# Parent-mediated early intervention for young children with autism spectrum disorders (ASD) (Review)

**Oono IP, Honey EJ, McConachie H**

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[Intervention Review]

# Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Inalegwu P Oono[1], Emma J Honey[2], Helen McConachie[1]

[1]Institute of Health and Society, Newcastle University, Newcastle upon Tyne, UK. [2]Complex Neurodevelopmental Disorders Services, Northumberland, Tyne and Wear NHS Foundation Trust, Newcastle upon Tyne, UK

Contact address: Helen McConachie, Institute of Health and Society, Newcastle University, Sir James Spence Institute, Victoria Road, Newcastle upon Tyne, NE1 4LP, UK. h.r.mcconachie@newcastle.ac.uk.

**Editorial group:** Cochrane Developmental, Psychosocial and Learning Problems Group.
**Publication status and date:** Edited (no change to conclusions), published in Issue 10, 2013.
**Review content assessed as up-to-date:** 28 February 2013.

**Citation:** Oono IP, Honey EJ, McConachie H. Parent-mediated early intervention for young children with autism spectrum disorders (ASD). *Cochrane Database of Systematic Reviews* 2013, Issue 4. Art. No.: CD009774. DOI: 10.1002/14651858.CD009774.pub2.

## ABSTRACT

### Background

Young children with autism spectrum disorders (ASD) have impairments in the areas of communication and social interaction and often display repetitive or non-compliant behaviour. This early pattern of difficulties is a challenge for parents. Therefore, approaches that help parents develop strategies for interaction and management of behaviour are an obvious route for early intervention in ASD. This review updates a Cochrane review first published in 2002 but is based on a new protocol.

### Objectives

To assess the effectiveness of parent-mediated early interventions in terms of the benefits for both children with ASD and their parents and to explore some potential moderators of treatment effect.

### Search methods

We searched a range of psychological, educational and biomedical databases including CENTRAL, MEDLINE, Embase, PsycINFO and ERIC in August 2012. As this is an update of a previous review, we limited the search to the period following the original searches in 2002. Bibliographies and reference lists of key articles were searched, field experts were contacted and key journals were handsearched.

### Selection criteria

We included only randomised controlled trials of early intervention for children with ASD. The interventions in the experimental condition were mediated by parents; the control conditions included no treatment, treatment as usual, waiting list, alternative child-centred intervention not mediated by parents, or alternative parent-mediated intervention of hypothesised lesser effect than the experimental condition.

### Data collection and analysis

Two review authors (HM and IPO) independently screened articles identified in the search and decided which articles should be retrieved in full. For each included study, two review authors (IPO and EH) extracted and recorded data, using a piloted data collection form. Two review authors (IPO and HM) assessed the risk of bias in each study. We performed data synthesis and analysis using The Cochrane Collaboration's Review Manager 5.1 software.

### Main results

The review includes 17 studies from six countries (USA, UK, Australia, Canada, Thailand and China), which recruited 919 children with ASD. Not all 17 studies could be compared directly or combined in meta-analyses due to differences in the theoretical basis underpinning interventions, the duration and intensity of interventions, and the outcome measurement tools used. Data from subsets of 10 studies that evaluated interventions to enhance parent interaction style and thereby facilitate children's communication were included in meta-analyses. The largest meta-analysis combined data from 316 participants in six studies and the smallest combined data from 55 participants in two studies. Findings from the remaining seven studies were reported narratively.

High risk of bias was evident in the studies in relation to allocation concealment and incomplete outcome data; blinding of participants was not possible. Overall, we did not find statistical evidence of gains from parent-mediated approaches in most of the primary outcomes assessed (most aspects of language and communication - whether directly assessed or reported; frequency of child initiations in observed parent-child interaction; child adaptive behaviour; parents' stress), with findings largely inconclusive and inconsistent across studies. However, the evidence for positive change in patterns of parent-child interaction was strong and statistically significant (shared attention: standardised mean difference (SMD) 0.41; 95% confidence interval (CI) 0.14 to 0.68, P value < 0.05; parent synchrony: SMD 0.90; 95% CI 0.56 to 1.23, P value < 0.05). Furthermore, there is some evidence suggestive of improvement in child language comprehension, reported by parents (vocabulary comprehension: mean difference (MD 36.26; 95% CI 1.31 to 71.20, P value < 0.05). In addition, there was evidence suggesting a reduction in the severity of children's autism characteristics (SMD -0.30, 95% CI -0.52 to -0.08, P value < 0.05). However, this evidence of change in children's skills and difficulties as a consequence of parent-mediated intervention is uncertain, with small effect sizes and wide CIs, and the conclusions are likely to change with future publication of high-quality RCTs.

### Authors' conclusions

The review finds some evidence for the effectiveness of parent-mediated interventions, most particularly in proximal indicators within parent-child interaction, but also in more distal indicators of child language comprehension and reduction in autism severity. Evidence of whether such interventions may reduce parent stress is inconclusive. The review reinforces the need for attention to be given to early intervention service models that enable parents to contribute skilfully to the treatment of their child with autism. However, practitioners supporting parent-mediated intervention require to monitor levels of parent stress. The ability to draw conclusions from studies would be improved by researchers adopting a common set of outcome measures as the quality of the current evidence is low.

## PLAIN LANGUAGE SUMMARY

### Early intervention delivered by parents for young children with autism spectrum disorders

Autism spectrum disorders (ASD) affect more than 1% of children and is usually evident in behaviour before the age of three years. A child with ASD lacks understanding of how to interact with another person, may not have developed language or understand other people's communication, and may insist on routines and repetitive behaviours. This early pattern of difficulties is a challenge for parents. Therefore, helping parents to develop strategies for interaction and management of behaviour is an obvious route for early intervention. The present review brings up to date one published in 2003, which found only two well-designed studies. This review, based on a new protocol, includes 17 randomised controlled trials, most published since 2010, in which interventions delivered by parents were compared with no treatment or local services, or alternative child-centred intervention such as nursery attendance, or another parent-delivered intervention that differed in some way from the main condition. We were able to combine outcome information and so increase confidence in the results. All the studies were rated on the quality of their evidence, which was then taken into account in judging how firmly conclusions could be drawn.

The studies varied in the content of what parents were trained to do, and over what length of time parents had contact with professionals. Parents received training either individually with their child or in groups with other parents. In the majority of the studies, the interventions aimed to help parents be more observant and responsive during interactions with their child in order to help their child develop communication skills.

In summary, the review finds sufficient evidence that the ways in which parents interacted with their children did change as intended. The review also suggests improvement in child outcomes such as understanding of language and severity of autism characteristics as a result of interventions delivered by parents. However, important outcomes such as other aspects of children's language, children's adaptive skills and parent stress did not show change. The evidence is not yet strong for any outcome and would benefit from researchers measuring effects in the same ways.

## SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

**Child and parent outcomes following parent-mediated interventions for young children with autism spectrum disorders (ASD)**

**Patient or population:** children aged 1 year to 6 years 11 months with diagnosis of ASD
**Settings:** home, clinic, or both, interventions delivered through group or 1-to-1 sessions
**Intervention:** parent-mediated early intervention
**Comparison:** no treatment or treatment as usual (including alternative child-centred intervention not mediated by parents, alternative parent-mediated intervention that differed in some way from the experimental condition and waiting list control groups, for example, intensity)

| **Outcomes** | **Illustrative comparative risks* (95% CI)** | | **No of participants (studies)** | **Quality of the evidence (GRADE)** | **Comments** |
|---|---|---|---|---|---|
| | **Assumed risk** | **Corresponding risk** | | | |
| | **No treatment or treatment as usual** | **Parent-mediated early intervention** | | | |
| **Language - joint (direct or independent assessment)**<br>EIDP/PSDP, PLS-IV/CASL[1] | - | The mean language - joint (independent assessment) in the intervention groups was<br>**0.45 standard deviations higher**<br>(0.05 lower to 0.95 higher) | 64<br>(2 studies) | ⊕⊕○○<br>**low** [2] | SMD 0.45 (-0.05 to 0.95) . Higher scores indicate improvement. Duration of intervention ranged from 12 weeks to 1 year. This is small effect [3] |
| **Communication (reported)**<br>VABS[1] | The mean communication (reported) ranged across control groups from<br>**60.93 to 67.7** | The mean communication (reported) in the intervention groups was<br>**5.31 higher**<br>(6.77 lower to 17.39 higher) | 228<br>(3 studies) | ⊕⊕○○<br>**low** [2] | The mean value was 5.31 points higher for the intervention group. Higher scores indicate improvement. Duration of interventions ranged from 1 to 2 years |
| **Language - expression (direct or independent assessment)**<br>PLS-IV, MSEL[1] | - | The mean language - expression (direct assessment) in the intervention groups was<br>**0.14 standard deviations higher**<br>(0.16 lower to 0.45 higher) | 264<br>(3 studies) | ⊕⊕○○<br>**low** [2] | SMD 0.14 (-0.16 to 0.45) . Higher scores indicate improvement. Duration of interventions ranged from 12 weeks to 2 years. This is a small and uncertain effect [3] |

| | | | | | |
|---|---|---|---|---|---|
| **Language - Comprehension (direct or independent assessment)**<br>PLS, MSEL[1] | - | The mean language - comprehension (direct assessment) in the intervention groups was<br>**0.29 standard deviations higher**<br>(0.2 lower to 0.78 higher) | 200<br>(2 studies) | ⊕⊕○○<br>**low** [2] | SMD 0.29 (-0.2 to 0.78) . Higher scores indicate improvement. Duration of intervention ranged from 1 to 2 years in the studies. This effect size is small and uncertain [3] |
| **Parent-child interaction (parent synchrony)** | - | The mean parent-child interaction (parent synchrony) in the intervention groups was<br>**0.9 standard deviations higher**<br>(0.56 to 1.23 higher) | 244<br>(3 studies) | ⊕⊕○○<br>**low** [2] | SMD 0.9 (0.56 to 1.23). Higher scores indicate improvement. Duration of intervention ranged from 12 weeks to 1 year. This is large effect size [3] |
| **Parents'level of stress**<br>PSI, SAC[1] | - | The mean parents' level of stress in the intervention groups was<br>**0.17 standard deviations lower**<br>(0.7 lower to 0.36 higher) | 55<br>(2 studies) | ⊕⊕○○<br>**low** [2] | SMD -0.17 (-0.7 to 0.36) . Lower scores indicate improvement. Duration of interventions ranged from 12 weeks to 1 year. This is a small and uncertain effect [3] |
| CI: confidence interval; SMD: standardised mean difference | | | | | |
| GRADE Working Group grades of evidence<br>**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.<br>**Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.<br>**Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.<br>**Very low quality:** We are very uncertain about the estimate. | | | | | |

[1] CASL: Comprehensive Assessment of Spoken Language, quotients; EIDP: Early Intervention Developmental Profile; MSEL: Mullen Scales of Early Learning; PLS-IV: Preschool Language Scale-IV; PSDP: Preschool Developmental Profile; PSI: Parental Stress Inventory; SAC: Stress Arousal Checklist; VABS: Vineland Adaptive Behavior Scales.

[2] Quality of evidence has been rated as low across domains due to the small numbers of studies combined.

[3] Cohen's interpretation of effect size (rule of thumb): 0.2 is considered a small effect, 0.5 is considered a moderate effect and 0.8 or higher is considered as large effect.

# BACKGROUND

## Description of the condition

Autism is the core disorder of the pervasive developmental disorders as defined in the International Classification of Diseases and Related Health Problems, 10th edition (ICD-10) (WHO 2010) and the Diagnostic and Statistical Manual of Mental Disorders IV, Text Revision (DSM-IV-TR) (APA 2000). It is evident before the age of three years and is characterised by impairments in communication and social interaction and the presence of restricted and repetitive behaviours and impaired imagination. The prevalence of core autism is accepted to be around four per 1000 (Baird 2006). Autism is, however, understood to be on a continuum rather than being a distinct category, with clinical agreement on a range of difficulties that can be classified as 'autism spectrum disorders' (ASD). The prevalence for all ASD is around 11 per 1000, with a male: female ratio of 3.3:1 (Baird 2006). Young children with difficulties on the autism spectrum pose challenges to family members and others who interact with them: they lack understanding of how to initiate and respond to joint attention with another person, have difficulties in social timing of communication and may not understand other people's intentions as expressed through language and gestures, even though they may appear affectionate and want to be with other people socially. They have difficulty organising their responses and inhibiting repetitive behaviours and interests. Children with ASD frequently pose considerable behaviour challenges to their parents and other family members.

## Description of the intervention

Previous literature reviews have suggested the effectiveness of a number of early intervention programmes (Dawson 1997; Rogers 1998a; Smith 1999), as have more recent reviews of the evidence (Ospina 2008; Rogers 2008), but the quality of the evidence base is still weak. The field of ASD remains controversial, with a range of questionable claims for efficacy of therapies and few successful replication studies (Diggle 2002).

ASD early intervention programmes vary considerably in their theoretical background (Prizant 1998). Some approaches use applied behaviour analysis (ABA) or early intensive behavioural interventions (EIBI) in intensive programmes that are based at home but delivered primarily by trained therapists (for example, Howlin 1987; McEachin 1993; Sallows 2005; Reichow 2012). Others have an educational framework, such as project TEACCH (Treatment and Education of Autistic and related Communication handicapped CHildren), with an emphasis on structuring class environments through visual cueing, communication routines and individual tasks (for example, Lord 1994). The TEACCH project aims to increase children's independence and is designed to work on their existing strengths rather than focusing on weaknesses. Other programmes focus more on communication partners such as parents and emphasise the creation of naturalistic communication opportunities, enhancing reciprocity between communication partners, enhancing children's motivation for social interaction and prompting specific social behaviours (for example, Rogers 1991; Koegel 1995; Aldred 2004).

Research in this area has typically involved children aged between one and seven years (for example, Koegel 1996; Jocelyn 1998; Smith 2010); and although these programmes may differ in content, they all advocate treatment implementation as early as possible as a matter of clinical urgency. The age at which intervention starts has been reducing since the early 2000s with the advent of earlier identification and diagnosis of ASD (Charman 2010). However, a diagnosis of ASD, based on behavioural observation, is not given before the age of 12 months, as children's impairments in social communication cannot be interpreted until the second year of life at the earliest. Stability of diagnosis before 30 months can be poor (Turner 2007).

Some reviews have suggested that successful early intervention programmes have important similarities, whatever their apparently different theoretical foundations (for example, Dawson 1997; Prizant 1998). Indeed, Rogers conducted a comparative analysis of the elements of apparently contrasting programmes to demonstrate how each may address the underlying neuropsychological processing difficulties evidenced by children with ASD, including intersubjectivity (interpersonal sharing including establishing joint attention to objects), and emotional functioning and imitation (Rogers 1998). It has been suggested that successful programmes are those in which the 'dose' is intensive (a significant number of hours per week and rigorous levels of structure and instruction are introduced into the child's world (Eldevik 2009)). Programmes may thus have to effect a change through the family system in order to treat ASD successfully, as well as offer expert educational support.

The involvement of parents in implementing intervention strategies designed to help their autistic children has a history stretching back to the 1970s (for example, Schopler 1971). Within the ASD treatment literature there have been a number of studies that evaluate specific parent training approaches in dealing with behaviour problems (for example, Howlin 1987; Vriend 2011), in improving parent-child interactions (for example, Koegel 1996; Dawson 1997; McConachie 2005), in facilitating communication (for example, Prizant 1997; Aldred 2004), and in implementing an ABA approach (for example, Smith 2000). In addition, there are evaluations of the added value of parent involvement to a daycare or nursery programme (for example, Jocelyn 1998; Rickards 2007). A review by Boyd 2011 concludes that "many of the promising focused intervention practices and comprehensive treatment models (CTMs) involve components of naturalistic interventions for teaching pivotal skills in natural environments and parent-implemented approaches where carers learn strategies to better support their children's development". Harnessing the skills of parents allows the opportunity for generalisation of child learning between environments, and consistency of management strategies.

## How the intervention might work

Training parents as 'therapists' allows intervention to begin early, with the aim that parent interaction strategies help enhance children's earliest social relationships. It is important, given the nature of the children's impairments, that parents support the child in establishing shared interest in each other and in objects, and learn the power of imitation. If parents act in a way that is 'synchronous' with their child's focus and intentions, then language and communication are enhanced (Siller 2008). The secondary effects may be reduced frustration for the child, as well as increased parent confidence and skills. Increased parental skills allow for continual opportunities for child learning in a range of situations. Furthermore, training parents in new skills has frequently been carried out in groups, allowing for mutual support and potential reduction of parental stress. Where parent training is an adjunct to an education-based intervention, the amount of ASD-appropriate intervention is increased, with generalisation of child learning across different people and environments.

## Why it is important to do this review

Since the mid 2000s, there has been an increase in research publications that seek to address issues surrounding early identification and early interventions for children with ASD (Boyd 2011). The earlier version of this Cochrane review, Diggle 2002, found only two randomised controlled trials (RCT) of parent-mediated early intervention. From 2009 onwards, there has been a surge in the publication of RCTs of early intervention where parents are key to the delivery. In addition to improvement in research design, improvements in screening have enabled accurate detection of ASD at an age earlier than was documented about 30 years ago (that is, some children are now diagnosed as early as two years of age). However, doubt remains about which interventions are effective for young children with ASD and what constitutes an objective assessment of improvement. Furthermore, the increased number of studies raises a potential opportunity to link ASD and other characteristics to the outcomes of intervention. However, these developments have not yet led to consensus answers to important questions for healthcare policymakers and parents alike: What intervention should money be spent on? Which children, and which parents, will benefit most from what intervention? Is there evidence of greater benefit with earlier detection of ASD and thus earlier intervention? How long should interventions last?

# OBJECTIVES

The primary aim of this review is to assess the effectiveness of parent-mediated early interventions in terms of the benefits for both children and their parents. A secondary aim is to attempt to explore some potential moderators of treatment effect.

# METHODS

## Criteria for considering studies for this review

### Types of studies

We included only RCTs in this review as studies where participants are not randomly allocated to groups are more liable to bias.

### Types of participants

- Parents of children with ASD, aged between one year and six years eleven months. Studies that include child participants whose ages fall outside of this range of one year to six years eleven months may be included in the review, for example, if fewer than 5% of the children are above six years eleven months at the start of the study. The term 'parent' was used to include carers who take on a parental role.
- Diagnosis of ASD to include autism, Asperger's syndrome, Pervasive Developmental Disorder (PDD) and PDD Not Otherwise Specified (PDD NOS).
- Where a study included child participants with a variety of developmental disorders, it was included only if results were presented separately for the ASD group.

### Types of interventions

Interventions in which parents were trained by professionals in strategies designed to improve the management of their child's ASD-related difficulties. Parents must have received ongoing supervision and support from professionals. The training may have involved group or individual coaching of parents in a planned (potentially replicable) approach designed to help them promote their child's communicative and social development, learning, skills or control of behaviour.

The control conditions were no treatment, treatment as usual, a waiting list group, an alternative child-centred intervention not mediated by parents or an alternative parent-mediated intervention that differed in some way from the experimental condition. Where there are two alternative parent-mediated interventions, one is likely to be a 'contact control' and would be regarded as the 'control' group; where one is of higher intensity, it would be regarded as the 'experimental' intervention.

### Types of outcome measures

A range of measures is currently in use to confirm the diagnosis of ASD and characterise children with ASD. No particular measure or reporting of an outcome was used as an inclusion criterion for this review.

#### Primary outcomes

##### Child communication and social development

- Language development (comprehension and expression)*
- Social communication skills*
- Skills in interaction with parent*

##### Parental outcome

- Parents' level of stress*

#### Secondary outcomes

##### Child ability

- Developmental/intellectual gains
- Adaptive behaviour

##### Child problem behaviour

- Severity of autism characteristics*
- Maladaptive behaviour*

##### Parental outcomes

- Parents' satisfaction with therapy
- Parents' confidence in coping with child's disability and behaviour problems

##### Cost of intervention

- Any cost information provided by the authors

The outcomes marked with (*) are used to populate the Summary of findings for the main comparison.

#### Timing of outcome assessment

We collected pre-treatment (baseline) and outcome data. Outcome data were collected immediately post-treatment or at the time points closest to the following periods as appropriate: six months, one year, two years and four years.

## Search methods for identification of studies

We considered published or unpublished RCTs, with no language restrictions.

### Electronic searches

We searched the following databases between the year 2002 to August 2012 for relevant publications.

- Cochrane Central Register of Controlled Trials (CENTRAL), part of *The Cochrane Library* - from 2002 to August 2012.
- Ovid MEDLINE(R) - from 2002 to August 2012.
- Embase - from 2002 to August 2012.
- ERIC (Educational Resources Information Centre) - from 2002 to August 2012.
- PsycINFO - from 2002 to August 2012.
- CINAHL (Cumulative Index to Nursing and Allied Health Literature) - from 2002 to August 2012.
- Dissertation Abstracts International - from 2002 to August 2012.
- Social Sciences Abstracts - from 2002 to August 2012.
- Sociological Abstracts - from 2002 to August 2012.
- Linguistics and Language Behavior Abstracts - from 2002 to August 2012.
- Cochrane Database of Systematic reviews (CDSR), part of *The Cochrane Library* - from 2002 to August 2012.
- Database of Abstracts of Reviews of Effects (DARE) - from 2002 to August 2012.
- National Research Register (NRR) Archive - from 2002 to August 2012.
- LILACS (Latin American Health Sciences Literature) - from 2002 to August 2012.
- Turning Research into Practice (TRIP) database - from 2002 to August 2012.
- OpenGrey - from 2002 to August 2012.
- ASSIA (Applied Social Sciences Index and Abstracts) - from 2002 to August 2012.
- IBSS (International Bibliography of the Social Sciences) - from 2002 to August 2012.
- National Criminal Justice Reference Service Abstracts - from 2002 to August 2012.
- WHO International Clinical trials Registry Platform (ICTRP) - from 2002 to August 2012.
- metaRegister of Controlled Trials (mRCT) - from 2002 to August 2012.
- CinicalTrials.gov - from 2002 to August 2012.

