was likely to be influenced by lack of blinding, or where blinding could have been broken.
• Unclear risk of bias: if the term 'double-blinded' was mentioned, but no details were given with regards to how the outcome assessors were blinded to the intervention received by the participants.

5. Incomplete outcome data
• Low risk of bias: there were no missing outcome data, or the reasons for missing data were unlikely to be related to the true study outcome, or the numbers and reasons were balanced across intervention groups.
• High risk of bias: there were missing outcome data and the reasons are likely to be related to the true study outcome with either imbalance in numbers or reasons for missing data across intervention groups.
• Unclear risk of bias: there was insufficient reporting of attrition or exclusion, or both, to permit a judgement of low or high risk of bias.

6. Selective outcome reporting
We will assess the possibility of selective outcome reporting by checking study protocols, if available, and comparing the outcomes listed in the protocol with the published study report.
• Low risk of bias: it is clear that all of the study's prespecified and expected outcomes of interest have been reported in the prespecified way.
• High risk of bias: not all the study's prespecified outcomes have been reported, or one or more primary outcomes were reported in a way that was not prespecified, or one or more reported primary outcomes were not prespecified, or one or more outcomes of interest in the review were reported incompletely so that they cannot be entered in a meta-analysis, or the study failed to include results of a key outcome that would be expected to have been reported.
• Unclear risk of bias: there was insufficient information to permit a judgement of low or high risk of bias.

7. Other bias
• Low risk of bias: the study appeared to be free of other sources of bias.
• High risk of bias: there was at least one problem in the study that could put it at risk of bias. For example, the study has been claimed to have been fraudulent, or there was extreme baseline imbalance.
• Unclear risk of bias: there was a lack of information to permit a judgement of low or high risk of bias.

Where available, we will provide a quote from the study report together with a justification for our judgment in the 'Risk of bias' table (beneath the 'Characteristics of included studies' tables). We will summarize the 'Risk of bias' judgments across different studies for each of the domains listed, by graph and by text in the Results section of the review. Where information on risk of bias relates to unpublished data or correspondence with a trial author, we will note this in the 'Risk of bias' table.

When considering treatment effects, we will take into account the risk of bias for the studies that contributed to that outcome.

Measures of treatment effect

Dichotomous outcomes
We will calculate risk ratios (RRs) for dichotomous variables (e.g. clinical improvement or no clinical improvement), and present these with 95% confidence intervals (CIs). If a study only presents data for the change from baseline to follow-up in the published report, we will contact the corresponding author of the study to obtain data at each time point.

Continuous outcomes
For continuous data, we will calculate mean differences (MDs) provided that studies use the same measurement, or standardized mean differences (SMDs) when studies use different scales, together with their corresponding 95% CIs. We will ensure that higher scores for continuous outcomes have the same meaning for the particular outcome, explain the direction to the reader, and report where we have reversed the directions if this was necessary. If a study has not reported standard deviations (SDs) or standard errors, we will contact the corresponding author of the study to obtain this information. If necessary, we will seek to calculate effect estimates from t statistics, analysis of variance (ANOVA) tables or other statistics as appropriate.

Multiple outcomes
If included studies provide multiple, interchangeable measures of the same construct at the same point of time, we will calculate the average SMD across the outcomes and the average estimated variances for continuous variables; for dichotomous measures, we will choose only the most reliable measure based on the authors' statement or our judgment (e.g. measures from the most commonly used scales).

If included studies report the same outcomes (measured by the same scale/tool) differently (e.g. as a dichotomous variable in one study but as a continuous variable in another), we will attempt to transform them to uniform variables using the methods described in Chapter 9 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011b). In case a well-established cut-off point exists, we will transform continuous data to dichotomous data. Otherwise, we will require detailed information from the study authors when they report dichotomous results. Alternatively, we can use SMD (or log odds ratios) and their standard errors to combine dichotomous and continuous data, when possible, using the generic inverse variance method in RevMan (RevMan 2014). If we are unable to transform the variables (e.g. the study authors do not reply to our request) or to combine them appropriately, we will conduct separate analyses on the variables with different formats.

Unit of analysis issues
The unit of analysis will typically be the individual participant. We will assess trials with atypical study design, such as cluster-RCTs, further and will apply appropriate analysis (see below).