Search terms were adapted for each database using appropriate syntax and controlled vocabulary. As this is an update of a previous review (Diggle 2002), we limited the search to the period from 2002 to August 2012. The search strategies used for this update are reported in Appendix 1. To identify studies that were not yet indexed in the above databases, Google Scholar was searched. In order to keep up to date with new articles that may be added to databases after our search, alerts were set up in databases that had provision for this facility (for example, Ovid MEDLINE, Google Scholar, etc.)

### Searching other resources

We examined other sources of information including the bibliographies of systematic and non-systematic reviews and reference lists of key articles identified through the search strategy. We contacted experts in the field by letter in order to identify unpublished studies. We also handsearched key journals to identify studies not yet electronically catalogued in the databases searched, in addition to using Google Scholar to search the World Wide Web.

## Data collection and analysis

### Selection of studies

All citations generated through the search strategy were transferred to the reference management program EndNote Web X5. Two review authors (HM, expert in early autism, and IPO, expert in systematic reviews) independently screened titles and abstracts identified in the search, and indicated which reports should be retrieved in full. The full report of any title or abstract for which there were insufficient data was retrieved. The same review authors independently read full reports and determined whether these studies met the specified inclusion criteria. Multiple reports of the same study were sought. Two review authors (HM and IPO) independently assessed studies for inclusion from the pool of remaining studies.

### Data extraction and management

For each included study, two review authors (IPO, EH) extracted and recorded the following data, using a piloted data collection form: study location, funding source, study design, methods, participant details (diagnostic description and severity of impairments, parent characteristics), type of intervention (including the intensity and duration of intervention), measurement of adherence, outcome measures, any reported cost data, and key conclusions of study authors.

### Assessment of risk of bias in included studies

We used The Cochrane Collaboration tool for assessing risk of bias (Higgins 2011). Two review authors (HM and IPO) independently assessed the risk of bias for each included study based on the following six domains; judgements were rated as 'high', 'low' and 'unclear' risk of bias. Final judgements of risk of bias were then reached by consensus. This is summarised and presented in Risk of bias in included studies, which can be found in the results section.

**Random sequence generation:** we described the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

**Allocation concealment:** we described the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.

**Blinding of participants and personnel:** we described all measures used, if any, to blind personnel from knowledge of which intervention a participant received. As the focus of the review is on parent-mediated early intervention, the parent participants could not be blind, so the judgement depended on whether the outcome was likely to have been influenced by lack of blinding.

**Blinding of outcome assessment:** we described all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We also provided any information relating to whether the intended blinding was effective.

**Incomplete outcome data:** we described the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. We also stated whether attrition and exclusions are reported, the numbers in each intervention group (compared with total randomised participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.

**Selective outcome reporting:** we assessed the possibility of selective outcome reporting by the study authors by checking whether any of the stated outcomes were not reported at the end of the study.

In addition, for important outcomes included in Summary of findings for the main comparison, we assessed the overall quality of evidence using the 'GRADE' approach (GRADE working group). Factors taken into consideration before judgements were made (the GRADEpro criteria) include limitations of detailed designs and execution (risk of bias) in studies, inconsistency (heterogeneity), indirectness (population, intervention, comparison and outcome), imprecision and publication bias (see also below).

### Measures of treatment effect

Any procedures for making decisions set out in the protocol but not implemented in the review are summarised in Table 1 below.

#### Categorical data

Binary outcomes were not encountered in the present review. If encountered in future reviews, they will be analysed by calculation of the odds ratio (OR) with a 95% confidence interval (CI).

#### Continuous data

Continuous data encountered were analysed on the assumption that the means and the accompanying standard deviations (SD) were from a normally distributed sample with no evidence of skew.

Where studies used different measurement scales for assessing outcomes of a similar construct, we used standardised mean differences (SMD) with the 95% CI as a summary statistic. In cases where studies used a uniform measurement scale for assessing outcomes, the mean difference (MD) was preferred. While a number of the studies examined reported change from baseline, all studies reported means (and SD) at start and end (or provided this information upon request).Thus, end point means and accompanying SD were extracted. We calculated SMDs using Hedges *g*.

#### Multiple outcomes

In studies that provided multiple, interchangeable measures of the same construct at the same point in time (for example, multiple measures of child language), we intended to combine results across those measures that are most similar in their properties, that is, where authors used the same or similar wording to describe the outcome construct, and the method of administration was the same (for example, for parent questionnaires about child maladaptive behaviour). However, in this review, it was frequently judged that methods of administration were different, and constructs were dissimilar, and so separate analyses were conducted (for example, direct assessment of children's language skills analysed separately from parent-report; child comprehension of language separately from child expressive language). Where similar outcomes were combined, we used the reported average or combined means provided in eligible articles.

### Unit of analysis issues

#### Cluster-randomised trials

We did not find any cluster-randomised trials.

#### Studies with multiple treatment groups

In cases where studies compare more than one intervention condition, we intended to combine results across eligible (parent-mediated early intervention) intervention groups and compare these with the control group, making single, pair-wise comparisons. However, none of the studies included in the meta-analyses had multiple treatment groups.

#### Cross-over studies

Similarly, the only study that had a cross-over design (Wong 2010) was not included in the meta-analysis as it differed significantly in its choice of measures and methodology.

### Dealing with missing data

We contacted the authors of included studies to supply any unreported data (for example, group means and SDs, details of dropouts, and details of interventions received by the control group). We also described missing data and dropouts/attrition for each included study in the 'Risk of bias' table, and where necessary, discussed the extent to which these could impact upon the results/ conclusions of the review and provided reasons (as stated by authors) for missing data in the review.

### Assessment of heterogeneity

We intended to explore the possibility of assessing clinical variation across studies by comparing the distribution of duration and intensity of intervention. However, the information given in studies was not presented in such a way that hours of intervention could be estimated in order to make systematic comparisons. Heterogeneity according to focus of intervention, and whether the control condition was less (or more) intensive than the experimental intervention, was considered in choosing the studies included in meta-analysis (see Appendix 2 study characteristics). Type of intervention is addressed in the narrative results.

Statistical heterogeneity was assessed by computing the $I^2$ statistic (Higgins 2011), a quantity that describes approximately the proportion of variation in point estimates that is due to heterogeneity rather than sampling error. In cases where we combined only a few studies, we preferred direct comparison of any difference between papers over the $I^2$ values owing to the small numbers. Heterogeneity found in the analyses could be explained by the way outcomes were assessed in the articles (direct assessment versus reports), the coding schemes used by researchers, differences in follow-up intervals (which ranged from two to 13 months) and the varied nature of the interventions and outcomes reported. Thus, further statistical analyses were not carried out due to these differences.

### Assessment of reporting biases

We used funnel plots (estimated differences in treatment effects against their standard error) to subjectively assess reporting bias in the studies.

The extent of bias in the interpretation of results, for example, where the interpretation is based on results from treatment completers alone rather than the intention-to-treat analysis, or the significance of an inadequately powered studies is over-interpreted, or there is over-reliance on non-blinded measures, is addressed in the narrative results.

### Data synthesis

We synthesised results in a meta-analysis (using the inverse variance method) across interventions that were similar in their theoretical basis, the way in which parent-training was delivered, duration and intensity, and that used outcome measures with similar psychometric and psychological properties. We have reported results as means with SDs. We used both a fixed-effect and a random-effects model and compared the results to assess the impact of statistical heterogeneity. Unless the model was contraindicated (for example, if there was funnel plot asymmetry or a large difference between the results obtained from fixed-effect and random-effects meta-analyses), we have presented only the results obtained from the random-effects model. Data synthesis was conducted using the Review Manager 5.1 software (RevMan 2011).

### Subgroup analysis and investigation of heterogeneity

We conducted subgroup analyses to investigate the following possible sources of heterogeneity: how outcomes were assessed (direct reporting by outcome assessors such as trained psychologists, or reported by parents and carers of children). Due to variability in reporting methods, moderators such as duration, intensity, and type of intervention and parental education were not investigated directly in our analyses. Child intelligence quotient (IQ) could not be investigated as it was usually reported by group means rather than in ability bands. However, information relating to all these domains has been summarised and included in the narrative synthesis (Included studies).

### Sensitivity analysis

We conducted sensitivity analyses to determine whether findings were sensitive to restricting the analyses to studies judged to be at low risk of bias based upon:

- only studies judged to be of low risk of selection bias (associated with sequence generation or allocation concealment);
- only studies judged to be of low risk of performance and detection bias (associated with issues of blinding);
- only studies judged to be of low risk of attrition bias (associated with completeness of data).

In the analyses, we used the phrase 'No difference' to indicate instances where the overall conclusion or direction of effect remained unchanged. This does not take into account changes in the effect size estimate. The phrase 'There was a difference' was used to describe instances where there was a change in the overall conclusion that could be drawn from the initial estimates following sensitivity analysis (for example, a change from a statistically significant result to an inconclusive or non-significant one). In such cases, effects estimates are provided in the footnotes. See Table 2 below.

# RESULTS

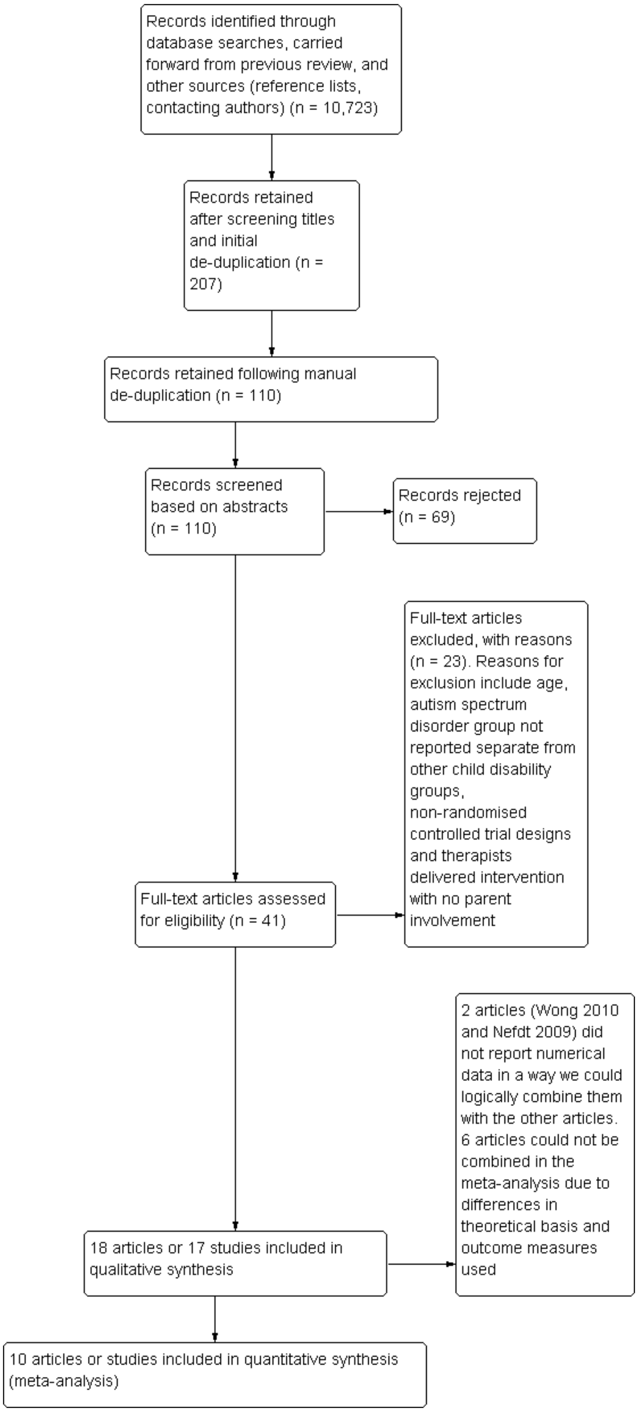
## Description of studies

### Results of the search

This review is an update of a previous review (Diggle 2002); as such the search was limited to papers published since 2002. (For details of the original 2002 search, see Appendix 3.) From a search of multiple databases, over 10,000 articles were initially identified, although this included a significant number of duplicate articles. All databases yielded relevant citations; however, most of the relevant articles originated from PsycINFO, ERIC and Ovid MEDLINE/PubMed. Twenty-seven additional articles were identified through handsearching of relevant websites for grey literature, contacting authors for unpublished articles and searching of reference lists of publications. Two articles were carried forward from the previous review.

After removal of duplicates, the remaining 110 articles were screened by two review authors (HM and IPO) and 69 records were rejected based on their titles and abstracts. The remaining 41 full-text articles were further assessed for eligibility and inclusion using a set of predefined inclusion and exclusion criteria. At this point 23 articles were excluded; the Cochrane Group were consulted about three articles and decision taken to exclude them (two had partial non-randomisation; one was not analysed as randomised). The excluded articles and reasons for their exclusion are listed in the Characteristics of excluded studies table. The remaining 18 articles were included in this review. Of these 18 articles, two were separate accounts of the same research evaluation study, with the earlier focusing on the parent outcomes and the later article focusing on the child outcomes. These two papers (Tonge 2006 and Tonge 2012) were thus combined. As a result we had 17 studies for the review. Figure 1 is a flow diagram showing a summary of the search and synthesis described above. Further details about these articles can be found in the Included studies section and Characteristics of included studies table.

Figure 1. Study flow diagram.



## Included studies

### Participants

There were a total of 919 children across the included studies. Fourteen studies (Jocelyn 1998; Drew 2002; Aldred 2004; Rickards 2007; Silva 2009; Dawson 2010; Green 2010; Kasari 2010; Smith 2010; Wong 2010; Carter 2011; Pajareya 2011; Roberts 2011; Siller 2012) reported on the numbers of males and females in their studies, with 645 males and 171 females (a male:female ratio of approximately 3.8:1). However, three studies (Tonge 2006/Tonge 2012; Nefdt 2010; Casenhiser 2011) did not report on the number of males and females. The smallest study in this review (Wong 2010) had 17 participants, while the largest (Green 2010) had 152 participants.

Children were aged between 17 months and six years with varied levels of functioning. In eight studies (Aldred 2004; Silva 2009; Nefdt 2010; Wong 2010; Carter 2011; Casenhiser 2011; Pajareya 2011; Roberts 2011), IQ was not directly assessed. However, in eight studies (Jocelyn 1998; Smith 2000; Drew 2002; Rickards 2007; Dawson 2010; Green 2010; Kasari 2010; Siller 2012), IQ was assessed in varying ways at baseline, and in three studies it was used as cut off for recruitment (for example, with participants having an IQ less than 35 being excluded from the studies) (Smith 2000; Dawson 2010; Green 2010). In one study (Tonge 2006/Tonge 2012) the Psychoeducational Profile-Revised (PEP-R) was used to assess functioning, and it was reported that scores obtained on this measure approximate IQ estimates on the Stanford-Binet Intelligence Scales. All child participants in the studies had a diagnosis of autism or ASD made by an assessing clinician or psychologist based on DSM-IV, DSM III-R and or ICD-10 classification; several of the studies used 'gold standard' instruments such as Autism Diagnostic Interview - Revised (ADI-R) or Autism Diagnostic Observation Schedule (ADOS), or both, to confirm diagnosis. None of the children had any comorbid or debilitating illness such as cerebral palsy, genetic syndromes, diagnosed hearing impairment, diagnosed visual impairment or seizures, or severe psychiatric disorders. Children were from a wide range of ethnicities including white, Hispanic, African, Caribbean, Asian, Latino and other mixed races.

### Intervention content

The content and theoretical basis of the interventions varied considerably. Fourteen of the studies had a principal focus on facilitating parent-child interaction and child communication skills through coaching of parents by therapists. In some studies, this principal focus was supplemented by educational and developmental techniques, such as those taken from Pivotal Response Treatment (Nefdt 2010) or Developmental, Individual-Difference, Relationship-Based (DIR) techniques (Casenhiser 2011; Pajareya 2011). One study focused on a massage intervention (Silva 2009), one on management of challenging behaviour (Tonge 2006/Tonge 2012), and one on early intensive behavioural intervention (Smith 2000).

### Control condition

The control conditions reported in the studies ranged from no treatment or 'treatment as usual' (local services) (Drew 2002; Aldred 2004; Tonge 2006/Tonge 2012; Green 2010; Kasari 2010; Carter 2011; Pajareya 2011) to alternative interventions (either not mediated by parents such as nursery attendance, or another parent-mediated intervention that differed in some way such as content or intensity) (Jocelyn 1998; Rickards 2007; Dawson 2010; Nefdt 2010; Silva 2009; Wong 2010; Casenhiser 2011; Siller 2012). In two studies the control condition was more intensive than the parent-mediated intervention condition (Smith 2000; Roberts 2011). In most of the studies (Jocelyn 1998; Smith 2000; Drew 2002; Tonge 2006/Tonge 2012; Rickards 2007; Dawson 2010; Green 2010; Kasari 2010; Casenhiser 2011; Roberts 2011; Siller 2012), the intervention group received the same local services as the control group. Thus it becomes difficult to judge the effectiveness of the experimental autism interventions in isolation from the services received in addition. Furthermore, there were multiple services available, with members of control groups being free to use any services of their choosing. In six studies, details of services received by the control condition were not given (Aldred 2004; Silva 2009; Nefdt 2010; Wong 2010; Carter 2011; Pajareya 2011).

### Setting

The delivery of training to parents took place in a range of different settings across the included studies. In seven of the studies, interventions were home-based (Smith 2000; Drew 2002; Rickards 2007; Dawson 2010; Pajareya 2011; Roberts 2011; Siller 2012). In six studies, interventions were centre- or clinic-based (Jocelyn 1998; Aldred 2004; Silva 2009; Green 2010; Kasari 2010; Wong 2010), and Roberts 2011 contrasted the home-based intervention with a centre-based intervention. One study used a combination of both home and centre locations for the delivery of the intervention to parents (Carter 2011). In two studies, it was unclear which locations were predominantly used for intervention delivery (Tonge 2006/Tonge 2012; Casenhiser 2011). Most of the interventions were delivered on a one-to-one basis but, in three studies, intervention was predominantly delivered to groups of parents (Jocelyn 1998; Tonge 2006/Tonge 2012; Carter 2011). In one study, the mode of delivery was self training from a manual and videotapes (Nefdt 2010). Across the studies, the implementation of taught techniques by parents was not constrained to particular settings; indeed, most encouraged parents to apply techniques opportunistically, thus generalising interventions into the child's natural environment, including home and out of home locations.

### Duration

The duration of intervention in the included studies varied greatly. Interventions lasted one week (Nefdt 2010), two weeks (Wong 2010), eight weeks (Kasari 2010), 12 weeks (Jocelyn 1998; Pajareya 2011; Siller 2012), 14 weeks (Carter 2011), 20 weeks (Tonge 2006/Tonge 2012; Silva 2009), 40 weeks (Roberts 2011), one year (Drew 2002; Aldred 2004; Rickards 2007; Green 2010; Smith 2010; Casenhiser 2011), and two years (Dawson 2010). The intensity of interventions varied considerable across studies and is presented in detail under the interventions section of individual studies in the Characteristics of included studies section of this review. Intensity of interventions mostly ranged between two to three hours per session, either in a group or for the parent and child with a therapist. Sessions were delivered at intervals ranging from twice a day through weekly and even monthly schedules. While most studies reported intensity and duration of interventions, many did not report outcome data immediately post-intervention, rather reporting values that were obtained at some later specified follow-up point.

### Location

The studies were conducted in six countries: seven were conducted in the USA (Smith 2000; Silva 2009; Dawson 2010; Kasari 2010; Nefdt 2010; Carter 2011; Siller 2012), three in the UK (England) (Drew 2002; Aldred 2004; Green 2010), three in Australia (Tonge 2006/Tonge 2012; Rickards 2007; Roberts 2011), two in Canada (Jocelyn 1998; Casenhiser 2011), one in Thailand (Pajareya 2011), and one in China (Hong Kong) (Wong 2010).

### Moderators

In eight of the studies (Drew 2002; Aldred 2004; Silva 2009; Dawson 2010; Nefdt 2010; Wong 2010; Pajareya 2011; Roberts 2011), small numbers precluded analyses to explore the potential impact of moderators such as child's age, child's baseline IQ and parental education or family socioeconomic status on reported outcomes. However, nine studies did report their attempts to explore the impact of certain baseline factors on the reported outcomes of interest. Carter 2011 reported that their intervention particularly facilitated communication development in children with lower levels of interest in objects at time 1. In Casenhiser 2011, changes in language scores were found to be significantly predicted by pre-treatment developmental quotient (DQ), initiation of joint attention and involvement; they also identified enjoyment of interaction as a marginally significant predictor of outcome following intervention. In Green 2010, analyses were carried out to assess the impact of baseline characteristic such as age, socioeconomic status, parental education, child ability (non-verbal ability and language level), centre where study was conducted and severity of disability on severity of autism symptoms. However, in this large study it was found that these variables did not significantly impact on the findings (which is a reduction of autism social-communication symptom severity). Similarly, in Jocelyn 1998 analyses of the impact of baseline IQ and severity of autism symptoms as measured by the Childhood Autism Rating Scale (CARS) were conducted and these variables were not found to have any impact on the analysis. However, the level of reduction in autism symptomatology in this study failed to reach statistical level of significance and was only described as a trend. Analyses carried out by Kasari 2010 suggested that higher carer quality of involvement scores significantly predicted increased joint engagement scores post-intervention. The relationship between family stress and outcome of intervention was explored by Rickards 2007, identifying that families with greater stress levels were likely to benefit most from the additional home-based sessions added to nursery intervention for the child. Smith 2000 analysed the relationship between diagnostic grouping, intake IQ and early mastery of verbal skills; gains in IQ were not related to baseline IQ, but were greater for children who had a diagnosis of PDD-NOS rather than autism, and for children who made greater progress within the first three months of treatment. In contrast, Siller 2012 suggested that only children with expressive language skills below 12 months evidenced reliable treatment effects on language outcomes following intervention. Furthermore, it was concluded that only parents classified as insightful at baseline effectively changed their communication in response to the experimental intervention. Finally, analyses conducted by Tonge 2006/Tonge 2012 suggested that the effect of treatment was dependent on pre-test levels of communication skills; children whose parents were in the parent education and behaviour management (PEBM) group and who had lower pre-treatment scores in communication skills domains (and by implication lower communication skills levels) registered greater gains in this domain post-intervention when compared with the control group.

### Training fidelity

Most studies reported on the fidelity of training delivered by therapists to parents. However, only five studies provided information on parent implementation of intervention procedures (adherence). For some studies this related to self report measures of either number of hours (Dawson 2010; Pajareya 2011) or weekly examination of carer diaries and carer involvement scales (Kasari 2010). In Nefdt 2010, parent-recorded videos were scored for fidelity of implementation of techniques, and parents self rated their level of confidence. Similarly, in Casenhiser 2011, video recordings were scored for fidelity of implementation of intervention techniques. However, in the remaining 13 studies, the authors did not report on adherence/parent implementation. The picture of what intervention children actually received is further complicated by scant details provided in most studies about the additional services and interventions being received by children as 'treatment as usual'. Such information is provided only by Dawson 2010, Green 2010 and Kasari 2010.

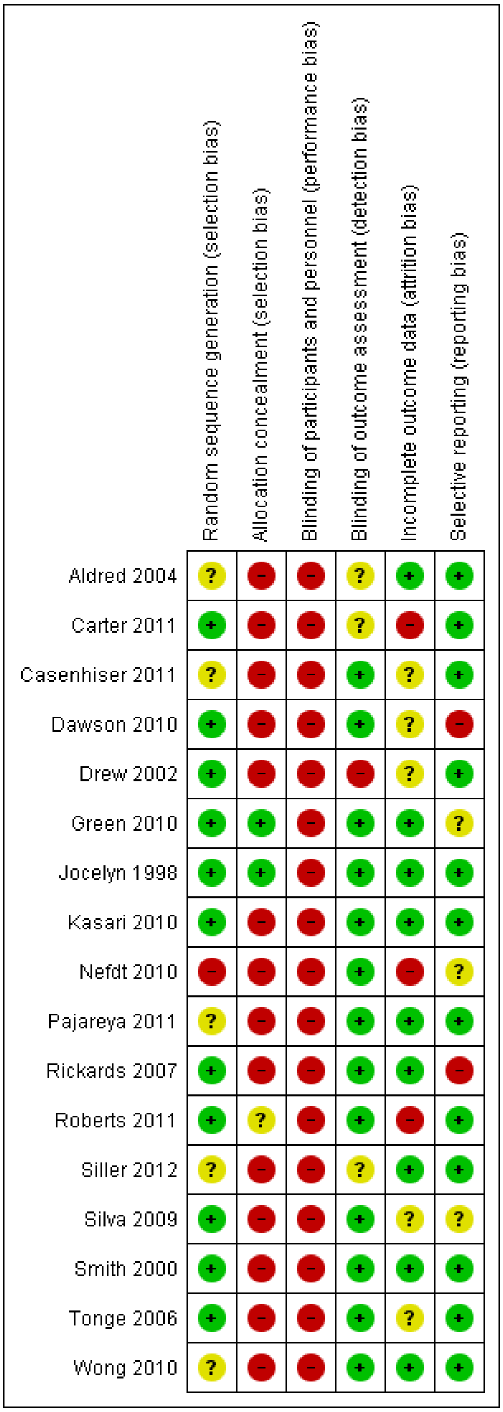
### Outcome measures

Another important factor to note about the studies included in this review is the wide variation in outcome measures used. Thus, combining the results from these measures in a meta-analysis, and by implication the inferences that may follow from such analysis, can be potentially misleading. Since a number of these measures were not applied consistently across studies, data were aggregated only across outcome measures of similar psychometric properties that assess outcomes of similar constructs. A summary of the outcome measures aggregated and a definition of these outcome measures have been included (Table 3; Table 4).

### Missing data

Missing data were judged to have been well accounted for in this review based on Cochrane guideline for assessing risk of bias (see 'Risk of bias' assessment of studies under Characteristics of included studies section and Figure 2 for details). In one paper (Carter 2011) included in the meta-analysis, we thought the degree of missing data could lead to an alteration in our estimates and in this case we conducted a sensitivity analysis to assess the impact of missing data by excluding the study from the analysis (Analysis 1.8). It was observed that there was no change in the conclusions that could be made from the analysis before and after the sensitivity analysis. In the meta-analyses, estimates from 499 participants (that is 54.2% of total study participants) were combined.

**Figure 2.**



| | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) |
|---|---|---|---|---|---|---|
| Aldred 2004 | ? | − | − | ? | + | + |
| Carter 2011 | + | − | − | ? | − | + |
| Casenhiser 2011 | ? | − | − | + | ? | + |
| Dawson 2010 | + | − | − | + | ? | − |
| Drew 2002 | + | − | − | − | ? | + |
| Green 2010 | + | + | − | + | + | ? |
| Jocelyn 1998 | + | + | − | + | + | + |
| Kasari 2010 | + | − | − | + | + | + |
| Nefdt 2010 | − | − | − | + | − | ? |
| Pajareya 2011 | ? | − | − | + | + | + |
| Rickards 2007 | + | − | − | + | + | − |
| Roberts 2011 | + | ? | − | + | − | + |
| Siller 2012 | ? | − | − | ? | + | + |
| Silva 2009 | + | − | − | + | ? | ? |
| Smith 2000 | + | − | − | + | + | + |
| Tonge 2006 | + | − | − | + | ? | + |
| Wong 2010 | ? | − | − | + | + | + |

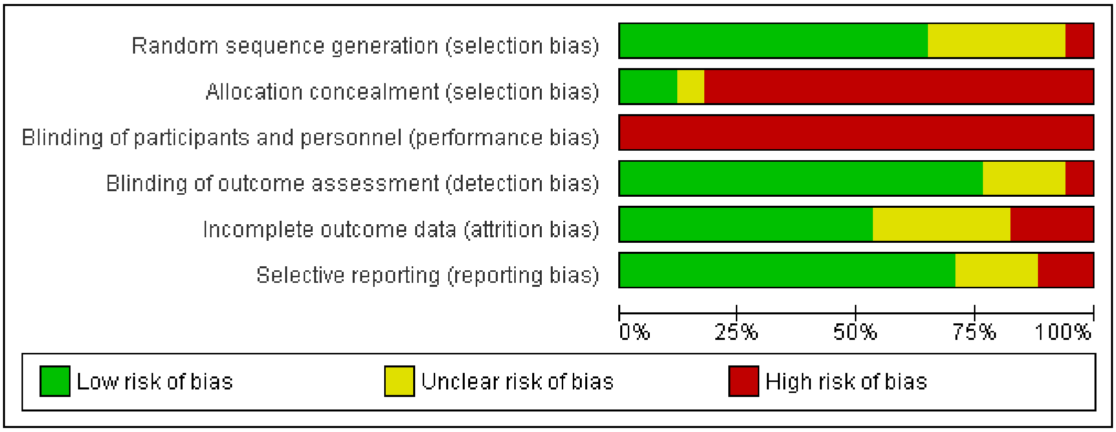
### Excluded studies

Following the electronic search, handsearching of articles and reference lists and a process of sifting as described above, 23 articles were excluded. Eight articles were excluded as they were not "parent-mediated" interventions and instead delivered by therapists or education staff (Warreyn (unpublished); Giarelli 2005; Sallows 2005; Kasari 2006; Yoder 2006; Whalen 2010; Landa 2011; Kaale 2012). Six were excluded as the primary focus was on child participants outside the age range of interest (Whittingham 2009; Frankel 2010; Lopata 2010; Sofronoff 2011; Sung 2011; Gantman 2012). Five articles were excluded as they did not provide results separately for the ASD group included in their studies (Rickards 2009; Shin 2009; Balkom 2010; Romski 2010; Tang 2011). Three were excluded as they were not full RCTs either in the process of recruitment or in the process of analysis (Oosterling 2010; Smith 2010; Silva 2011). Finally, one article (Gulsrud 2010) presents a descriptive analysis of participants in one of the included studies (Kasari 2010), not separated by condition. Further details about reasons for exclusion can be found in the Characteristics of excluded studies table.

## Risk of bias in included studies

Risk of bias was assessed across a number of domains in the articles included in this review. Figure 3 provides a 'Risk of bias' graph showing review authors' judgements about each risk of bias item presented as percentages across all included studies. Figure 2 provides a 'Risk of bias' summary on review authors' judgements about each risk of bias item or domain for each included study.

Figure 3.



### Allocation

Eleven of the articles were judged to have conducted the randomisation process in a way that fell within the 'low risk' for bias category (Figure 2; Figure 3). Low and unclear levels of risk of bias were pre-specified as acceptable for the inclusion of studies in a meta-analysis. Only one study (Nefdt 2010) was judged to be at 'high risk' for bias in this domain (Figure 2). The authors did not report the randomisation sequence generation process, and they stated "Parents were randomly assigned to either [condition] based on the order in which the family information was received".

### Blinding

The domain "Blinding of participants and personnel (performance bias)" was rated as 'high risk' for all the studies; as parents deliver the intervention, it is not logically possible to blind parents and training personnel from the intervention being delivered. Therefore, care was taken in the meta-analysis to analyse parent-report measures separately from direct (blinded) assessment measures. However, detection bias was not found to be a major issue; studies did ensure that the outcome assessors were blind to the group status and baseline characteristics of the participants. Only one article (Drew 2002) was judged to be at 'high risk' for detection bias.

### Incomplete outcome data

Fourteen of the studies addressed attrition in ways judged to be at 'low risk' or 'unclear risk' of bias (Figure 2; Figure 3). Three studies (Nefdt 2010; Carter 2011; Roberts 2011) were judged to be at high risk of bias in this domain because they reported group results for those completing intervention, with considerable attrition.

### Selective reporting

Fifteen studies reported their results in ways judged to be at 'low risk' or 'unclear risk' of bias. Two studies were judged to be at high risk of bias in this domain either because emphasis was placed upon an outcome ('change in diagnosis') not pre-specified (Dawson 2010), or because results relating to only some of the measures used were reported (Rickards 2007).

### Summary

In summary, only the study Jocelyn 1998 was found to have low risk of bias in all domains.

## Effects of interventions

See: **Summary of findings for the main comparison**

Ten studies were included in meta-analyses (Jocelyn 1998; Drew 2002; Aldred 2004; Dawson 2010; Green 2010; Kasari 2010; Carter 2011; Casenhiser 2011; Pajareya 2011; Siller 2012); this group of studies all evaluated intervention focusing on parent interaction style in facilitating children's communication and had a 'treatment as usual' comparison condition (that is, the intervention condition was more intensive than the control; Appendix 2). The numbers of participants involved in meta-analyses ranged from 55 in the smallest analysis to 316 in the biggest (see Data and analyses section).

### Primary outcomes

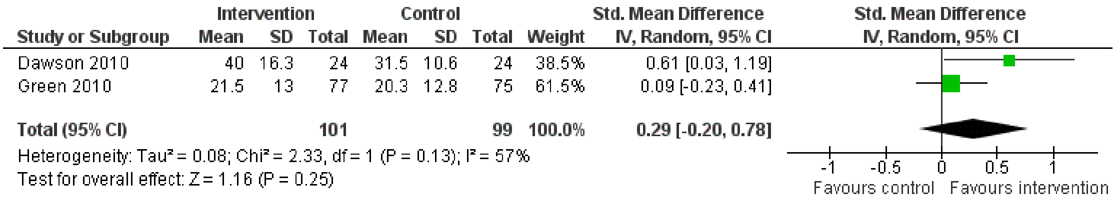
#### Child communication and social development

#### 1. Language development

A range of measures were used to assess language development. Outcomes have been reported in studies either as a total score or as comprehension and expression scores separately. Measures used included either direct assessments by blinded outcome assessors or parent/carer reports and so have been grouped accordingly in analyses.

- **Comprehension (direct or independent assessment)** : a random-effects meta-analysis (SMD) of end point means obtained from two studies (Dawson 2010; Green 2010) involving 200 children indicated a non-significant difference between the parent-mediated intervention group and the control condition (SMD 0.29; 95% CI -0.20 to 0.78, P value > 0.05) (Analysis 1.5). From the Forest plot, it is clear that the two studies are inconsistent in their effects size estimates (Figure 4). The quality of evidence for this outcome was assessed as 'low' based on the GRADE approach for assessing quality of evidence (Summary of findings for the main comparison) (GRADE working group).

**Figure 4. Forest plot of comparison: 1 Child communication and social development, outcome: 1.5 Language - Comprehension (direct or independent assessment).**



| | Intervention | | | Control | | | | Std. Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| Dawson 2010 | 40 | 16.3 | 24 | 31.5 | 10.6 | 24 | 38.5% | 0.61 [0.03, 1.19] |
| Green 2010 | 21.5 | 13 | 77 | 20.3 | 12.8 | 75 | 61.5% | 0.09 [-0.23, 0.41] |
| **Total (95% CI)** | | | **101** | | | **99** | **100.0%** | **0.29 [-0.20, 0.78]** |

Heterogeneity: Tau$^2$ = 0.08; Chi$^2$ = 2.33, df = 1 (P = 0.13); I$^2$ = 57%

Test for overall effect: Z = 1.16 (P = 0.25)

- **Comprehension (parent report)** : a random-effects meta-analysis of end point means obtained from three studies (Drew 2002; Aldred 2004; Green 2010) using the same measure (Macarthur Communicative Development Inventory) and involving 204 children found the presence of a statistically significant effect in favour of the parent-mediated intervention group (MD 36.26; 95% CI 1.31 to 71.20, P value < 0.05) (Analysis 1.6). This estimate was fairly consistent across the studies combined in the meta-analyses.

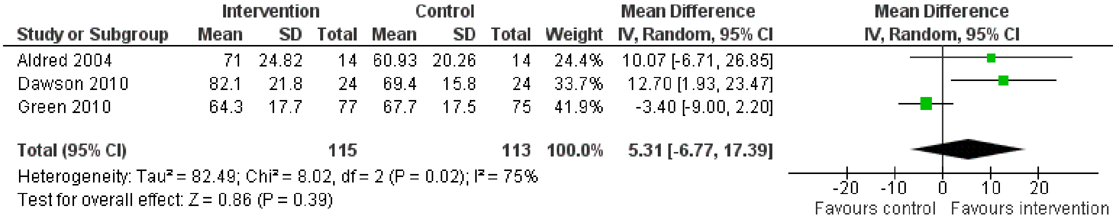
- **Expression (direct or independent assessment)** : a random-effects meta-analysis (SMD) of end point means from three studies (Dawson 2010; Green 2010; Siller 2012) involving 264 children indicated a non-significant effect on language expression between the parent-mediated intervention group and the control condition (SMD 0.14; 95% CI -0.16 to 0.45), P value > 0.05) (Analysis 1.3). This estimate was consistent across the studies combined in this analysis. Again, the quality of evidence was rated as 'low' (Summary of findings for the main comparison) (GRADE working group).

- **Expression (parent report)** : the random-effects meta-analysis of data obtained from three studies (Drew 2002; Aldred 2004; Green 2010) involving 204 children, that used the same measure (Macarthur Communicative Development Inventory) a non-significant difference between the parent-mediated intervention group and the control condition (MD 29.44; 95% CI -14.99 to 73.86, P value > 0.05). This estimate was consistent across the studies combined in the meta-analysis (Analysis 1.4).

- **Joint language (direct or independent assessment)** :a random-effects meta-analysis of means obtained from two studies (Jocelyn 1998; Casenhiser 2011) involving 64 children indicated a statistically non-significant effect on joint language between the parent-mediated intervention group and the control condition (SMD 0.45; 95% CI -0.05 to 0.95, P value = 0.08). In the two studies combined, there was considerable overlap in their CIs and a fairly consistent effects size estimate (Analysis 1.1). The quality of evidence was rated as 'low' (Summary of findings for the main comparison) (GRADE working group).

- **Child communication (parent or teacher report)** : a random-effects meta-analysis of means obtained from three studies (Aldred 2004; Dawson 2010; Green 2010) that used the same measure (Vineland Adaptive Behavior Scales) and involving a total of 228 children indicated a statistically non-significant effect between the parent-mediated intervention group and the control condition (MD 5.31; 95% CI -6.77 to 17.39, P value > 0.05) (Analysis 1.2). From the Forest plot (Figure 5), it is evident that one study (Green 2010) had an effect size that is at odds with the other two studies (Aldred 2004; Dawson 2010). This difference may be explained by the method of reporting adopted (teacher reports in Green 2010 as opposed to parent reports in Aldred 2004 and Dawson 2010). When Green 2010 was excluded from the analysis, the results for parent-reported child communication was a statistically significant difference in favour of the parent-mediated group (MD 11.93; 95% CI 2.87 to 21.00, P value < 0.05) . The quality of evidence was rated as 'low' for this outcome (Summary of findings for the main comparison) (GRADE working group). The overall evidence for this outcome is therefore inconclusive.

**Figure 5. Forest plot of comparison: 1 Child communication and social development, outcome: 1.2 Communication (reported).**



| | Intervention | | | Control | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI |
| Aldred 2004 | 71 | 24.82 | 14 | 60.93 | 20.26 | 14 | 24.4% | 10.07 [-6.71, 26.85] |
| Dawson 2010 | 82.1 | 21.8 | 24 | 69.4 | 15.8 | 24 | 33.7% | 12.70 [1.93, 23.47] |
| Green 2010 | 64.3 | 17.7 | 77 | 67.7 | 17.5 | 75 | 41.9% | -3.40 [-9.00, 2.20] |
| **Total (95% CI)** | | | **115** | | | **113** | **100.0%** | **5.31 [-6.77, 17.39]** |

Heterogeneity: Tau² = 82.49; Chi² = 8.02, df = 2 (P = 0.02); I² = 75%

Test for overall effect: Z = 0.86 (P = 0.39)

These analyses indicate that directly assessed language effect size estimates were fairly consistent across studies, and though not statistically significant they suggest an effect of intervention upon children's language skills. Assessments of language development in the meta-analyses of data obtained by parent report indicated a similar pattern (apart from report of expressive vocabulary) suggesting that lack of blinding of parents may not distort estimates of effect for language development.

### 2. Social communication skills

Carter 2011 used a directly observed assessment measure, the Early Social Communication Scales, and found no difference after intervention. Studies using a parent-report of socialisation skills, the Vineland Adaptive Behavior Scales (Smith 2000; Roberts 2011; Tonge 2012) found a varied picture depending on the contrast condition, but suggesting some improvement within the more intensive treatment group. Despite the treatment focus being on physical massage, Silva 2009 also reported a significant improvement on a measure of teacher-reported social and language skills.

### 3. Skills in interaction with parent

Several studies included a standard situation where parent and child played with toys for 10 to 20 minutes. The filmed session was then coded by observers blind to group and time. Three proportional measures were derived: duration of time in which parent and child showed shared attention to each other or joint attention to the same toy; proportion of child communicative acts that were spontaneous initiations of verbal, vocal or non-verbal communication to the parent and proportion of parent communicative acts that were parent responses to the child that had a quality of synchrony, that is, picking up the child's focus of interest, making statements (and not making requests or changing focus).

- **Shared or joint attention (coding of parent-child interactions)** : the random-effects meta-analysis of means obtained from three studies (Aldred 2004; Green 2010; Kasari 2010), which recruited 215 children, indicated that there was a statistically significant small effect in favour of the parent-mediated intervention group (SMD 0.41; 95% CI 0.14 to 0.68, P value < 0.05) (Analysis 1.7).

- **Child initiations (coding of parent-child interactions)** : a random-effects meta-analysis of means obtained from four studies (Green 2010; Kasari 2010; Carter 2011; Casenhiser 2011), which involved 268 children, indicated that there was no statistically significant difference between the intervention and control groups (SMD 0.38; 95% CI -0.07 to 0.82, P value > 0.05) (Analysis 1.8). There was moderate heterogeneity between the studies combined for this outcome ($I^2 = 60\%$).