Cluster-randomized trials
We will include cluster-RCTs along with individually-RCTs in the analysis. We will assess cluster-RCTs carefully (in terms of recruitment bias, baseline imbalance, loss of clusters and
comparability with individually-RCTs for potential unit of analysis errors. If it is unclear whether or not an included study applied proper controls for clustering, we will contact the corresponding author for further details. If the study did not use appropriate controlling we will request individual participant data from the study authors and we will reanalyze the data using appropriate multilevel models. We will perform the analyses according to the approach described in Chapter 16 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011c). We will analyze effect sizes and standard errors in RevMan using the generic inverse method (RevMan 2014). For adjustment for clustering (reducing the size of effect of each clustered trial to its 'effective sample size'), we will use an estimate of the intracluster correlation coefficient (ICC) extracted from the trial (if possible), or from another source (external estimates obtained from similar studies, and several resources that provide examples of ICCs), as described in Chapter 16 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011c). Where we derive ICCs from other sources, we will state this clearly in the Results section and will conduct a sensitivity analysis to investigate the effects of variation in the ICC (see Sensitivity analysis).

**Trials with multiple treatment arms**

If a single trial reports multiple treatment arms, we will only include the relevant trial arms. If more than one intervention arm is relevant to our review, we will first estimate if they are sufficiently similar to be combined. For instance, arms with the same intervention but different frequency of application, or arms with essentially the same intervention but with minor modifications in each group, can be treated as a whole treatment group. If so, we will combine all eligible intervention groups and compare them with the combined results of eligible control groups, thus making single, pair-wise comparisons. Where two comparisons (e.g. intervention A versus control and intervention B versus control) must be entered into the same meta-analysis separately, we will halve the number of participants in the control group to avoid double counting of participants.

**Dealing with missing data**

For studies without complete reports (studies identified by abstract only) or without complete information in full reports (critical data cannot be found in report), we will contact investigators or study sponsors to obtain the missing data, where possible. We will document any details provided by the study authors and use for further analysis.

For studies with missing data due to loss of follow-up/attrition, we will conduct analyses using intention-to-treat (ITT) principles. We will impute the outcomes for the missing participants using both a 'best-case' and 'worst case' scenario for dichotomous data. In the case that the missing data are continuous variables (i.e. no mean or SD reported), we will attempt to calculate them using the standard errors, CIs and t values, according to the methods described in Chapter 16 of Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011c).

If we are unable to retrieve or derive the missing data, we will describe the missing data for each trial included in the review in the 'Risk of bias' tables (beneath the 'Characteristics of included studies' tables); and if the proportion is large (greater than 20%), we will consider to decrease the quality level of a body of evidence. We will discuss the extent to which missing data could affect the results and mention it in the Authors' conclusions section. We will also conduct a sensitivity analysis to explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect (Sensitivity analysis), using the strategy described in Chapter 9 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011b).

**Assessment of heterogeneity**

We will assess clinical heterogeneity by comparing the differences between trials in terms of participant factors (age, gender, diagnostic subtypes, IQ) and intervention factors (type, duration). We will assess methodological heterogeneity by comparing the variability between the studies for issues such as concealment of allocation, blinding, and ways in which the included studies evaluated outcomes.

We will perform tests for heterogeneity using the Chi² test to assess whether observed differences in results are compatible with chance alone. Furthermore, we will use the I² statistic to quantify inconsistency across studies. We will define the presence of heterogeneity by a P value of less than 0.10 from the Chi² test and an I² statistic value of greater than 50%, as described in Chapter 9 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011b). We have been aware that in the case of small sample size or few included studies, a non-significant result of heterogeneity analyses must not be taken as evidence of no heterogeneity. We will explore possible sources of heterogeneity by subgroup analysis and investigation of heterogeneity (see Subgroup analysis and investigation of heterogeneity) and sensitivity analysis (see Sensitivity analysis).

**Assessment of reporting biases**

For outcomes where we are able to pool outcome data from 10 trials or more, we will draw a funnel plot (intervention effect estimate versus standard error of intervention effect estimate) to examine the possibility of reporting bias. If we find funnel plot asymmetry, we will further investigate clinical heterogeneity of studies as a possible explanation. We will use the 'contour-enhanced' funnel plot (Peters 2008), to distinguish asymmetry due to publication bias from that due to other factors; asymmetry is more likely caused by factors other than publication bias when the supposed missing studies are in areas of higher statistical significance.