- **Parent synchrony (coding of parent-child interactions)** : a random-effects meta-analysis of three studies (Aldred 2004; Green 2010; Siller 2012), which recruited 244 children, suggested the presence of a large and statistically significant effect in parent synchrony in favour of the parent-mediated intervention group (SMD 0.90; 95% CI 0.56 to 1.23, P value < 0.05) (Analysis 2.2). The quality of evidence was rated as 'low' (Summary of findings for the main comparison) (GRADE working group).

### Parents' level of stress

- Based on random-effects meta-analysis of means from two studies (Jocelyn 1998; Drew 2002), which recruited 55 children, there was no statistically significant difference in parent stress between the parent-mediated intervention groups and the control groups (SMD -0.17; 95% CI -0.70 to 0.36, P value > 0.05) (Analysis 2.1). The quality of evidence was rated 'low' (Summary of findings for the main comparison) (GRADE working group).

The reported findings from studies not included in the meta-analysis had similar conclusions (Aldred 2004; Tonge 2006; Rickards 2007; Roberts 2011) (Table 5).

## Secondary outcomes

### Child ability

- **Developmental/intellectual gains**: five studies (Smith 2000; Drew 2002; Rickards 2007; Dawson 2010; Tonge 2012) with varying theoretical basis and methods for assessing developmental/intellectual gains reported on this outcome. Dawson 2010 and Rickards 2007 suggest that small gains were made in this domain following intervention. However, Drew 2002 and Tonge 2012 (individual and group intervention, respectively) did not report any difference in this domain between intervention and control groups following intervention. Smith 2000 found greater gains for the intensive therapist-delivered intervention condition. Evidence for gains from parent-mediated intervention therefore may be suggested. However, gains in formal assessment may in part reflect child co-operation.

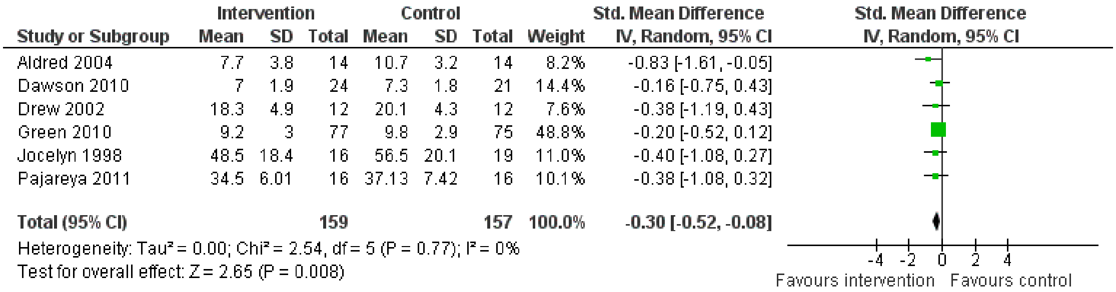
- **Adaptive behaviour**: based on random-effects meta-analysis of means from two studies (Dawson 2010; Green 2010), which recruited 197 children and used the Vineland Adaptive Behavior Scales composite score, found no statistically significant difference between the intervention and control groups following intervention (MD 1.06; 95% CI -2.95 to 5.06, P value > 0.05) (Analysis 1.10). Green 2010 reported teacher interview (after one year), and Dawson 2010 reported parent interview (after two years). Smith 2000 found no difference between parent-mediated and intensive therapist-mediated groups on adaptive behaviour (after four years), though Rickards 2007 did suggest a small effect in favour of additional parent-mediated intervention (after one year).

### Child problem behaviour

- **Maladaptive behaviour** : four studies (Smith 2000; Tonge 2006/Tonge 2012; Rickards 2007; Roberts 2011) reported on this outcome. Due to significant and important differences between these studies in theoretical basis and outcome measures used, a meta-analysis could not be conducted. None found a significant difference in maladaptive behaviour in favour of the intervention group, even where that was the focus of intervention (Tonge 2012).

- **Severity of autism characteristics**: autism severity was assessed across the studies using a number of measures (Table 3; Table 4). A random-effects meta-analysis of means obtained from six studies (Jocelyn 1998; Drew 2002; Aldred 2004; Dawson 2010; Green 2010; Pajareya 2011), which recruited 316 children, indicated there was a statistically significant effect in reduced severity of autism characteristics after intervention between the parent-mediated group and the control condition (SMD -0.30; 95% CI -0.52 to -0.08, P value < 0.05). There was no significant heterogeneity between the studies combined in the analysis (Analysis 1.9) (Figure 6).

**Figure 6. Forest plot of comparison: 1 Child communication and social development, outcome: 1.9 Autism severity.**



| | Intervention | | | Control | | | | Std. Mean Difference |
|---|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Mean** | **SD** | **Total** | **Mean** | **SD** | **Total** | **Weight** | **IV, Random, 95% CI** |
| Aldred 2004 | 7.7 | 3.8 | 14 | 10.7 | 3.2 | 14 | 8.2% | -0.83 [-1.61, -0.05] |
| Dawson 2010 | 7 | 1.9 | 24 | 7.3 | 1.8 | 21 | 14.4% | -0.16 [-0.75, 0.43] |
| Drew 2002 | 18.3 | 4.9 | 12 | 20.1 | 4.3 | 12 | 7.6% | -0.38 [-1.19, 0.43] |
| Green 2010 | 9.2 | 3 | 77 | 9.8 | 2.9 | 75 | 48.8% | -0.20 [-0.52, 0.12] |
| Jocelyn 1998 | 48.5 | 18.4 | 16 | 56.5 | 20.1 | 19 | 11.0% | -0.40 [-1.08, 0.27] |
| Pajareya 2011 | 34.5 | 6.01 | 16 | 37.13 | 7.42 | 16 | 10.1% | -0.38 [-1.08, 0.32] |
| **Total (95% CI)** | | | **159** | | | **157** | **100.0%** | **-0.30 [-0.52, -0.08]** |

Heterogeneity: Tau² = 0.00; Chi² = 2.54, df = 5 (P = 0.77); I² = 0%

Test for overall effect: Z = 2.65 (P = 0.008)

Silva 2009 found a significant differential reduction in autism characteristics reported by teachers after a massage intervention, though Tonge 2012 found no differential effect of their group intervention on two separate measures.

### Parental outcomes

- **Parents' satisfaction with therapy** : only one study reported on this outcome and it was stated that "customer" satisfaction was high with mean ratings of 5.48 (out of 6) on the group experience questionnaire and 3.46 (out of 4) on the group leader experience questionnaire (Carter 2011).

- **Parents' confidence in coping with child's disability and behaviour problems** : in the Nefdt 2010 (Table 5) study, observers rated parent confidence in carrying out procedures with their child; parents in the intervention group appeared to be more confident compared with those in the control conditions.

### Cost of intervention

- The majority of studies did not provide information on the cost of intervention. One study stated that the cost of the home-based programme was one teacher's salary for one year plus some expenses for travelling (this travelling estimate was not provided) (Rickards 2007). In another study, the authors estimated that the cost per child was AUD6383, adding that this is a small cost compared to a range of other interventions currently available to children and families with autism in that area (Roberts 2011). Casenhiser 2011 reported that the intervention programme (MEHRIT) cost is approximately CAD5000 per child per year, which they considered to be less than the estimates of therapy for most therapist-delivered programmes that typically provide 20 to 30 hours treatment. In two studies, though no detailed cost analyses were reported, the authors hinted that the parent-mediated interventions would cost less than available alternatives as they employed low-cost and widely applicable "professional-as-consultant, parent-as-therapist" models (Drew 2002; Pajareya 2011). In general, most studies tended to report that the interventions would be more cost effective in the long run when compared with existing alternatives. However, to reach a definite conclusion about the cost effectiveness of intervention vis-a-vis alternative therapies, such arguments require health economic evaluation of the cost implications of the interventions. The study reported by Green 2010 included a health economics evaluation that is expected to be published.

### Sensitivity analyses

- **Based on risk of bias**

in this analysis, we restricted the included studies only to those we judged to be at low and unclear risk of bias in pre-specified domains. For the results see Table 2. A statement of "no difference" in this table implies that the overall direction of inference was preserved following the analysis and one of “not applicable” was used to describe analyses in which all studies had low or unclear risk of bias.

# DISCUSSION

## Summary of main results

Overall, the review and meta-analyses demonstrate that children with ASD may make gains in language skills following parent-mediated interventions. These gains have been reported fairly consistently across reviewed studies in directly (blinded) assessed composite language scores, and separately for expressive language, and language comprehension. This pattern of gains was also reported by parents, with statistically significant findings in reported language comprehension (Analysis 1.6). Furthermore, six studies reported on overall severity of children's autism characteristics, with meta-analysis suggesting reduction in autism severity following intervention (Analysis 1.9). However, this finding certainly requires further investigation in future, especially to explore whether earlier intervention may be more efficacious. The strongest effect found was for the proximal effect of interaction coaching, that is, improvement in parent synchrony in observed interaction (Analysis 2.2). This is the assumed mediator for positive child outcomes from intervention (Aldred 2012), along with an increase in shared or joint attention during play. In this review, gains in child initiations within observed interaction, improvement in social communication skills, and reductions in child maladaptive behaviour have not been consistently found across studies, with effect estimates associated with significant degrees of uncertainty. The gains reported in the studies, especially in language development, could have the potential to enhance other areas of the child's development. Though the effect sizes for child outcomes were typically small, for a serious neurodevelopmental disorder such as autism even effect sizes of this magnitude could serve as pointers to what may be potentially effective approaches to managing autism in early childhood. How much benefit these gains will add to the longer-term quality of life of children and families is a question that needs further investigation and follow-up.

No significant reduction in parent stress was demonstrated in this review (Analysis 2.1). This could be due to the fact that the content of most of the interventions was primarily aimed at improving child outcomes rather than reducing parent stress. It was not possible to explore further questions about parent stress, such as whether the demands of receiving training and delivering intervention might lead to an increase in stress experienced. Rickards 2007 found that families with fewer resources and greater stress benefited most from the addition of home sessions with the parent to the child's experience of autism-specific nursery.

## Overall completeness and applicability of evidence

One strength of a parent-mediated approach to intervention in autism is that it should be possible to create therapeutic experiences spread out across the child's day and natural environments. This approach, however, makes it difficult to quantify the amount of time spent in therapy. This is because many of the approaches encourage parents to use techniques learned during training sessions in their daily interactions with their children. In order to explore the relationship between duration and intensity of intervention and impact, a consistent system for report of parent implementation would be necessary. As each study had different numbers and distribution of contact training hours with parents, it was also not possible to describe intensity of intervention as delivered to the parent.

The studies reviewed varied in the extent to which they were embedded in community services, and thus approached an evaluation of ’effectiveness’ rather than efficacy of the intervention (Smith 2007). It was notable that two community studies (Oosterling 2010; Smith 2010) had to be excluded as compromises had been made to randomisation. These studies raise questions about the feasibility of strict randomisation where young children with ASD share nursery provision, and parents meet in groups for support. Cluster-randomised studies may be prohibitively expensive. A further issue identified is the tension between, on the one hand, good research design, which requires evaluation of an intervention where the key elements are clearly specified and controlled, and, on the other hand, the needs of families of children with ASD for comprehensive support and good educational provision for the child.

It was not possible to investigate any potential moderators through subgroup analyses. Though the evidence was variable, some of the individual studies suggested that children of lower ability (however measured) made greater progress in certain domains (for example, expressive language skills in Siller 2012 and pre-treatment communication skills scores in Tonge 2006/Tonge 2012). This is generally in contrast to the findings of long-term follow-up of cohorts (for example, Magiati 2011) and reviews of early intensive behavioural intervention (for example, Howlin 2009) where greater gains are made by higher functioning children. Resolution of questions about moderators of treatment effect requires individual level data meta-analysis (cf Eldevik 2009; Reichow 2012).

In the introduction we posed some important questions to which parents, professionals and policy makers would like to have answers. What intervention should money be spent on? Which children, and which parents, will benefit most from which intervention? Is there evidence of greater benefit with earlier detection of ASD and thus earlier intervention? How long should interventions last? The available evidence has enabled us to make very little preliminary exploration. The variability in interventions including length and intensity, variability in content and delivery, the lack of direct comparisons between interventions, variability in recruitment and in ways of describing characteristics of children and parents, means that these important questions cannot yet be answered. Therefore, these factors need to be considered when making any generalisations. However, the review provides a basis for concluding that parent-mediated early intervention does appear on average to lead to positive changes in parent-child interaction, and to possible gains for children in language, with reduction in severity of autism characteristics.

## Quality of the evidence

This review considered 17 RCTs representing 919 young children with ASD. This is a considerable increase in numbers of RCTs since the original review (Diggle 2002), which included only two RCTs. In the meta-analyses, estimates from 499 children were combined (252 of these estimates were from the individuals in 'intervention' conditions while 247 were from the 'control' conditions), though only a maximum of 316 in one meta-analysis. For the studies included in the review, we used the Cochrane guideline for risk of bias assessment and it was observed that there were repeated problems with allocation concealment, incomplete outcome data, blinding and reporting bias (including emphasis on outcomes not pre-specified) (Figure 2; Figure 3). Though all of the studies assessed failed to blind parents (not possible given the nature of the interventions), it is however suggested that this did not impact on the quality of the evidence as most studies also included outcome measures from 'blinded' assessors and these outcomes were considered separately. For important outcomes included in the Summary of findings for the main comparison, we assessed the overall quality of evidence using the 'GRADE' approach (GRADE working group). Factors taken into consideration before judgements were made (the GRADEpro criteria) include limitations of detailed designs and execution (risk of bias) in studies, inconsistency (heterogeneity), indirectness (population, intervention, comparison and outcome), imprecision and publication bias.

## Potential biases in the review process

We relied heavily on published data in the course of this review with limited access to individual participant records; however, attrition was low in 14 of the 17 studies. The individual studies aggregated in this review vary considerably in their design, tools used for measuring outcomes, degree of utilisation of community or local services, as well as definition of control and intervention conditions. This limited our capacity to make full use of published data in the meta-analyses as we were only able to combine data from studies considered to be most similar in content and control condition.

## Agreements and disagreements with other studies or reviews

The findings of this updated review add considerably to the original review (Diggle 2002) as the increased number of studies allows greater power to draw conclusions. However, many of the same difficulties with sample sizes, multiple outcome measures and variable follow-up times remain. The general direction of findings presented is in keeping with those of other reviews of early intervention (see, for example, Ospina 2008; Warren 2011) though these do not focus on parent-mediated intervention per se and include a range of ages and research designs. This review suggests more caution in the interpretation of results than is espoused by other reviewers (for example, Rogers 2008) on account of the rigorous consideration of weaknesses in study design and analysis. Even where studies have been well designed (for example, Jocelyn 1998; Dawson 2010; Green 2010) there remain some potential problems with design and biases in their analyses and reporting.

# AUTHORS' CONCLUSIONS

## Implications for practice

The findings of this review have a number of implications for practice. First, given a conclusion that there is sufficient evidence of the effectiveness of parent-mediated interventions in treatment of ASD in young children, there is then a need for local service providers to pay increased attention to models and approaches that facilitate parent participation as part of available therapies. Three studies tested a combination of parent-mediated interventions with other locally available services, and this might be expected to be the preferred pattern for local autism treatment provision so that the burden on parents is shared (Jocelyn 1998; Rickards 2007; Dawson 2010). Aspects of intervention that aim to reduce parents' stress might also be given more attention in future. Second, some of the studies reviewed hinted at the fact that not all therapies may suit all families and individuals, highlighting the need for treatment of ASD to be individualised. The benefits of an increase in parent interaction skills (such as a 'synchronous' style of interacting) will be likely to generalise therapy strategies into the natural environments of children with ASD, and therapist coaching of parents can be tailored to individual needs with some degree of ease and flexibility.

## Implications for research

Most of the studies had methodological flaws that, if avoided, would improve the quality of evidence available, and thus increase our confidence in the effect estimates (Risk of bias in included studies; Figure 3; Figure 2). First, there is need for larger RCTs recruiting greater numbers of participants; only Green 2010 was adequately powered. Larger sample sizes will help increase power to detect the presence of a true effect if there is one, and to explore important moderators and mediators of effects. Second, most of the included studies failed to report on the process of allocation concealment, an important step in limiting bias in RCTs. Other weaknesses frequently observed were incomplete outcome data and variable blinding of assessors, and could be remediated in future studies. Third, the variability in outcome measures used, and the lack of evidence for their measurement properties, suggests there is an urgent need to explore what might be an optimum battery of outcome measures for early intervention (Cunningham 2012), with pre-specification of the primary outcome and full reporting. There is a particular problem with assessment of improvement in the core social-communication skills impaired in autism. Progress towards consistent and robust measurement requires further development and cross-site agreement on measures of coding parent-child interaction, and direct assessment of child social and communication skills, so as to ensure sensitive and objective outcome measures are used in future studies. Finally, researchers should include an estimate of the costs of their interventions, as well as any adverse effects, as these have important implications for future translation of research findings into practice. To arrive at more robust conclusions, there is need for studies of better quality, including attention paid to blinding, allocation concealment and fidelity of implementation, and more studies with outcome measure data that could readily be combined.

# ACKNOWLEDGEMENTS

We would like to thank all the members of the Cochrane Developmental, Psychosocial and Learning Problems Review Group (CDPLPG) editorial team, with special thanks to Geraldine Macdonald, Laura MacDonald and Margaret Anderson for the provision of ongoing guidance and support. On occasions where judgements about articles were not clear cut, assistance and support was sought from the CDPLPG editorial board.

We would also like to thank the Nuffield Foundation for the financial support of this and the original review.

We acknowledge the authors of the original review who were not involved in this update: Tim Diggle and Val Randle.

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* *Indicates the major publication for the study*

# CHARACTERISTICS OF STUDIES

## Characteristics of included studies *[ordered by study ID]*

**Aldred 2004**

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|---|---|
| Methods | An RCT. There were a total of 28 children: 14 children in the intervention (target treatment) group and 14 children in the control (routine care) group. 25 of the children were males and 3 were females. The study used a combination of centre-based sessions attended by parents and their children and home-based sessions between parents and their children. Parents were the primary “therapists” in the study |
| Participants | **Child participants:** participants were drawn from northwest England. Inclusion criteria were a clinical diagnosis of autistic disorder made by an assessing professional, English as a first language and a desire to interact with adults. Exclusion criteria were the presence of severe global developmental delay, severe environmental deprivation in infancy, a diagnosed hearing impairment and a diagnosed visual impairment. The parents of children included in the study had no known chronic psychiatric or physical illness<br>The children were aged 2 to 5 years 11 months: the median age for those in the intervention group was 48 months (range 29 to 60 months) while that for the control group was 51 months (range 24 to 71 months). ADI and ADOS were used to assess diagnostic criteria. Other measures used in the study were the MCDI, VABS, Parenting Stress Index and coding of parent-child interaction videos. Children were placed into ability categories based upon ADOS scores and chronological age. The following groups were created. Young High Functioning (aged 24-47 months, total ADOS score 11-17) , Young Low Functioning (aged 24-47 months, total ADOS score 18-24), Older High Functioning (aged 48-71 months, ADOS score 11-17) and Older Low Functioning (aged 48-71 months, ADOS score 18-24)<br>**Parent participants:** it was reported that the parent sample was predominantly middle-class. Median years in education were 17.6 years (range 16 to 21 years) for fathers and 16.5 years (range 16 to 21 years) for mothers. 2 mothers were African-Caribbean and the other parents were described as Caucasians. No parent had a known chronic psychiatric or physical illness |
| Interventions | **Control group:** those in the control group were said to have received “routine care alone”<br>**Intervention group:** the intervention (which was based on a social communication model) was designed to last for 12 months: some workshops for parents, then 6 months of monthly individual sessions for parents and children and 6 months of less frequent maintenance sessions. The intervention group was also free to use the routine care available to those in the control group |
| Outcomes | Child-parent communication, reciprocal social interaction, expressive language, parental stress and adaptive functioning. Outcomes were assessed at baseline and 12 months after intervention. There was no report on adherence (fidelity of parent training and report of parent implementation) in the study |
| Funding source | The Shirley Foundation |

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| Study main findings | The active intervention group was reported to make significant improvement compared with control on the primary outcome measure (ADOS total score, particularly in reciprocal social interaction) and on secondary measures of expressive language, communicative initiation and parent-child interaction. Suggestive but non-significant results were found in VABS (Communication Subdomain) and ADOS stereotyped and restricted behaviour domain. There was no report of any analysis of moderators. In the control group there were improvements in autistic symptoms for the young low functioning subgroup only. There was an increase in demands and intrusive language in the parent-child interaction. There were no significant changes in parenting stress for either of the groups |
| Missing data | No missing data reported |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Randomisation was done by an independent statistician but details of method employed were not provided in the publication (page 1423) |
| Allocation concealment (selection bias) | High risk | The process did not appear concealed |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | The authors reported that the researchers were blind to the group status of the participants. Details about the blinding process were provided in the report (page 1423) |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Dropout from the study after randomisation was handled by replacement with equivalent stratified cases and analysis was based on an intention- to- treat basis (page 1423) |
| Selective reporting (reporting bias) | Low risk | ADOS, VABS, MCDI, parent-child interaction and PSI were all reported |

**Carter 2011**

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|---|---|
| Methods | An RCT. There were 62 children in the study in total: 51 males and 11 females. 32 were in the intervention (HMTW) group while 30 were in the control (treatment as usual) group. Training was given to parents at locations outside of their homes. Parents and carers were the primary targets of the training and were responsible for the delivery of the intervention to their children |
| Participants | **Child participants:** the study was conducted in 3 project sites across cities in the south, southeast and northeast US and families were recruited from ASD specialty clinics, early intervention programmes, paediatric and neurology practices, and the online Interactive Autism Network. The sample was drawn from a population of children whose ethnicity were described by their parents as white (47.6%), Hispanic or Latino (38.6%), black (3.5%) and other mixed groups. Inclusion criteria were no genetic disorder and a diagnosis of ASD (PDD-NOS and autistic disorder) made through expert clinical impression (based upon DSM-IV) and STAT. The ADOS was applied but only at time 3 (9 months into the study). Baseline characteristics (time 1) were assessed using MSEL; DPA, and VABS II. A clinical assessment of DSM-IV symptom criteria for ASD using the Stat was also conducted. Outcomes were assessed through coding of recorded PCFP, ESCS, PIA-CV<br>The ESCS, PCFP and PIA-CV were also completed at time 2 and time 3, 5 and 9 months after the time 1 visit, respectively. The MSEL, VABS-II and ADOS were completed again at time 3 along with the clinical assessment of DSM-IV symptom criteria for ASD (Stat and ADOS). The children's mean age at baseline was 20 months (SD 2.6). Children's ability was assessed using the MSEL. Using the expressive language age scale (in months), children in the intervention group had a mean score of 8.22 (SD 6.01, range 1.00 to 29.00 months) while those in the control group had a mean score of 7.33 (SD 3.71, range 1.00 to 16.00)<br>**Parent participants:** 16% of the parents had up to high school education; 33% had some college coursework, an associate's degree or vocational/trade degree; 35% had a college degree and 16% had advanced degrees |
| Interventions | **Control group:** further details about intervention in this group was not provided<br>**Intervention group:** the intervention entailed 8 group sessions with parents only and 3 in-home individualised parent-child sessions interspersed. The strategies taught to parents by trained speech and language therapists were based on social communication models and targeting 2-way interaction, more mature and conventional ways of communicating, better skills in communicating for social purposes and improved understanding of language. This intervention was delivered over 3.5 months |
| Outcomes | Primary outcomes were child social communication skills development. Secondary outcomes were exploration of the role of potential moderators such as pre-treatment child characteristics, communication and object interest on treatment outcome and parents' responsivity at the end of the programme. Time 1 was defined as the start of the study. Times 2 and 3 were 5 months and 9 months after the start of the study, respectively. Baseline assessments were made at time 1 while outcomes were assessed at time 2 and 3, 5 and 9 months after time 1 assessments. Fidelity of parent training was assessed through checklists for sessions held by speech and language therapists. It was reported that the intervention was implemented with 88% delivery of intended items at group sessions and 89.9% delivery of intended items at individual sessions. Parent implementation was reported as low with mean family attendance at sessions put at 3.57 (SD 2.29, range 1 to 10) when compared to the standard minimum of 8 families per group set by the |

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| | researchers |
| Funding source | Autism Speaks and Marino Autism Research Institute |
| Study main findings | There were no main effects of the HMTW intervention on either parental responsivity or children's communication and did not reach statistical significance. It was gathered that the intervention facilitated communication in children with lower levels of time 1 object interest with attenuation of growth in this domain in children with higher levels of object interest |
| Missing data | There were a number of missing data as a sizeable number of individuals (7) withdrew from the study or were lost to follow-up. There were also missing data at different time points in the study with 28 having data at time 2 and 25 at time 3 for the intervention group and 24 and 25, respectively at time 2 and 3 for the control group |
| Notes | *Only 46 out of the 50 assessed at time 3 by ADOS and DSM-IV were said to have met the criteria for ASD |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | The use of a "software that utilises a random number generator" for randomisation (page 742) |
| Allocation concealment (selection bias) | High risk | There was no mention of this process in the report and it did not appear that the process has been concealed in any way. It is highly unlikely, from the published report, that this was done |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | It was reported that "the majority of assessors and all observational coding of children's behaviour were blind to treatment condition". 2 outcome measures were coded blind (and 1 more was a parent questionnaire) |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Authors "elected not to carry forward values from earlier periods to later periods when participants were missing Time 1 data for a particular procedure or to use multiple imputations". They also conducted what was referred to as "partial" in- |

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| | | tent to treat on the ground that full intent to treat analysis would require imputation for all missing data. In addition it was reported that "because a large minority of participants had missing scores for several variables, estimation would have increased the risk of producing non-replicable results" (page 742). Partial intention-to-treat analysis is a unconventional way of handling missing data and the fear of non-replicable results entertained by the authors should estimations have been done for certain missing data makes one think that the way missing data have been handled by the authors could also have significant impact on the observed effect size. The analysis done also appeared to have used different time points, determined by availability of data rather than a chosen time point |
| Selective reporting (reporting bias) | Low risk | The study reported on pre-specified outcomes (pages 742, 747 and 748) |

**Casenhiser 2011**

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|---|---|
| Methods | An RCT. There were 51 children in the study; 25 children were in the intervention (MEHRIT) group while 26 children were in the control (community treatment) group. Therapy was delivered by a therapist with the parent and child for 2 hours per week and then by the parent for at least 3 hours a day in interactions with the child. The location of the therapist sessions were not indicated |
| Participants | **Child participants:** the population was recruited from the Greater Toronto Area, Canada. Children with neurological or developmental diagnoses other than ASD were excluded from the study. The diagnostic category in this study was ASD, with diagnosis based upon ADOS and ADI scores. Participants were aged between 2 years and 4 years 11 months (mean 42.52 months, SD 8.76 in the intervention group and mean 46.38 months, SD 8.29 in the control group). Child ability levels were not reported in the study. ADOS and ADI were used for baseline assessments of ASD. An mCBRS was used to rate children's interactions with parents at baseline and 12 months. PLS IV and CASL were used to assess receptive and expressive language skills at baseline and 12-month follow-up<br>**Parent participants:** in the treatment (MEHRIT) group, 24 of 25 families were of married or partnered status. 23 parents spoke English most often at home. Of the 25 families, English was the native language of 15 mothers. 12 families had an income more than 100,000 CAD, 6 had an income between 50,000 and 100,000 CAD and 4 an income of less than 50,000 CAD. 3 families chose not to provide this information. 2 mothers had advanced degrees, 15 had Bachelor's degrees, 7 had some university/college education and 1 had an associate degree. In the control (community treatment) group, |

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| | out of 26 families, 22 were married or partnered, 23 families spoke English as the main language at home. In 12 families (in the control group) the mother's native language was English. 11 families in the control condition had an income of 100,000 CAD or more, 4 had an income between 50,000 and 100,000 CAD and 8 an income less than 50, 000 CAD. 6 mothers had advanced degrees, 11 had a Bachelor's degree, 3 had associate degrees, 4 had some university/college education and 2 had high school education |
| Interventions | **Control group:** children in the community treatment group were encouraged to seek treatment for their child while waiting for treatment through the study. On average, the community treatment group received 3.9 hours of treatment per week. No family received more than 15 hours of treatment per week. Treatments were received solely or in combination with other therapies like traditional speech therapy, ABA, occupational therapy, social skills group specialised part-time day care and other treatments such as hyperbaric oxygen therapy and specialist diets<br>**Intervention group:** The MEHRIT programme aims to improve children's social interaction and communication abilities. It is based on DSP interventions, which teach children functional skills in a sequence consistent with typical child development and help children develop social communication capacities in a natural social context. The MEHRIT programme lays emphasis on carer involvement in intervention and the use of sensory motor supports and co-regulation and it uses a set of developmental capacities to guide treatment. Treatment was delivered by licensed speech and language pathologists or occupational therapists who received approximately 3 weeks of intensive hands-on training from faculty members before the start of therapy. Weekly meetings and summer institutions provided ongoing supervision. The primary goals of therapists were to assess strengths and challenges of the child (with regards to speech and communication, sensory, cognitive and motor abilities), to teach parents about their child's strengths and challenges and to devise a set of strategies appropriate for the child and family. Therapists met with children and carers for 2 hours a week for 12 months. Midway through each session the child received a 15- to 20-minute break. During this time the therapist consulted with the carer about the therapy. In addition, carers met every 8 weeks with therapists to discuss progress and review recordings of play sessions of carers and their child to assess therapeutic approach and address any questions. Parents were required to spend at least 3 hours per day interacting with their child |
| Outcomes | Assessments were made at baseline and 12 months into the study. The following aspects of social interaction were examined using the mCBRS; attention to activity, compliance, involvement, initiation of joint attention and enjoyment in interaction. Language and DQ of the child was measured using the PLC and CASL. Parent behaviours were measured using the MEHRIT Fidelity Scale in terms of co-regulation, expression of enjoyment of the child, joining, use of affect, support of reciprocity sensory-support and support of independent thinking |
| Funding source | The Harris Steel Foundation and the Harris family, the Unicorn Foundation, Cure Autism Now, the Public Health Agency of Canada, the Templeton Foundation and York University |
| Study main findings | Results indicated that overall significant improvements were made in scores pre- to post-treatment. These changes differed and were marginally significantly between the groups. The MEHRIT group made significantly greater changes than the community treatment |

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| | group in attention to activity, involvement, initiation of joint attention and enjoyment in interaction as measured by the mCBRS. Changes in language scores were found to be significantly predicted by pre-treatment DQ, initiation of joint attention and involvement. Enjoyment of interaction was a marginally significant predictor. The intervention group (MEHRIT) improved significantly in all areas of carer behaviour measured with the exception of sensory-support. The community treatment group remained largely unchanged with the exception of joining behaviours, which declined. There was significantly more improvement in the MEHRIT group than the community treatment group over the course of 12 months on the parent fidelity measures of co-regulation, expression of enjoyment of the child, joining, use of affect and support of reciprocity. The authors stated that the cost associated with the MEHRIT therapy programme is approximately CAD5000 per child per year, which is considerably less than the estimates of therapy for most therapist-delivered programmes that typically provide 20-30 hours of treatment |
| Missing data | No missing data were reported |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Participants were "selected" from a randomised programme, which is not further explained. In each cohort, children were stratified by age and baseline level of language function, and were randomly assigned to 1 of 2 groups using random.org's random number generator (pages 5 and 6) |
| Allocation concealment (selection bias) | High risk | There was no mention of this in the report and it did not appear this was done |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Those assessing outcome and coding videos or child-parent interactions were blind to the group status of participants (pages 10 and 11) |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | The reasons for the withdrawal of children from the programme, and therefore lost to follow-up, were fully accounted for. Analyses of results was limited to study completers alone (page 17) |

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| Selective reporting (reporting bias) | Low risk | PLS, CASL, and mCBRS for interaction were all reported |

**Dawson 2010**

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| Methods | An RCT. 48 children participated in the study. There was a male:female ratio of 3.5:1. The intervention (ESDM) was delivered in the child's natural environment (the home) and delivered by trained therapists and parents of children with ASD. The control group was the A/M group. 24 children were in the A/M group and 24 were in the ESDM group |
| Participants | **Child participants:** this study was conducted in Washington, US and participants were recruited from "Birth to three" centres in areas including Seattle. Participants were children who resided within 30 minutes of the University of Washington. Participants' ethnicities were as follows: Asian (12.5%), white (72.9%), Latino (12.5%) and Multi-racial (14.6%). Inclusion criteria were being younger than 30 months at entry, meeting criteria for autistic disorder on the Toddler Autism Diagnostic Interview, meeting criteria for autism or ASD on the ADOS and a clinical diagnosis based on DSM-IV criteria using all available information, residing within 30 minutes of the University of Washington and willingness to participate in a 2-year intervention. Exclusion criteria were the presence of a neurodevelopmental disorder of known significant sensory or motor impairment, a major physical problem such as a chronic serious health condition, seizures at time of entry, use of psychoactive medications, history of a serious head injury or neurologic disease (or both), alcohol or drug exposure during the antenatal period and ratio IQ below 35 as measured by mean age equivalence score/chronological age on the visual reception and fine motor subscales of the MSEL. Measures used in this study were the toddler version of the ADI-Revised, ADOS, MSEL, VABS and RBS. All measures were administered at baseline, 1 year after onset of the intervention and either 2 years after the onset of intervention or 48 months of age whichever yielded the longest time frame. Children were aged 18-30 months: A/M group mean age was 23.1 months (SD 3.9) and ESDM group mean age was 23.9 months (SD 4.0). Children had diagnoses of either autistic disorder or PDD-NOS. Child level of ability was assessed using ADOS severity score: A/M group mean was 6.9 (SD 1.7) while the ESDM group mean was 7.2 (SD 1.7)<br>**Parent participants:** parent characteristics were not reported in the study |
| Interventions | **Control group:** families in this group were given resource manuals and reading materials at baseline and twice yearly throughout the study. The group reported a mean of 9.1 hours of individual therapy and a mean of 9.3 hours/week of group interventions (for example, developmental preschool programmes) across the 2-year period. Developmental preschool programmes vary but typically include special education and related services. There are a number of private ABA providers in the community therefore the control group likely to have used ABA interventions<br>**Intervention group:** those in this group were provided with intervention by trained therapists for 2-hour sessions, 5 days per week, for 2 years, using a manual. Intervention was delivered using manuals by graduate level trained lead therapist who had a minimum of 5 years' experience providing early intervention to young children with autism, with ongoing consultation from a clinical psychologist, speech-language pathologist and developmental behavioural paediatrician. Parents were asked to use ESDM strategies dur- |

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| | ing daily activities and to keep track of the number of hours during which they used these strategies. ESDM uses teaching strategies that involve interpersonal exchange and positive affect, shared engagement with real-life materials and activities, adult responsivity and sensitivity to child cues, and focus on verbal and non-verbal communication, based on a developmentally informed curriculum that addresses all developmental domains. Each child's plan was individualised. Mean therapist-delivered intervention hours were 15.2 hours (SD 1.4). Parents reported spending a mean of 16.3 hours per week (SD 6.2) using ESDM strategies |
| Outcomes | Primary outcomes were child cognitive and adaptive behaviour while secondary outcome was impact of intervention on the severity of ASD. Time points for outcome assessments were baseline, time 1 (1 year) and time 2 (2 years). Reports of parent implementation was through therapists supervision and parent reports |
| Funding source | National Institute of Mental Health Grant - U54MH066399 |
| Study main findings | The study reported significant gains in language and adaptive behaviour in addition to the observation that children in the ESDM were more likely to experience a change in diagnosis from autism to PDD, not otherwise specified, than the comparison group. The authors also came to the conclusion that parents' use of intervention strategies at home during their daily activities likely was an important ingredient of its success. No stated moderator analysis in the study |
| Missing data | Yes. 3 losses to follow-up in the A/M group |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Randomisation was done using random permuted blocks of 4 (page 19) |
| Allocation concealment (selection bias) | High risk | There is no mention of this in the published article |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | It is very likely that outcome assessors were blind to the group status of participants in the study |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | There were losses to follow-up in the study; 1 in the first year and 2 in the second year. These losses were not accounted for and results were analysed on the basis of study |

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| | | completers in the second year |
| Selective reporting (reporting bias) | High risk | ADOS, MSEL, VABS, RBS - all reported but no defined primary outcome. Also authors reported "change in diagnosis" (done blind), though not pre-specified |

**Drew 2002**

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|---|---|
| Methods | An RCT. There were 24 children in the study: 19 males and 5 females. 12 children were in the intervention (parent training) group and 12 were in the control (local services) group. The intervention was a home-based model in which parents were trained as the sole therapists of their children with ASD |
| Participants | **Child participants:** this study was conducted in the UK and children recruited for the study were those identified to be at high risk for autism through the shortened version of CHAT. Inclusion criteria were fulfilment of ICD-10 criteria for childhood autism using the ADI-R and a structured Child-Adult Interaction Assessment to elicit examples of social interaction, reciprocity, non-verbal social communication abilities and affective responsivity. ICD-10 diagnoses of childhood autism were achieved using all available clinical, historical and psychometric information. A consensus clinical judgement was reached by 2 clinicians highly experienced in the diagnosis of autism and related PPDs. Measures used in the study includes MCDI, Griffith's Scale of Infant Development (D and E scales), ADI-R and PSI. All measures were applied at baseline and at follow-up, a mean of 12.3 (SD 1.6) months after the initial assessments. Overall mean age of the children was 23 months: parent training group mean age was 21.4 months (SD 2.7) and the local services group mean age was 23.6 months (SD 3.8). 11 of 12 children in both study groups were non-verbal (having fewer than 5 words) on the ADI-R scale<br>**Parent participants:** their characteristics were not given in the report |
| Interventions | **Control group:** those in this group had locally available treatment services for ASD including speech and language therapy sessions, portage home worker input and other paramedical therapy services<br>**Intervention group:** in this group, parents acted as everyday sole therapists. Parents were visited at home by a speech and language therapist every 6 weeks for a 3-hour session over a period of 12 months. Activities and aims for the 6-week period were set by therapists and parents of the child along the communicative and cognitive level of the child. Activities lasted initially for 2-3 minutes but were stepped up gradually to 5 minutes per activity. Therapists were available for telephone support and parents were encouraged to take up locally available therapy or preschool services available to them in addition to the intervention. The intervention adopted a psycholinguistic and social-pragmatic approach to language development |
| Outcomes | Primary outcomes were expressive and receptive language and the domain scores on the ADI-R. Secondary outcomes were parent stress. Time points for assessments were baseline and 12 months after baseline assessments and intervention. To measure input from other health and education services (for example, speech and language therapy sessions, part-time placement in a nursery) for both groups, an activities checklist was |

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| | completed every 3 months by parents. There was a lack of data on the implementation of the parent training approach |
| Funding source | Grants from Medical Research Council and Special trustees of Guy's Hospital to SBC, AC and GB |
| Study main findings | There was marginal and statistically non-significant difference in language comprehension between the 2 groups in favour of the parent training group. In the parent training group more children moved from being non-verbal (which was the assessment at baseline for both control and intervention groups) to spontaneous use of 3-word phrases, single-word speech and fewer than 5 words use. However, the authors did report that the language ability of children in both groups remained severely compromised at follow-up. There were no between-group differences in symptom severity on the ADI-R follow-up. There were no difference in PSI score between the 2 groups. No direct cost comparisons made but authors argued that the intervention will be a low cost and more effective alternative as the study employed a low-cost and widely applicable "professional-as-consultant, parent-as-therapist" model. No moderator analysis was made |
| Missing data | Yes. There were missing data for some outcomes in the control and intervention groups |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | The use of table of random numbers for allocation into groups (page 267) |
| Allocation concealment (selection bias) | High risk | The was no allocation concealment in the study and it appeared that only an open random allocation schedule was used |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | It was not stated if there was blinding and it is unlikely that this was done |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | Though stated that an intention-to-treat analysis was done, it is not clear to judge this from the information provided in the article. It also appears that analysis were done on the basis of treatment completers and reported that some questionnaire data were missing (pages 268 and 269 and Table 1 on page 270) |

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| Selective reporting (reporting bias) | Low risk | MCDI, non-verbal IQ, ADI, and PSI all reported |

**Green 2010**

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| Methods | An RCT. This study had 152 children and their families: 138 males and 74 females. There were 77 children in the intervention (PACT) group and 75 in the control (TAU) group. Intervention training was delivered to parents in centres (local primary care trusts) across London, Manchester and Newcastle (UK) by trained speech and language therapists. Parents were the primary target of the programme and both parents and their children with autism attended training sessions |
| Participants | **Child participants:** the research participants were drawn from London, Manchester and Newcastle (UK). Participating parents spoke English with their children at home. Inclusion criteria were families with a child aged 2 years to 4 years and 11 months, and meeting criteria for core autism according to the international standard diagnostic tests (social and communication domains of the ADOS-G, and 2 of 3 domains of the ADI-R algorithm). Exclusion criteria were children who had a twin with autism, children with a verbal age of 12 months or younger on the MSEL, children with epilepsy requiring medication, severe hearing or visual impairment in parent or child and a parent with a severe psychiatric disorder requiring treatment. Baseline characteristics were assessed using ADOS-G, ADI-R and MELS. The primary outcome measures was the ADOS-G social communication algorithm score (for autism severity). Secondary outcome measures were preschool language scales (for child language and social communication) - MDCI- infant form raw score, CSBS-DP - carer questionnaire, VABS teacher rating form for adaptive functioning outside of family and coding of videotaped child-carer interactions. Children were aged between 2 years to 4 years 11 months. Mean age of child participants was 45 months (range 26 to 60 months). The mean level of non-verbal ability of children (SD) for the intervention group was 27 months (10.0) while that for the control group was 25.3 months (9.5)<br>**Parent participants:** in the intervention group, 84% of the 77 participating families in that group had at least 1 parent with qualifications after age 16 years and 66% were in a professional or administrative occupation. While in the control (treatment as usual) group, 63% of the 75 participant families had at least 1 parent with qualifications after age 16 years and 59% were in a professional or administrative occupation |
| Interventions | **Control group:** this was described as limited to local intervention services for autism. The mean number of hours spent in therapies in this group is 9.8 hours (SD 12.9). Therapies in this group include language and speech therapies<br>**Intervention group:** those in this group received treatment as usual in addition to the PACT intervention, which is based on a social communication model and targets communication skills development. The intervention consisted of 1-to-1 clinic sessions between therapist and parent with the child present. Participants attended biweekly 2-hours session for 6 months then followed by monthly booster doses for 6 months. The mean number of hours spent in non-PACT treatment in this group was 9.5 hours per case (SD 16.3). A total of 18 sessions were to be delivered in the entire programme. Parents of children with autism were encouraged to engage in 30 minutes of home practice of taught methods at home with their child each day |