**Data synthesis**

We will use RevMan to pool all eligible trials that applied communication interventions on minimally verbal children compared to no treatment or usual treatment (RevMan 2014). In the primary analyses, we will pool data from all types of interventions together. Given that we expect to find substantial clinical heterogeneity — the included interventions will have been designed according to different theories and approaches — we will pool the available data using a random-effects model weighted by the inverse of the variance estimate as described in Chapter 9 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011b). We will thereby report the estimate of the between-study variance in a random-effects meta-analysis (known as tau²). We will conduct separate analyses for different types of intervention in subgroup analyses.
For outcomes where we are unable to conduct a meta-analysis (e.g., studies do not report data or are very heterogeneous), we will present a narrative description of the results.

'Summary of findings' tables

We will assess the overall quality of the body of evidence using the GRADE approach (Guyatt 2008). Using this approach, we will grade the quality of the body of evidence from high to very low according to the presence of the following criteria: limitations in the design and implementation of studies; indirectness of evidence; unexplained heterogeneity or inconsistency of results; imprecision of results; and high probability of publication bias. We will provide the reasons why we downgrade the quality of the evidence for studies in the footnotes. Two review authors (HS, AB) will complete the quality assessment. We will create a 'Summary of findings' table for the main comparisons and outcomes, as listed under the 'Types of outcome measures' section.

Subgroup analysis and investigation of heterogeneity

We plan to perform the following subgroup analyses in relation to the primary outcomes.

1. Age: preschool (aged under five years with more than two years mental age) versus school-aged children (aged six to 12 years with more than two years mental age).
2. Baseline language capability: children with ASD who have different language levels at baseline (totally non-verbal versus one to 10 functional words; non-verbal versus 10 to 20 functional words).
3. Type of intervention: verbally-based interventions, AAC interventions, combined interventions, comprehensive interventions with a communication focus.
4. Duration of intervention: number of weeks.
5. Dose of intervention: number of hours per week.

We will examine differences between subgroups by visually inspecting their CIs. Non-overlapped CIs indicate a statistically significant difference in treatment effect between subgroups. We will then use the approach developed by Borenstein 2008 to formally investigate differences between two or more subgroups. This method conducts a standard test for heterogeneity across subgroup results rather than across individual study results, and has been implemented in RevMan (RevMan 2014). If there are a small number of studies or small sample sizes, or both, we will use caution when we interpret the subgroup analyses and we will discuss the limitations of the findings (e.g., potential for confounding) to avoid over-interpretation of the results. For ethical reasons most intervention studies in the field of ASD do not conduct RCTs using a ‘true’ control group (i.e. one group that receives an intervention and the other receives no intervention at all). Most studies use a treatment-as-usual (TAU) control group. TAU means the children may be receiving a range of interventions in the community (e.g., one session of speech pathology per week) but these interventions are not an intervention arm in the RCT. We will discuss the limitations of interpreting data when a study has used TAU control groups.

Sensitivity analysis

We will perform sensitivity analyses to assess the impact of each of the following on the effect estimate.

1. Performance of missing data imputation based on a 'best-case' or 'worst case' scenario assumption of missing data.
2. Exclusion of unpublished studies.
3. Exclusion of studies at high risk or unclear risk of bias (related to randomization, blinding or attrition).
4. Exclusion of studies with high levels of missing data.
5. Fixed-effect model versus a random-effects model.
6. Variations in the ICC (where we have derived ICC’s from other sources).

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Abidin 1995

ADDM Network 2014

Alessandri 2005

Anderson 2007

APA 2013

Biklen 1990

Bondy 1998

Borenstein 2008

Bott 1997

Charman 2003

Chaste 2012

Chumpelik 1984

Croen 2002

Dawson 2010

De Fossé 2004

Delprato 2001

Emerson 2013

Freitag 2009

Ganz 2004

Gillberg 1999
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Lawton 2012

Liberati 2009

Lorah 2015

Lord 1994

Lord 2000

Lord 2010
Lord C. Who remains non-verbal? What are the characteristics of this population?. NIH Workshop on Non-verbal School Age Children with Autism; 2010 April 13-14; Rockville, Maryland. Rockville, Maryland, 2010.

Lovaas 1987

Luyster 2008

McClintock 2003

Merinda 2009

Mesibov 2005

Millar 2006

Mundy 1990

Mundy 2007

NIH 2010

Norrelgen 2015

Owens 2009

Paul 2008

Paul 2013

Peters 2008
Pickett 2009

Prizant 1998

Prizant 2006

Reichow 2009

RevMan 2014 [Computer program]

Rogers 2000

Rogers 2009

Romski 1996

Rutter 2003

Schoen 2011

Schopler 1986

Shriberg 2011

Sigafoos 2000

Sparrow 2005

Stanfield 2008

Strain 1998

Sussman 2001

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Thomas-Stonell 2013

Thunberg 2013

Thurber 2007
Thurber L, Lord C, Lee LC, Newshaffer C. Predictors of language acquisition in preschool children with autism spectrum...

**Thurm 2015**

**WHO 1992**

**Wing 2002**
Wing L, Leekam SR, Libby SJ, Gould J, Larcombe M. The Diagnostic Interview for Social and Communication Disorders:

**APPENDICES**

**Appendix 1. Ovid MEDLINE search strategy**

1 exp child development disorders, pervasive/
2 Developmental Disabilities/
3 pervasive development$ disorder$.tw,kf.
4 (pervasive adj3 child$).tw,kf.
5 (PDD or PDDs or PDD-NOS or ASD or ASDs).tw,kf.
6 autism.tw,kf.
7 asperger$.tw,kf.
8 kanner$.tw,kf.
9 childhood schizophrenia.tw,kf.
10 Retts.tw,kf.
11 or/1-10
12 exp Communication/
13 exp communication disorders/
14 language development disorders/
15 exp Language Development/
16 nonverbal communication/
17 Verbal Behavior/
18 exp Verbal learning/
19 ((communicat$ or speech or language) adj5 (need$ or dysfunction$ or impair$ or disabil$ or disabl$ or delay$)).tw,kf.
20 (minimal$ adj1 (speech$ or verbal$)).tw,kf.
21 (limited adj1 (speech$ or verbal$)).tw,kf.
22 (nonverbal or non-verbal or "no speech").tw,kf.
23 (pre-linguistic or prelinguistic).tw,kf.
24 vocabulary/
25 (vocabular$ or lexicon$).tw,kf.
26 functional word$.tw,kf.
27 Mutism/
28 (mute or mutism).tw,kf.
29 or/12-28
30 randomized controlled trial.pt.
31 controlled clinical trial.pt.
32 randomi#ed.ed.ab.
33 placebo$ .ab.
34 drug therapy.fs.
35 randomly.ab.
36 trial.ab.
37 groups.ab.
38 or/30-37
39 exp animals/ not humans.sh.


**Wodka 2013**

**Yoder 2006**
CONTRIBUTIONS OF AUTHORS

HS conceived the protocol.
AB, HS, JZ and CS designed the protocol.
AB, HS and JZ co-ordinated the protocol.
AB, HS and JZ designed the search strategies.
AB, HS, JZ, CS and ATM wrote the protocol.
AB, DL and ATM provided general advice on the protocol.
AB, HS, JZ and DL performed previous work that was the foundation of the current study.

Amanda Brignell is the guarantor for this review.

DECLARATIONS OF INTEREST

Amanda Brignell is employed by the University of Melbourne as a Research Assistant, which is funded by the William Collie Trust. During the time of this protocol Amanda is completing a systematic review on language outcomes for autism spectrum disorders (ASDs), as well as conducting a study looking at communication trajectories in children with ASD. Amanda will not assess the eligibility or extract data from any studies that she is involved in should they appear in the searches for this review.

Huan Song - none known.
JianWei Zhu - none known.
Chen Suo - none known.
DongHao Lu - none known.

Angela Morgan is employed by the University of Melbourne and Murdoch Childrens Research Institute. She receives funding from the National Health and Medical Research Council for a Practitioner Fellowship (#APP1105008) and Centre of Research Excellence grants (#APP1023493; #APP1023043). Angela also receives royalties for a book she edited entitled “Dysphagia post Trauma”, which is unrelated to autism or communication therapies in autism.

Authors who are involved in studies that are eligible for inclusion in the review will not assess the eligibility or extract data from those studies.

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Internal sources

- Karolinska Institutet, Sweden.
  Provided fellowship to Huan Song
- National Health and Medical Research Council, Australia.
  Provided fellowship to Angela Morgan

External sources

- None, Other.