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| Outcomes | The primary outcome was social communication severity while the secondary outcomes were parent-child interaction, child language and adaptive functioning in school. Assessments were made at baseline and 13 months' post-intervention. A median of 13.4 criteria (12.5 to 14.0) per session was reported as fidelity, how this was assessed was not reported. Adherence was reported as high: median of 16 (IQR 13 to 17) out of the 18 sessions possible, details of how this was assessed were not stated |
| Funding source | UK Medical Research Council, UK Department of Health and UK Department for Children, Schools and Families |
| Study main findings | A statistically non-significant reduction in social communication difficulties, positive treatment effect for parental synchronous response to child and small gains in child language and adaptive functioning were reported. Analysis were carried out to assess impact of baseline characteristic such as age, socioeconomic status, parental education, child ability (non-verbal ability and language level), centre where study was conducted and severity of autism on outcome of interest post-intervention. It was found that these variables did not significantly impact on the study outcomes. No cost information was provided in this publication. However, cost analysis were performed and will be published in a separate paper |
| Missing data | Missing data were accounted for and analysis was on intent-to-treat basis. Multiple imputation done for missing data |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Randomisation was done using a computer-generated allocation schedule created by an independent statistician (page 2) |
| Allocation concealment (selection bias) | Low risk | Done centrally by trial manager informing clinical sites (page 3) |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | "Endpoint ADOS-G ratings were made, from anonymised videotapes, by an assessor from a different trial site to the ADOS-G administrator, unaware of the case details and treatment status" (page 3) |

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|---|---|---|
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Data were analysed on intention to treat basis and missing data were imputed |
| Selective reporting (reporting bias) | Unclear risk | 1 primary and 5 secondary outcomes all reported, separated by mode of assessment (blind/not) |

**Jocelyn 1998**

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|---|---|
| Methods | An RCT. There were 36 children in the study: 35 males and 1 female. 16 of these children were randomised into the intervention (APP) group and 19 into the control (community day care - standard services) group. The intervention was delivered in centres to families or daycare staff (or both) of children with autism |
| Participants | **Child participants:** children newly diagnosed with either autism or PDD using DSM-III-R criteria, resident no more than 60 miles outside of Winnipeg, Canada were recruited for the study. Exclusion criteria were being outside the age range of 24 to 72 months, physical disabilities that would preclude completion of developmental test items and enrolment in school at time of diagnosis. The ethnicity of participants was only stated as “Caucasian or others”. Baseline assessments were made using Hollingshead’s 4 factor index of social status, Leiter international performance scale and CARS. Outcome measures were the TRE-ADD autism quiz - mothers’ score, ABC, EIDP, PSDP stress arousal checklist, client satisfaction questionnaire, and family assessment measure. Children were all aged 24-72 months and had a diagnosis of autism. Mean age of children in the intervention group was 42.6 months (SD 9.2) while that for the children in the control group was 43.8 months (SD 9.0). 21 of the children had mild-to-moderate autism (CARS scores $\leq 37$) and 14 severe autism (CARS scores > 37). Children in the intervention group had a mean IQ score of 58.44 (SD 27.5), children in the control group had a mean IQ score of 67.1 (SD 27.5)<br>**Parent characteristics:** 8 out of the 35 participating families had single parents. Further details about the families were not provided |
| Interventions | **Control group:** children in this group were given a standard intervention for autism in the community in use before the development of APP. Children in this group attended community daycare centres where they got support from child care workers. Children received 15 hours of day care during the 12 weeks in addition to social worker support<br>**Intervention group:** the intervention (based on an educational model), lasted for ”twelve weeks” and involved training parents and daycare staff of children with autism through hospital-based seminars (5 weekly 3-hour classes) and on-site consultations with autism behaviour specialists (3 hours per week for 10 weeks). Interventions were primarily directed at the parents and daycare staff of children with autism rather than the children and the children in this group also attended the daycare centres just like children in the control condition |
| Outcomes | Primary outcomes were impact of intervention on knowledge of carers about need of children with autism, developmental outcome of children with autism, and parental stress and family functioning. Assessments were made at the start of the programme (baseline assessments) and 12 weeks (outcome assessments).There was no report on adherence in |

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| | the study |
| Funding source | National Health Research and Development Program. Grant number 6607-1649-62 |
| Study main findings | "Clear" difference in favour of the intervention group was reported in the language development domain by the authors. No difference was reported in the overall autistic symptomatology between the 2 groups and there was no difference between the 2 groups in the family functioning outcome (no significant change in stress or arousal on the Stress Arousal Checklist) though gains were reported in parents' confidence and knowledge about coping with their children's behaviour. Analysis of the impact of baseline IQ and CARS scores on outcome was made and none of these was found to have impacted on the outcomes of interest in the study. No cost implications mentioned |
| Missing data | Yes: 1 participant in the intervention group whose data were not included in analysis as he was withdrawn by his parents from the study |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | This was done by an independent statistician using a random numbers table (page 327) |
| Allocation concealment (selection bias) | Low risk | The use of sealed opaque envelopes (page 327) |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Assessments were conducted by psychologists who were blind to participants' ' group assignment (page 327) |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Though 36 children were recruited for the study. One 1 withdrew for a stated reason before randomisation was done |
| Selective reporting (reporting bias) | Low risk | Stated measures of the study were all reported on (pages 327, 329, 330, 331 and 332) |

**Kasari 2010**

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|---|---|
| Methods | An RCT. 38 children and their families: 29 males and 9 females, participated in the study. There were 19 in the intervention (immediate treatment) group and 19 in the control (waiting-list) group. The intervention was delivered across a number of locations including home and school centres. Parents and carers (mainly mothers) were responsible for the delivery of intervention |
| Participants | **Child participants:** the authors noted that earlier studies indicated that children with minimal language impairment were most likely to benefit from intervention; as such, the focus of this intervention was children with minimal language problems. The sample was drawn from areas only described as “middle class areas in Western United States”. About 40% of the sample was drawn from ethnic minority groups<br>Inclusion criteria for the study were meeting DSM-IV criteria for autism on the ADI-R and chronological age below 36 months. Exclusion criteria were the presence of seizures, sensory or physical disorders, or comorbidity with any other psychological disorder or disease. Baseline characteristics were assessed using MSEL. Outcomes were assessed through coding of child-parent play interactions using methods described by Adamson 2004, Kasari 2006 and Kasari 2008 . At baseline and 12-month follow-up carer-child interaction was assessed along with the MSEL. At the end of intervention (8 weeks) only the carer-child interaction was assessed. The children were aged 21-36 months, with a mean age of 30.82 months. The mean age of children in the intervention group was 30.35 months (SD 0.93). The mean age of children in the control group was 31. 31 months (SD 0.90). The intervention group had a mean chronological age of 30.35 months (SD 0.93) while the control group had a mean chronological age of 31.31 (SD 0.90). Children’s level of ability as measured by the MSEL. The intervention group had a mean mental age of 19.83 months (SD 1.80) and a DQ of 64.80 (SD 5.35). The control group had a mean mental age of 18.57 (SD 1.09) and a mean DQ of 59.81 (SD 3.14)<br>**Parent participants:** the mean age of parents in the study was 34.5 years. The majority of the participants were not in employment (74% in the intervention group and 63% in the control group, respectively). Regarding level of education, only 21% of those in the intervention group and 31% of those in the control group had their highest level of education at professional/graduate level with the majority reporting their highest level of education as college or some college/vocational training |
| Interventions | **Control group:** those in this group received only interventions available locally (table 6 in the original report). This included varying hours (1-30 hours) of ABA, school-based instruction, speech therapy, occupational therapy and ’miscellaneous’<br>**Intervention group:** those in this group received 8 weeks of intervention (that is, 24 therapist sessions with carer and child, delivered at 3 sessions per week with each session lasting about 45 minutes). These sessions were focused on joint attention/engagement skills development. 10 modules were included in the intervention; these were individualised for each carer-child dyad with the starting point of the intervention determined by the baseline carer-child interaction. Each 45-minute session included the interventionist coaching the carer and child in engaging in play routines. The approach included developmental procedures of responsive and facilitative interaction methods as well as aspects of ABA. Some principles included were following the child’s lead, imitating the child and making environmental changes. 30 minutes of directed instruction, modelling, guided practice and feedback from the interaction was followed by handing out of summary sheets and then 10 minutes of practice |

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| | Interventions were run by trained interventionists who were all graduate students in educational psychology with experience working with children with autism. There were 4 interventionists each working with 8 or 9 families. Interventionists were trained using 2 pilot families and supervision prior to the study commencing and continued to receive weekly group supervision for 1 hour per week during the study. In addition to the intervention, numbers of hours spent in other intervention programmes were recorded. These were quite varied and were presented in table 6 in the report. This included varying hours (from 0.5 to 30 hours) of ABA, school-based instruction, speech therapy, occupational therapy and 'miscellaneous' |
| Outcomes | Primary outcomes were related to engagement state, in particular the presence of joint attention and assessed through carer child interactions. Secondary outcomes were interventionist-rated carer quality of involvement in the intervention, carer-rated adherence to the intervention and competence in the delivery of the intervention as well as the type and amount of other intervention services accessed. At baseline and 12-month follow-up carer-child interaction was assessed along with the MSEL. At the end of intervention (8 weeks) only the carer-child interaction was assessed. Parent/carer implementation of the intervention was assessed weekly using carer diaries and carer involvement scales. As regards fidelity of treatment, an overall average score of 3.37 (SD 0.32) was found with a range of 2.56 to 3.94. This was stated as high fidelity by the authors |
| Funding source | National Institute of Mental Health grant MH064927 |
| Study main findings | It was reported that the intervention group made significant changes in targeted areas of joint attention following the intervention (joint attention and joint engagement showing significantly less object related play) with maintenance of the skills 1 year post intervention. However, they did not show greater initiations of joint attention or increased diversity of symbolic play than the waiting list group following the intervention. Analysis of carer quality of involvement scale and the parent-rated adherence and competence scales were conducted to examine their relationship to the primary outcome measures. A regression analysis by the authors tend to suggest that higher carer quality of involvement scores significantly predicted increased joint engagement scores post-intervention<br>No cost information was provided |
| Missing data | Missing data were well accounted for in the publication - 3 participants were missing data from the control group at the end of the study |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Randomisation was done using a random number list (page 1048) |
| Allocation concealment (selection bias) | High risk | There was no mention of allocation concealment procedures in the report and it did not appear this was done |

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| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Primary outcome assessors were reported as blind to the case control status of participants |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Though not explicitly stated, it appeared from table 4 that analyses were based on intent to treat rather than on treatment completers alone |
| Selective reporting (reporting bias) | Low risk | The study reported on all outcomes of interest stated in the publication (pages 1052 and 1053) |

**Nefdt 2010**

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|---|---|
| Methods | An RCT. 27 children with ASD were included in the study. No information was provided about gender. There were 13 families in the Intervention (treatment) group and 14 in the control (wait-list) group. Parents delivered the intervention strategies to their children following self-directed learning, using an interactive DVD and accompanying manual |
| Participants | **Child participants:** the study was conducted in US. Inclusion criteria were children under the age of 60 months at the start of the intervention who met DSM-IV criteria for ASD with an ability level “less than twenty functional words”. Parents could not have had any previous training in the implementation of PRT. Parents must have been waiting for services at either the time of referral or at a distance from the centre and must have access to have video recorder and a DVD player in order to be enrolled in the study. The majority of participant children with autism were Caucasian (81%) and male (92.6%). A large percentage of the children were firstborn (~ 70%). The mean age of the children in the treatment and control group was 38.92 months (SD 14.57) and 38.43 months (SD 11.20), respectively. Baseline measures were a 10-minute video of parent-child interaction in which parents attempt to elicit speech, demographics and the Parenting Stress Index. 1 week after baseline the video was repeated, satisfaction questionnaire and DVD usage sheet completed<br>**Parent participants:** the mean age of parents in the intervention group was 36.31 years (SD 5.38) while that of the parents in the control group was 36.21 years (SD 4.54) . Parents in both groups were reported to have clinically significant levels of stress. Of the entire sample approximately 88% were mothers who were married. 15% of parents had a graduate degree, approximately 51% had completed college and around 29% had completed some college. Approximately 4% had completed high school only. Around 52% of participants were stay-at-home parents, approximately 37% were employed as full time with 11% employed as part-time staff. Yearly incomes ranged from less than USD15,000 to more than USD75,000. 41% of families lived in small cities, with the remainder were divided equally between metropolitan areas and towns |

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| Interventions | **Control group:** there were no details of the control condition other than that they were a waiting list control<br>**Intervention group:** a self-directed learning programme that consisted of an interactive DVD with an accompanying manual covering the procedures used in PRT to teach first words to children with ASD was used. The DVD aimed to teach parents strategies to increase child motivation to engage in social communication. Motivation techniques included child choice, incorporation of maintenance factors, reinforcers and reinforcement attempts. Basic behavioural techniques were also taught including clear prompts and immediate contingent consequences. The primary target was expressive verbal language. There were 14 chapters in the DVD each followed by a test. The test was self guided and available in DVD and workbook formats. Parents were asked to complete a chapter and the corresponding test before moving on to the next chapter. At the end of the DVD was a review of the material presented and an interactive learning task including video clips of parents implementing the procedures which they then judged for accuracy of implementation. Information on the DVD was provided in written format on the screen with an audio presentation of the writing. Each chapter had approximately 2 or 3 video clips and a total running time of 1 hour 6 minutes |
| Outcomes | Time points in the study were baseline and 1 week post-intervention. Expressive verbal language was the primary outcome. This was scored from parent-child interaction videos. Language opportunities, functional verbal utterances and observed parent confidence were coded from this. In addition, post-intervention a satisfaction questionnaire and DVD usage sheet were completed |
| Funding source | Not given in the publication |
| Study main findings | Parents who completed the intervention were found to use significantly more motivational procedures of pivotal response training than the waiting list control group at post test. Parents in the treatment group used significantly more language opportunities at post test than the control group. There was a significant difference between the treatment and waiting list control group in parent confidence at post test. Parents in the treatment group were more confident than parents in the waiting list control group at post test. All parents in the treatment group reported that the DVD was easy to understand, useful and informative and that it changed the way they interacted with their child. The majority of parents enjoyed completing the intervention with their child and felt their child was trying to communicate more. No cost information provided |
| Missing data | Yes there were loses to follow-up though not clearly stated how these were handled |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | High risk | Authors only reported that participants were randomly assigned into study groups but failed did not to provide details about |

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| | | the sequence generation process. Parents were randomly assigned to either treatment or control based on the order in which the family information was received (page 25) |
| Allocation concealment (selection bias) | High risk | There was no mention of allocation concealment and it did not appear this was done in the study |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Tapes were presented in a random order for scoring and reliability (p Page 27). Raters were blind to group conditions |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | It is clear that not all the participants who started the study completed it. The reason (s) for losses to follow-up and how data were handled to address the loses were not provided in the publication (page 27) |
| Selective reporting (reporting bias) | Unclear risk | Four 4 targets coded from video, all reported. However, key data were coded by undergraduate students |

**Pajareya 2011**

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|---|---|
| Methods | An RCT. There were 32 children: 28 males and 4 females. 16 children were in the intervention (DIR/Floortime-supplemented treatment) group and 16 were in the control (typical) group. Intervention was a home-based programme delivered by parents of children with ASD following training |
| Participants | **Child participants:** the study was conducted in Mahidol University, Thailand. Participant recruitment was conducted by paper, advertising the DIR/Floortime model. Inclusion criteria were children aged 2-6- years whose diagnoses were confirmed by a developmental paediatrician and met clinical criteria for autistic disorders according to the DSM Mental Disorders. Exclusion criteria were a) any additional medical diagnosis (for example, genetic syndromes, diagnosed hearing impairment, diagnosed visual impairment or seizures); b) geographically inaccessible for follow-up visits or c) parents were not literate or had known chronic psychiatric or physical illness. The primary outcome measure was the FEAS. Secondary outcome measures were the FEDQ and CARS. Each of these measures was used at baseline and at the end of the study. Children's level of ability was assessed through CARS rating: mild autism (CARS score of 30-40) and severe autism (CARS score of 41-60). The mean age for the intervention group was 51.5 months (SD 13.9) and that for the control group was 56.6 months (SD 10.1). The diagnostic groups in this study were autistic disorder and PDD-NOS. 10 of 16 children (62.5%) of the |

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| | control group and 13 of 16 children (81.2%) of the intervention group were diagnosed with autistic disorder. The remaining children were classified with PDD-NOS. In both the intervention and control groups there were 8 children in the mild autism group and 8 children in the severe autism group<br>**Parent participants:** 24 families had parents (mothers) who had Bachelor's degrees or higher and 10 families (mothers) were in full- or part-time employment. 29 families were 2-parent households |
| Interventions | **Control group:** this group received therapies only stated as the typical (entailed varying types of and amounts of interventions)<br>**Intervention group:** this intervention was targeted at parents of children with autism rather than the children themselves. Parents in the intervention group attended a 1-day training workshop with the first author, to learn about the DIR/Floortime model in addition to a 3-hour DVD lecture. The intervention was developmentally sequenced, according to the 6 functional developmental levels of the model: 1) self regulation and interest in the world; 2) engagement and relating; 3) purposeful emotional interaction; 4) social problem solving; 5) creating ideas and 6) thinking logically. The intervention was delivered at 15.2 hours per week for 3 months |
| Outcomes | Primary outcome was children's functional emotional development as measured by the FEAS. Secondary outcomes included the impact of intervention on autistic symptoms as measured by the CARS and child's developmental rating on the FEDQ. Assessments were taken at baseline or start of the study and 3 months (at the end of intervention). There was no report of fidelity of treatment, however, parents reported the number of hours they spent in delivering the intervention (report of parent implementation) and it was stated that 9 parents delivered intervention for ≥ 10 hours per week while 6 parents reported doing so for < 10 hours per week |
| Funding source | Not stated |
| Study main findings | It was reported that the intervention group (compared with the control group) made significantly greater gains in all 3 measures FEAS, CARS and FEDQ. There was no report on any moderator analysis done in the study. Though no cost information was mentioned, authors hinted that the intervention would cost less than alternatives as it employed a low-cost and widely applicable professional-as-consultant, parent-as-therapist model |
| Missing data | Data from 1 participant was reported missing |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Random sequence generation only stated as "Stratified random sampling based on age and symptom severity" |

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|---|---|---|
| Allocation concealment (selection bias) | High risk | Participants who were registered for the study were arranged in a sequence before screening. Following screening, those eligible for the study were allocated into groups with no mention of any attempt to conceal allocations |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Assessment team consisted of two 2 developmental psychologists who were blind to the children' 's group allocation (page 570) |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Precise numbers for each main outcome category was not stated but of the 32 randomised only one 1 from the intervention group was lost to follow- up and reason for this was stated. Analysis was on intention- to- treat basis and differences between group still remained statistically significant even when the outcome for the drop out was treated as " "worst-case scenario: zero change in effect from baseline" " (page 572) |
| Selective reporting (reporting bias) | Low risk | Report included all expected outcomes |

**Rickards 2007**

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|---|---|
| Methods | An RCT. There were 59 children in the study: 47 males and 12 females. 30 children were in the intervention (treatment or home-based) group and 29 were in the control (or centre-based) group. A combination of home- and centre-based programmes were employed in the study. Parents were the primary target of the home-based programme whereas parents and teachers were involved in the activities carried out in the centre-based programme |
| Participants | **Child participants:** the study was conducted in Melbourne Australia at Uncle Bob's Child Development Centre or Westarc Early Intervention Centre and participants were recruited from these centres. Inclusion criteria were delays in 2 or more areas of development based on play observations, parental interview, and information supplied by the referring agency. The centres included children with communication disorders, developmental delay, physical disabilities and PDDs. Children with ASD had been diagnosed by an autistic assessment team according to the criteria listed in DSM-IV or more recently by the ADI-R and the ADOS. All children were eligible for inclusion except those with cerebral palsy and those whose families had inadequate English language skills to enable them to understand the home-based teacher and to complete the questionnaires. Measures used were the Bayley Scales of Infant Development, 2nd edition (for children |

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| | functioning below 3.5 years), Wechsler Preschool and Primary Scale of Intelligence (for children functioning above 3.5 years), VABS, Bayley Behaviour Rating Scale, Behaviour Screening Questionnaire, PBCL, Questionnaire of resource and stress, Family Empowerment Scale and Family Support Scale. These measures were administered at baseline and follow-up. Children were aged 3-5 years. The intervention group had a mean age of 44.6 months (SD 6.1) while the control had a mean of 43.1 months (SD 6.5). The diagnostic groups in this study were ASD, developmental delays and language delay. There were 18 children in the treatment group with ASD, 7 with developmental delay and 5 with language disorder. In the control group there were 21 with ASD, 2 with developmental delay and 6 with language disorder. Mean IQ for the intervention group was 60.2 (SD 20.0) and for the control group it was 60.6 (SD 21.8). Mean VABS scores for the intervention group were 61.2 (SD 18.8) and for the control group 55.0 (SD 14.6)<br>**Parent participants:** in the intervention group, 30% of parents in the group rated high for social status on Daniel's scale; 48.3% of the mothers had less than 12 years of education; 20% were single mothers and 30% used other language in addition to English at home. Similarly, in the control group, 37.9% of parents rated high for social status on Daniel's scale; 50% of the mothers had less than 12 years of education; 3.4% were single mothers and 13.8% used other language in addition to English at home |
| Interventions | **Control group:** those in this group received the centre-based programme, which was a formulated programme designed by a multidisciplinary team in conjunction with the parents and which was tailored to each child and determined by the child's developmental level, learning style and interests and covered all areas of development. This intervention consisted of 5 hours spread over 2 sessions weekly during school terms for 1 year<br>**Intervention group:** in this group a home-based programme was administered and was carried out in the home setting in addition to the centre-based intervention described above. The additional home-based programme was undertaken at a convenient time for families with the aim of providing continuity and generalising skills across the child's environment. A home visitor visited the home during term time for 1-1.5 hours per week for 40 weeks (over a 12-month period) during which relevant concerns about achieving goals and priorities were discussed with the family |
| Outcomes | Primary outcomes were cognitive development and behaviour, family skills, and stress and parental empowerment. Secondary outcomes were effectiveness of a home-based intervention versus a centre-based programme and description of the characteristics of children and families who may benefit most from the home-based intervention. Assessments were made at baseline (time 1) and 13 months after time 1 (time 2). There was no report of fidelity of parent training or report of parent implementation in the study |
| Funding source | Supported by the Murdoch Children's Research Institute and the Jack Brockhoff Foundation |
| Study main findings | There was a reported increase in mean IQ from time 1 to time 2 in the intervention group. Both groups had made no progress in the verbal domain at time 2. There was no statistically significant difference between the groups for change in family measures. It was also reported that the improvements recorded in cognitive functioning at time 2 were sustained in the follow-up<br>The authors correlated stress with outcome and came up with a conclusion that families |

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| | with greater stress were likely to benefit most from the home-based intervention<br>Though no direct cost calculations were made, the authors did state that the cost of the home-based programme was one teachers' salary for 1 year plus some expenses for travelling (though a precise estimate was not given). They were confident that the costs were modest and may likely reduce in the long run if the improvements described were sustained over time |
| Missing data | Yes. 6 children who did not complete the study were accounted for. 1 of those who withdrew from the control group did so because the family felt the intervention group was being favoured |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | After assessment, they were paired according to their DQ, their names placed on folded cards so the names were hidden, and each pair placed in a bowl. The director of Uncle Bob's Child Development Centre randomly and blindly chose 1 of each pair for the home-based intervention and the other for the control group. The director always had another staff member present to witness the validity of the randomisation (page 309) |
| Allocation concealment (selection bias) | High risk | There is no mention of this in the published article and it is not likely that this was carried out |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | The psychologist who did the assessments was blind to the participants groups (page 309) |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | 6 children who did not complete the study were accounted for. One 1 of those who withdrew from the control group did so because the family felt the intervention group was being favoured (page 312) |
| Selective reporting (reporting bias) | High risk | No primary measure specified in the report. For children with autism, only re- |

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| | | ported IQ and PBCL (teacher rating of behaviour) were reported. VABS, an important expected outcome, was missed out with no explanation |

**Roberts 2011**

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| Methods | An RCT. There were 95 children in the study: the exact male/female numbers were not given but it was stated that 90.5% of the children were males. The study had 3 groups: centre-based intervention group, a home-based intervention and a control group (which was not selected at random). The number of participants in each group were: home-based 34, centre-based 33 and WL (waiting list?) 28 (these were total numbers recruited from 2006 and 2007). The centre-based intervention was delivered predominantly at centres outside of the home and with less emphasis on parent involvement as compared with the home-based arm in which there was greater parent emphasis and the intervention was delivered in the child's natural environment, which was the home |
| Participants | **Child participants:** the study was conducted in Sydney, Australia. Participants were drawn from locations not specified in the article (but most likely New South Wales - NSW). Recruitment into the study was done in 2 iterations: 2006 and 2007. Inclusion criteria were children of preschool age at the start of the programme, a diagnosis of autistic disorder, Asperger syndrome or PDD-NOS according to DSM-IV made by a referring clinician (medical practitioner or psychologist, or both), domicile within reasonable distance of a centre-based group and consent to be involved. Parents and staff also judged the child's readiness for a centre-based programme; in a few cases it was agreed that the child was not ready for a centre-based programme and these children were therefore not eligible for inclusion in the study. Baseline measures were the ADOS, GMDS - Extended Revised and the Beach Centre Family Quality of Life Scale. Outcome measures were the VABS II, RDLS-III, the Pragmatics Profile, the DBC, PSI (Short form) and the Beach Family Quality of Life Questionnaire. Mean child age was 3.5 years (range 2.2 to 5.0, SD 0.61). The home-based group had a mean age of 41.5 months (range 26.5 to 59.4); the centre-based group had a mean age of 43.1 months (range 26.3 to 60.0) and the WL group had a mean age of 43.7 months (range 27.6 to 60.3). These figures are based on data from 85 children. Diagnostic groups in the study were autism, Asperger syndrome and PDD-NOS. Level of ability of children was assessed through Griffiths Developmental Quotient: home-based group had a mean of 57.0 (SD 11.7), the centre-based group had a mean of 66.5 (SD 17.7) and the WL group had a mean of 63.3 (SD 15.5), based on data from 85 participants<br>**Parent participants:** out of 78 families with data available for income level of families, 45 (57.7%) earned more than AUD75,000 per year, 8 (10.3%) earn less than AUD40,000 per year while the remainder (25, that is, 32%) earn between AUD50,000 and AUD75,000 per year. Out of 73 mothers, 10 (13.7%) had high school education, 28 (38.4%) had college or post-high school training, 23 (31.5%) had Bachelor's degrees and 12 (16.4%) had postgraduate education. The mean number of family members supported by income was 4 (SD 1.2) out of the 78 families whose data were reported in the article. A mean of 73.0 (SD 23.0) families out of 80 families who gave this information had ranking within NSW in terms of their socioeconomic status and the mean age of mothers was 36.6 years (SD 4.3) based on data from 75 participants. Most of the families spoke |

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| | English language at home with 12 (15.4%) speaking a language other than English and 2 (2.6%) speaking English language in addition to another language at home |
| Interventions | **WL group:** the WL group who got neither of the 2 interventions above but rather attended routine interventions available in the local community. This group was not randomised<br>**Centre-based (control) group:** children in this programme attended 40 weekly 2-hour sessions. The centre-based programme comprised 6 playgroups of 4-6 children, with 6 concurrent parent support and training groups. The child playgroup component involved children participating in a condensed preschool programme with the goal of preparing children for integration into regular preschool settings by focusing on the development of social play skills, functional communication skills and participation in small-group activities. During these activities, staff worked with children to address individual needs through direct intervention (for example, speech difficulties, sensory routines, social skills). Children were also given time to engage in routines and activities that were less directed. The parent training and support group component operated concurrently with the child programme and provided parents with an opportunity to meet weekly with other parents and professionals to discuss a range of set topics, which were prioritised according to individual interests and needs, and included positive behaviour support, communication, self help issues, school options, specialist services and sensory issues. Parents were also encouraged to share information, concerns and achievements and form a support network<br>**Home-based (intervention) group:** children in the home-based programme received a visit for 2 hours once every 2 weeks over a 40-week period (20 sessions maximum) from a member of the transdisciplinary team. Staff from the programme worked in the home with the family to address identified needs (for example, speech, sensory, social skills). An individual programme was designed for each child in conjunction with parents and other professionals involved in the child's programme. Major areas of focus included: assisting parents to manage their child's behaviour in a positive manner, teaching functional communication skills, enhancing social development, extending attending and play skills, addressing sensory processing issues, developing self help skills such as independent toileting, implementing visual communication supports, improving fine and gross motor skills, and developing pre-academic skills. During this time the team member worked with the child and also with their parents to help them develop skills in working with their child. Training techniques included direct modelling of skills, constructive feedback to the family on how they managed the child's education programme, and discussion of issues that were immediate to the needs of the family. There was emphasis on training and supporting parents to work effectively with their children through play and natural routines |
| Outcomes | Primary outcomes for children were communication, social skills, adaptive functioning and psychopathology. For the parents, primary outcomes were are levels of stress, perception of competence in managing their child and quality of life. Assessments were made at baseline (start of the study) and after 12 months. Fidelity of training was assessed through review of files of child participants and the use of checklists and the use of manuals for delivery of the interventions. No mention was made of any assessment of parent implementation |

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| Funding source | Australian Research Council Linkeage Projects grant number LP0562663 in conjunction with Autism Spectrum Australia (Aspect) |
| Study main findings | All 3 groups of children made gains over the intervention period. The centre-based group made significant improvement on VABS. Outcomes for parents were mixed and differences were non-significant. The authors concluded that the centre-based programme will not be suitable for some children and families. No moderator analysis was done. The cost effectiveness analysis for this study was limited to staff costs and outcomes as monitored for the trial. When costs are calculated on a staff hours per child basis the cost per child was AUD6383 regardless of which treatment the child received. The authors stated that this is a small cost compared to a range of other interventions that were available to children and families with autism at the time of the study |
| Missing data | Yes: 10 withdrawals (6 from the home-based group and 4 from the centre-based group) and 1 loss to follow-up in the home-based group |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "Randomisation was conducted by a statistician using computer generated random number tables and the project coordinator was informed of the randomisation result" |
| Allocation concealment (selection bias) | Unclear risk | The process described looks more like blinding (page 1555) |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Blinding of outcome assessors stated (but described as 'allocation concealment') (page 1555) |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Though not explicitly stated if analyses were based on intent to treat or study completers; however, looking at the information provided in table 4 it appears the latter was the case. A sizeable number of individuals withdrew from the study or were lost to follow-up. This could have significant impact on the effect size estimate (page 1560) |

**Roberts 2011** *(Continued)*

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| Selective reporting (reporting bias) | Low risk | The outcomes stated in the articles as outcomes of interest were reported on in the publication |

**Siller 2012**

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| Methods | An RCT. 70 children participated: 36 were in the intervention (FPI) group and 34 were in the control (PAC) condition. There were 64 males and 6 females in all and the therapy of interest (FPI) was a parent-centred one, which used in-home training of parents by trained graduate and postdoctoral students of developmental psychology and counselling |
| Participants | **Child participants:** the participants were recruited from multiple sources including other research projects or university clinics, online research directories, word-of-mouth and state funded regional centres in California, USA. Age at recruitment was said to be less than 6 years for all children. Mean age for the intervention group was 58.3 months (SD 2.7) while that for the control group was 55.9 months (SD 11.9). To participate in the study, children must have been previously diagnosed with ASD, must have shown limited or no use of spoken language (generally < 25 words and no phrases based on parent report), have a mother fluent in English and willing/available to participate in all assessment and treatment sessions, and live within a reasonable travel distance from the research laboratory (generally < 90 minutes). None of the participants indicated the presence of a genetic disorder. All children met diagnostic criteria for autistic disorder on the ADI-Re while 64 children met diagnostic criteria for autistic disorder on the ADOG-Generic. Measures used in this study included the ADI-R, ADOS-G, MSEL, the ESCS, the Insightfulness Assessment, observations of mother-child interaction, a medical history questionnaire and a survey of non-project services<br>**Parent participants:** the mean age of children's mothers in the experimental and control group was 36.0 years (SD 5.3) and 35.7 years (SD 6.1), respectively. There was an under representation of mothers with low educational attainment (that is, mothers who did not complete high-school). In the intervention group, 17 (47.2%) identified their ethnicity as Hispanic/Latino, 8 (22.2%) as white, 4 (11.1%) as Asian, 3 (8.3%) as black and 4 (11.1%) as mixed ethnicity. Annual household income ranged from below USD19,999 in 16.7% to above USD74,999 in 38.9% of families in the intervention group. 44.4% earn USD20,000-74,999 per household in this group. In the control group, 14 (41.2%) identified their ethnicity as Hispanic/Latino, 6 (17.6%) as white, 9 (26.5%) as Asian, 2 (5.9%) as black and 3 (8.8%) as mixed ethnicity. Annual household income ranged from below USD19,999 in 5.9% to above USD74,999 in 52.9% of families in the control group. 41.2% earn between USD20,000-74,999 per household in the control group. It thus appeared that the control group had more households that earn above USD74,999. 50% of parents in the intervention group did not work outside of their homes, 25% worked part time while 25% worked full time. In the control group, 45% did not work outside of the house with 27% working part time and 27% working full time |
| Interventions | **Control group:** this is a structured education programme that aims to promote the parents' ability to actively participate in the planning of their child's treatment and educational programme. Most families of children with autism in California participate in at least 2 annual planning meetings; 1 meeting was scheduled with a representative from the families' local California Regional Center (that is, Individual Program Plan) |

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| | ; the second meeting was scheduled with the child's teacher or representative from the child's the school district (that is, Individualized Education Program), or both. Families randomised to the control condition were invited to participate in 4 PAC sessions (1 session per month, 90 minutes per session). Given that the first sessions of PAC and FPI include several shared components (for example, gathering information on the family and the child's current intervention programme), families in the FPI intervention group were only invited to participate in 3 PAC sessions. While participating in PAC, parents learned about the structure of the individualised planning process and how to access available resources. They also participated in a structured conversation that aimed to identify developmental needs in the areas of health, daily-living skills, challenging behaviours, social integration, education and family supports. In addition to the detailed report about the results from the assessments, parents were provided with a written report summarising the needs identified during this parent interview<br>**Intervention group:** FPI is a parent education programme that involves 12 in-home training sessions (1 session per week for 12 weeks, 90 minutes per session) and follows a standardised treatment manual (the treatment manual is available as an online resource to this manuscript). FPI uses a capacity building approach to promote co-ordinated toy play between parent and child, and includes an ordered sequence of 8 topics. Each treatment session consists of 2 parts. The first part (30-60 minutes) involves both parent and child and provides ample opportunities for parent and interventionist to take turns interacting with the child. After the intervention team enters the home, parent and child are provided with a suitcase that includes a standard set of toys. Parent and child are invited to remove the toys from the suitcase and play for a period of 10 minutes. After this initial episode of parent-child interaction, the interventionist joins the dyad on the floor, and provides the parent with a short overview of the session's topic (2-4 minutes). After this initial introduction of the topic, parent and interventionist take turns interacting with the child for additional 15-45 minutes. In the context of these interactions, the interventionist demonstrates strategies that relate to the session's topic, provides specific and concise feedback on the parent's play (accentuating her positive contributions) and comments on the child's responses. All interactions between parent, child and interventionist are videotaped and captured live using a laptop computer. The second part of each session (30-60 minutes) involves only the parent (a co-interventionist is available to help with child care). During this time, each intervention topic is elaborated using a range of adult learning strategies, including an illustrated workbook for parents (the workbook is available as an online resource to this manuscript), video feedback, conventional teaching and review of weekly homework assignments. Particular emphasis is given to video feedback where parent and interventionist review specific moments of the videotapes captured during the first half of the session. The interventionist carefully chooses these moments to illustrate specific activities, adult behaviours or child responses as they relate to the topic of the respective session. In discussing the challenges that a parent may face in engaging her young child with autism in co-ordinated toy play, the interventionist aims to maintain a collaborative working relationship and engage the parent in active problem solving |
| Outcomes | Outcomes of interest are responsive parental communication (maternal synchronisation) , children's expressive language abilities and the impact of moderators on some outcomes (for example, impact of maternal insightfulness, a potential moderator, on maternal synchronisation; the impact of baseline measures of expressive language on children's language outcomes and the impact of short-term gains in maternal synchronisation on |

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| | children's long term language outcomes). Regarding adherence, all intervention sessions were videotaped and at least 2 sessions per child were chosen at random and coded using a fidelity checklist. The interobserver reliability of this fidelity checklist was evaluated based on 20 videotaped sessions, revealing excellent agreement between 2 independent raters (intraclass correlation coefficient 0.85). Results from applying this checklist to 77 intervention sessions (at least 2 intervention topics were selected at random for each child) revealed that 88.3% obtained fidelity scores above 80% (mean 89.6%, SD 9.0%). There was no mention of parent implementation and the cost implications of the intervention in the publication. Time 1 in the study was baseline assessment, time 2 was "exit" assessment (immediately post-intervention) and time 3 assessment was at the end of 12 months (end of study) |
| Funding source | Not stated in the article |
| Study main findings | The authors reported a significant treatment effect of FPI on responsive parental behaviours. Findings also revealed a conditional effect of FPI on children's expressive language outcomes at 12-month follow-up, suggesting that children with baseline language skills below 12 months are most likely to benefit from FPI. Parents of children with more advanced language skills may require intervention strategies that go beyond FPI's focus on responsive communication. From the moderator analyses done in the study, it was concluded that only parents classified as insightful at baseline effectively changed their communication in response to the experimental intervention. Similarly, only children with expressive language skills below 12 months evidenced reliable treatment effects on language outcomes |
| Missing data | While there were 5 dropouts from the intervention group and 3 from the control conditions, it was stated that the analyses were based on intent to treat. Multiple imputation for missing data was carried out by the authors |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
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| Random sequence generation (selection bias) | Unclear risk | It was only stated that children were "randomised in clusters of 4". Further details about the process was not provided in the article |
| Allocation concealment (selection bias) | High risk | There was no mention of any attempt at allocation concealment in the study |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |

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| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | Interactions were coded by a team of 12 undergraduate research assistants who were blind with regards to the research hypotheses, assessment wave and treatment condition |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | While there were 5 dropouts from the intervention group and 3 from the control conditions, it was stated that the analyses were based on intent to treat. Multiple imputation for missing data was carried out by the authors |
| Selective reporting (reporting bias) | Low risk | All measures were reported |

**Silva 2009**

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| Methods | An RCT. There were 47 children in the study: 33 males and 14 females. 28 were in the intervention (QST Home Program) group and 19 were in the control (waiting-list) group. Though treatment/training support were delivered at centres, it was expected that strategies learned would be generalised into the child's environment through daily routines. Trainers as well as parents were involved to different extents in the delivery of intervention but parents appeared to be the primary target of the intervention in the study. Children were present during parent sessions with trainers |
| Participants | **Child participants:** participants were drawn from children receiving autism services in local, state-sponsored early intervention preschool programmes in Salem and Portland areas of Oregon, USA. The participants were children aged under 6 years, receiving early intervention services for autism and had no complicating medical diagnoses or chronic medication, including no active medical therapies for autism. Children who already had a diagnosis of autism were recruited but details of how this diagnosis was arrived at was not stated in the report. Measures used in the study include ABC, Parent version of PDDBI, Approach/Withdrawal problems composite, Receptive/Expressive social communication abilities composite and PSI. These measures were used for both baseline and outcome assessments. The children in the study were aged 3-6 years (mean age of those in intervention group was 65.2 months (SD 20.7) and those in the control group had a mean of 53.3 months (SD 18.7) and autism was the only diagnostic group in the study. The level of ability of the children was not stated in the study<br>**Parent participants:** no information about the parents were provided in the published article |
| Interventions | **Control group:** this was only stated as the wait-list group and no further details were provided<br>**Intervention group:** this is the QST Home Program, lasting 5 months, and during which parents or carers were trained through 3-hour group sessions until parents were comfortable with procedures followed by coaching and support programme delivered in 7 weekly support meetings lasting 30 minutes. Parents, carers, or both were responsible for delivery of intervention at home to their children with autism. The QST protocol |

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| | takes approximately 15 minutes for parents to deliver |
| Outcomes | Outcomes of interest in the study were impact of intervention on sensory and self regulatory impairment and autistic behaviour. Assessments were made at baseline and 4 months in the study. Fidelity of parent training was assessed through training of trainers (trainers were all graduates of 80-hour QST skill-based training) and report of parent implementation was through trainer reports and records of activities |
| Funding source | Curry Stone Foundation and Northwest Health Foundation |
| Study main findings | The authors concluded that the intervention was suitable for home delivery and is an effective early intervention for autism. This was based on a reported gain in ABC scores and the parent PDDBI in the intervention group compared with the waiting-list group. No analysis of moderators was reported. No cost information was reported |
| Missing data | Yes |
| Notes | Uneven group numbers following randomisation (28 in intervention group and 19 in control group) was said to have been due to sibling pairs in the study |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | This was done using a random sequence generator (page 426) |
| Allocation concealment (selection bias) | High risk | There was no mention of any attempts at concealing the allocation groups and it did not appear like it was done |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Outcome assessors (teachers) were blind to the group status of the participants (pages 423, 425 and 428) |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | The study did not address this outcome and it is unclear if there had been any dropout |
| Selective reporting (reporting bias) | Unclear risk | The primary outcomes of interest were not clearly outlined in the study. Teacher and parent PDDBI, ABC and self regulation checklist. All reported |

**Smith 2000**

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| Methods | An RCT. 28 children were in the study: 23 males and 5 females. 15 of these children were in the intervention* (intensive treatment) group and 13 were in the control (parent training) group. In the intensive intervention group, intervention was taught to parents of the participants through 1-to-1 discrete sessions at the participants' homes followed by a shift to more naturalistic environments (schools) after a period of about 12 months. Intervention was delivered primarily by a team of student therapists and children's primary carers |
| Participants | **Child participants:** this study was conducted in Los Angeles, USA and participants were children with diagnosis of autism or PDD-NOS made by licensed psychologists. The children had no other major medical problem, resided in regions within 1 hour's drive from research centre or hospital, had IQ score of 35-75 and were in the age range of 18-42 months. Participants were drawn from a number of ethnic groups: white (14 children); Hispanic (6 children); black (4 children) and Asian (4 children). Participants were referred to the University of California, Los Angeles young autism project between 1989 and 1992. Diagnostic criteria were not stated. Baseline assessments were done using Stanford-Binet, RDLS and VABS. Outcome measures include VABS, Achenbach Child Behaviour Checklist administered by carers, Wechsler Individualized Achievement Test, Early Learning Measure and family satisfaction questionnaire. Mean age of those in the intensive treatment group was 36.07 months (SD 6.0) while those in the control group had a mean of 35.77 months (SD 5.37). The study diagnostic groups were autism and PDD-NOS. At baseline, most of the children (83%) were non-verbal on RDLS. 50% obtained a raw score of 0 on Merrill-Palmer and VABS scores were reported to be far below the national average<br>**Parent participants:** 8 of the participating children were from single parent homes. Mothers in the intensive treatment group had about 12 years of schooling (range 10 to 16+) while those in the parent training group had about 15 years of schooling (range 12 to 16+). Household income for participating families was about USD40,000 to 50,000 (ranging from less than USD10,000 to 100,000) for both groups |
| Interventions | **Control (intensive treatment) group:** 30 hours of intervention per week was the intended intensity of intervention for the intensive treatment group (but a mean of 25 hours was actually delivered in the end) and intervention was delivered by a team of 4-6 student therapists working under close supervision. Children's primary carers were asked to do 5 hours per week of treatment while working alongside a student therapist for the first 3 months. Once the children could speak in short phrases, play appropriately with toys and acquire some self care skill at approximately 1 year from introduction of intervention, the attention then shifted to more naturalistic environments like classrooms as opposed to homes at the start of intervention. This intervention was based on Lovaas et al manual (1981) (Lovaas 1981). It appears that therapists delivered hours were greater than the number of carer delivered hours in this group<br>**Intervention (parent training) group:** parents were trained at home for about 5 hours per week (delivered in 2 sessions) and children enrolled in special education classes in public schools for up to 10-15 hours. Treatment was also based on based on Lovaas et al manual (1981) (Lovaas 1981) |
| Outcomes | IQ, language development (comprehension and expression) and socialisation skills. Baseline evaluations were made at 3 months before intervention was commenced. Outcomes were assessed at follow-up, which was in the third year of the study. Fidelity was assessed through notes made of start and stop times of interventions by the student therapists |

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| | in the intensive treatment group. The monthly summaries indicated that these children received a mean of 24.56 hours of intervention per week (SD 3.69, range 18.40 to 30.79). It was reported that similar methods were applied to those in the parent training group and in addition the student therapists needed to obtain a satisfactory grade on a number of tests. Parent implementation was assessed through "parent ratings" |
| Funding source | Department for Education grant number H133G80103 and UCLA Regents account number 4-444040-LS-60090 |
| Study main findings | The intensive training group was found to afford statistically significant advantage over the parent training group in IQ, visual-spatial skills and language development but not in adaptive behaviour in everyday settings. Parents in both groups reported moderate gains but this is highly unreliable given the nature of how the assessments were made. No direct cost implications were stated. However, the intensive intervention appears to be more expensive compared to the parent training given the author's comparison of the two. Analyses of the impact of intake IQ and early learning measure (verbal ability) on outcome after treatment was done and while there was no significant relationship between intake IQ and outcome, it was stated that the verbal ability at intake may be predictor of outcome at follow-up following intervention. No cost information provided |
| Missing data | The initial plan was to include children with "mental retardation" and no PDD but as there were only four, they were excluded from data analyses. It was stated that this did not alter the results following sensitivity analysis. There were no reported losses to follow-up in the study |
| Notes | *For the purpose of this review, the group with the parent component was treated as the intervention with the intensive treatment group being considered the control |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Random sequence generation was done using a table of random numbers and by an independent statistician (page 272) |
| Allocation concealment (selection bias) | High risk | The use of an open random sequence alone in the study (page 272) |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Parents who completed surveys were told that their responses would not be disclosed to the treatment personnel, and examiners were blind to children' 's group assignment and treatment history (page 277) |

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| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | The initial plan was to include children with mental retardation and no pervasive developmental disorder PDD. But following the low numbers of participants in this category, those recruited and randomised (4 of them), they were excluded from data analyses. It was stated that this did not alter the results following sensitivity analysis. There were no reported loses to follow up in the study |
| Selective reporting (reporting bias) | Low risk | Primary and secondary outcomes of interest were not clearly stated by the authors. All measures reported |

**Tonge 2006**

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| Methods | An RCT. 105 children and their families participated in the study: there were 35 children in the PEAC group, 35 in the PEBM group and 35 in the control group. In the parent arm of this study (Tonge 2006), which was reported separately, data were analysed for only 33 parents/carers in the PEAC group. Treatments were centre-based and directed at carers or parents of children with autism. Sessions were delivered to parents in small groups. Children were not present in the PEAC sessions but were present in the PEBM skills training sessions. All children were said to be living with their parents |
| Participants | **Child participants:** the study was conducted in Australia and sample was drawn from a wide range of nationalities including English, Irish, Italian, Greek, Vietnamese, Chinese, Cambodian, Sudanese, Saudi Arabian, Lebanese, Pacific Islander, and Indigenous Australian groups. These participants were recruited from areas simply described as rural or metropolitan. Children met the criteria for the diagnosis of autism. No other inclusion/exclusion criteria were stated in the report. Diagnostic criteria were the DSM-IV criteria. Baseline measures included VABS, DBC, CARS, PEP-R, Developmental score, DQ and RDLS- III. The same measures were administered post intervention. Children were aged 2.5-5 years. Mean age was 43.24 months (SD 7.35) for the PEAC group and 46 months (SD 8.11) for the PEBM group. Child level of ability was characterised using a number of instruments including DBC TBPS into mild autism (37%), moderate autism (29%) and severe autism (34%); CARS (mean scores) of 43.54 (SD 5.60) for PEAC group, 41.23 (SD 5.25) for PEBM and 38.9 (SD 5.79) for control; and mean DQ of 48.71 (SD 21.72) for PEAC group, 64.74 (SD 27.41) for the PEBM group and 63.31 (SD 28.52) for the control group all taken at baseline<br>**Parent participants:** parental occupations included professional and business management, farming, trades, semi-skilled and unskilled workers and unemployed. A detailed breakdown of parents characteristics was not provided in the report |
| Interventions | **Control group:** children had no intervention of interest but were allowed to use local services available for autism. Children received on average 7.9 hours per week of these services<br>**PEAC group:** parents in this group received a manual-based education programme. The |

| | |
|---|---|
| | educational material in the manual for PEAC group discussion sessions was the same as for the PEBM group. Individual sessions were for parents only and the child was not present. No skills training or homework tasks were set and emphasis was on non-directive interactive discussion and counselling<br>**PEBM skills training group:** parents in this group attended sessions aimed at educating them about autism; features of communication, social, play and behavioural impairments; principles of managing behaviour and change; teaching new skills; improving social interaction and communication; how to access available services; managing parental stress, grief and mental health problems; sibling, family and community responses to autism, and individual sessions included the child as well<br>Both interventions lasted 20 weeks and were based on educational models. In both groups participants were allowed to use locally available services (average use was up to about 7.3 hours per week) in addition to the intervention |
| Outcomes | Primary outcomes were child's adaptive behaviour and parent stress. Secondary outcomes were autism symptoms, child's emotional and behavioural state, level of cognitive and language development and the impact of specific parent skills training and coaching methods on child outcomes as compared to parent education alone. The study time point were baseline or pre-treatment and 6 months after the completion of treatment (12 months after baseline). There was no mention of adherence in the report |
| Funding source | National Health and Medical Research Council Project Grant (124303) |
| Study main findings | The authors concluded that the PEBM (which incorporates skills training for parents of young children with autistic disorder) provided significant improvements in child adaptive behaviour and symptoms of autism post intervention and was a better programme compared to the PEAC programme. It was also reported that both treatments resulted in significant and progressive improvement in overall mental health at follow-up, especially those primary carers with the highest level of mental health problems and with the PEBM being more effective in alleviating a greater percentage of anxiety, insomnia, and somatic symptoms and family dysfunction than the PEAC. Moderator analysis suggested that the effect of treatment was dependent on pre-test level of communication skills; those in the PEBM group with lower pre-treatment scores will have greater gains when compared with the control group. No cost information provided but the authors suggested that group parent interventions may be more cost effective |
| Missing data | Dropouts from the study after randomisation were handled by replacement with equivalent stratified cases and analysis was on an intention to treat basis |
| Notes | For the purpose of this review, the PEBM group was treated as the intervention with the PEAC group was considered the control |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Participants were allocated into groups using computer-generated random sequences |

| | | |
|---|---|---|
| Allocation concealment (selection bias) | High risk | Use of open allocation schedule alone in the study |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Outcome assessment was done by a clinician blind to pre-treatment assessments and group membership |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | It was not reported if there was loss to follow-up in the study and though stated that 2 children did not complete 2 of the tests (PEP-R and RDLS-III), details of how this was handled was not reported in the article (page 20) |
| Selective reporting (reporting bias) | Low risk | The main outcome of interest (child behaviour measured using VABS) was reported on. All other outcomes reported |

**Wong 2010**

| | |
|---|---|
| Methods | An RCT with a cross-over design. It had 17 children: 16 males and 1 female. 9 children were in the intervention (autism 1-2-3) group and 8 children were in the control group. The study focused on a home-based intervention (autism 1-2-3) in which mothers and carers were the primary target |
| Participants | **Child participants:** children were consecutive newly diagnosed referral cases between January and December 2007. The study was conducted at the Duchess of Kent Child Assessment Centre of the University of Hong Kong, China. Child participants had no co-morbid neurological or psychiatric disorders and were children who had not received any communication or social skills training. Diagnostic criteria included DSM-IV, ADOS and ADI-R. Baseline measures were GMDS and CARS. Outcome measures were ADOS (module 1), RFRLRS, SPT and PSI/SF. The children were aged 17 to 36 months. Mean age of the intervention group was 25.33 months (SD 6.00, range 17 to 36) while that of the control group was 27.88 months (SD 5.57, range 18 to 36). ASD was the diagnostic group in the study. Children's level of ability was assessed using CARS score: mean score for the intervention group was 35.67 (SD 4.64, range 29.0 to 41.5) while that for the control group was 36.88 (SD 4.24, range 30.0 to 40.5)<br>**Parent participants:** not stated in the report |
| Interventions | **Control group:** this was only stated as the "no treatment arm" of the study. Those in this group did not receive the intervention during the first 2 weeks of the study, they only received intervention after the RCT phase was over and assessments were made before the cross-over began<br>**Intervention group:** based upon behavioural and social-pragmatic models, the autism 1- |

| | |
|---|---|
| | 2-3 intervention was designed to teach parents simple home-based techniques in training their children with autism to use eye contact, gestures and words to improve their quality of communication and social interaction. The autism 1-2-3 intervention was delivered daily for 5 days per week over a 2-week period |
| Outcomes | Primary outcomes included communication and social interaction (eye contact, gestures and words to improve their quality of life). The secondary outcome was parent stress. Time points in the study were baseline, time 1 (third week into the study and time for assessment of outcome for the RCT phase) and time 3 (week 5/6 of the study which marked the end of the cross-over design and assessment of outcome). Only assessments at baseline and time 1 were of interest for this review. There was no report on adherence in the report |
| Funding source | Not stated |
| Study main findings | It was reported that following the intervention children with autism improved in language/communication, reciprocal social interaction, and symbolic play and that parents perceived significant improvement in their children's language, social interaction and their own stress level. There were no significant changes in the control group. No cost information was provided |
| Missing data | No report of missing data in the study |
| Notes | |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | The authors only mentioned that participants were randomly assigned to group but failed to provide details about the randomisation sequence generation (page 679) |
| Allocation concealment (selection bias) | High risk | There was no mention of this in the study and it did not appear authors have done this |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Not possible |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Low risk | Outcome assessors only were blind to participants' case control status (p Pages 680 and 681) |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Though it was not explicitly reported in the study, a close look at the data analysed suggests that the study did not have any losses |

| | | |
|---|---|---|
| | | to follow-up nor was there any missing data (tables 1, 2, 3 and 4) |
| Selective reporting (reporting bias) | Low risk | Outcomes stated as outcomes of interest were reported on in the article |

ABA: applied behavioural analysis; ABC: Autism Behaviour Checklist; ADI-R: Autism Diagnostic Interview-Revised; ADOS: Autism Diagnostic Observation Schedule; A/M: Assess and Monitor; APP: Autism Preschool Program; ASD: autism spectrum disorder; AUD: Australian dollar; CAD: Canadian dollar; CARS: Childhood Autism Rating Scale; CASL: Comprehensive Assessment of Spoken Language; CHAT: Checklist for Autism in Toddlers; CSBS-DP: Communication and Symbolic Behaviour Scales Developmental Profile; DBC: Developmental Behaviour Checklist; DPA: Developmental Play Assessment; DQ: Developmental quotient; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; DSP: Developmental Social Pragmatic; EIDP: Early Intervention Developmental Profile; ESCS: Early Social Communication Scales; ESDM: Early Start Denver Model; FEAS: Functional Emotional Assessment Scale; FEDQ: Functional Emotional Developmental Questionnaire; FPI: Focused Playtime Intervention; GMDS: Griffiths Mental Developmental Scales; HMTW: Hanen More Than Words; ICD-10: International Classification of Diseases and Related Health Problems, 10th edition; IQ: intelligence quotient; IQR: interquartile range; mCBRS: modified Childhood Behaviour Rating Scale; MCDI: MacArthur Communicative Development Inventory; MEHRIT: Milton & Ethel Harris Research Initiative Treatment; MSEL: Mullen Scales of Early Learning; PAC: Parent Advocacy Coaching; PACT: Preschool Autism Communication Trial; PBCL: Preschool Behaviour Checklist; PCFP: Parent-Child Free Play; PDD: Pervasive Developmental Disorder; PDDBI: Pervasive Developmental Disorders Behaviour Inventory; PDD-NOS: Pervasive Developmental Disorder Not Otherwise Specified; PEAC: parent education and counselling; PEBM: parent education and behaviour management; PEP-R: Psychoeducational Profile-Revised; PIA-CV: Parent Interview for Autism - Clinical Version; PLS: Preschool Language Scales; PRT: Pivotal Response Treatment; PSDP: Preschool Developmental Profile; PSI: Parental Stress Inventory; PSI-SF: Parenting Stress Index Short Form; RBS: Repetitive Behaviour Scale; RCT: randomised controlled trial; RDLS-III: Reynell Developmental Language Scales III; FFRLRS: Ritvo-Freeman Real Life Rating Scale; SD: standard deviation; SPT: Symbolic Play Test; TAU: treatment as usual; TBPS: total behaviour problem score; VABS: Vineland Adaptive Behaviour Scales.

## Characteristics of excluded studies *[ordered by study ID]*

| Study | Reason for exclusion |
|---|---|
| Balkom 2010 | Focus was on developmental language delay |
| Frankel 2010 | Children in this study were 8-10 years old |
| Gantman 2012 | Adult study in which participants were aged above 6 years 11 months |
| Giarelli 2005 | In this study, the role of nurses in delivery of intervention was clearly defined but it was not clear that parents were carrying out the intervention. It is highly unlikely that parents were significantly involved in the intervention given the information provided |
| Gulsrud 2010 | A descriptive analysis of a new measure applied with participants in the Kasari 2010 study after all had received intervention |

(*Continued*)

| | |
|---|---|
| Kaale 2012 | Intervention was not primarily delivered by parents of the children. “Parents were not involved in the implementation of the intervention” |
| Kasari 2006 | The intervention in this study was not parent-mediated |
| Landa 2011 | Teachers delivered the intervention |
| Lopata 2010 | Children in this study were aged 7-12 years |
| Oosterling 2010 | Not fully an RCT: the randomisation process involved random assignments into groups, randomisation in clusters based on family residence and allocation that was not randomised for reasons stated as “pragmatic” |
| Rickards 2009 | This is a 2-year follow-up of the included study by Rickards 2007 (which reported results at 1 year). There was considerable attrition and results were not provided for the autism spectrum disorder group separately |
| Romski 2010 | Study was on children with language delay |
| Sallows 2005 | Therapist-delivered programme |
| Shin 2009 | Study was about children with intellectual disability |
| Silva 2011 | Not fully an RCT based on the method of analyses |
| Smith 2010 | Not an RCT (quasi-randomised) |
| Sofronoff 2011 | Study included children aged 10-12 years, and focused on intervention for anxiety |
| Sung 2011 | Study included children aged 9-16 years, and focused on intervention for anxiety |
| Tang 2011 | Study was on children with motor and developmental delay |
| Warreyn (unpublished) | Therapists delivered the intervention |
| Whalen 2010 | A computer-delivered intervention with no parent involvement |
| Whittingham 2009 | Study did not clearly state the age of participants but from the mean provided it is clear that the study had more than 5% of children aged above 6 years 11 months. The paper stresses the intervention is a “parenting intervention” and not child-focused |
| Yoder 2006 | The intervention, PECS and RPMT, was primarily therapist delivered with little or no emphasis on parent involvement |

PECS: Picture Exchange Communication System; RCT: randomised controlled trial; RPMT: Responsive Education and Prelinguistic Milieu Teaching.

# DATA AND ANALYSES

## Comparison 1. Child communication and social development

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Language - Joint (direct or independent assessment) | 2 | 64 | Std. Mean Difference (IV, Random, 95% CI) | 0.45 [-0.05, 0.95] |
| 2 Communication (reported) | 3 | 228 | Mean Difference (IV, Random, 95% CI) | 5.31 [-6.77, 17.39] |
| 3 Language - Expression (direct or independent assessment) | 3 | 264 | Std. Mean Difference (IV, Random, 95% CI) | 0.14 [-0.16, 0.45] |
| 4 Language - Expression (reported) | 3 | 204 | Mean Difference (IV, Random, 95% CI) | 29.44 [-14.99, 73.86] |
| 5 Language - Comprehension (direct or independent assessment) | 2 | 200 | Std. Mean Difference (IV, Random, 95% CI) | 0.29 [-0.20, 0.78] |
| 6 Language - Comprehension (reported) | 3 | 204 | Mean Difference (IV, Random, 95% CI) | 36.26 [1.31, 71.20] |
| 7 Parent-child interaction (Shared or joint attention time) | 3 | 215 | Std. Mean Difference (IV, Random, 95% CI) | 0.41 [0.14, 0.68] |
| 8 Child initiations (coding of parent child interactions) | 4 | 268 | Std. Mean Difference (IV, Random, 95% CI) | 0.38 [-0.07, 0.82] |
| 9 Autism severity | 6 | 316 | Std. Mean Difference (IV, Random, 95% CI) | -0.30 [-0.52, -0.08] |
| 10 Adaptive behaviour | 2 | 197 | Mean Difference (IV, Fixed, 95% CI) | 1.06 [-2.95, 5.06] |

## Comparison 2. Parent outcomes

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Parents' level of stress | 2 | 55 | Std. Mean Difference (IV, Random, 95% CI) | -0.17 [-0.70, 0.36] |
| 2 Parent-child interaction (parent synchrony) | 3 | 244 | Std. Mean Difference (IV, Random, 95% CI) | 0.90 [0.56, 1.23] |

## Analysis 1.1. Comparison 1 Child communication and social development, Outcome 1 Language - Joint (direct or independent assessment).

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 1 Child communication and social development

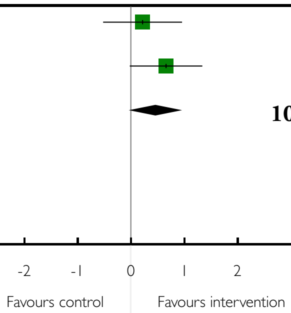
Outcome: 1 Language - Joint (direct or independent assessment)

| Study or subgroup | Intervention N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Casenhiser 2011 | 16 | 0.72 (0.39) | 13 | 0.64 (0.32) | | 46.5 % | 0.22 [ -0.52, 0.95 ] |
| Jocelyn 1998 | 16 | 30.2 (15) | 19 | 21.9 (9.6) | | 53.5 % | 0.66 [ -0.03, 1.34 ] |
| **Total (95% CI)** | **32** | | **32** | | | **100.0 %** | **0.45 [ -0.05, 0.95 ]** |

Heterogeneity: $\text{Tau}^2 = 0.0$; $\text{Chi}^2 = 0.74$, df = 1 (P = 0.39); $I^2 = 0.0\%$

Test for overall effect: Z = 1.77 (P = 0.077)

Test for subgroup differences: Not applicable



## Analysis 1.2. Comparison 1 Child communication and social development, Outcome 2 Communication (reported).

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 1 Child communication and social development

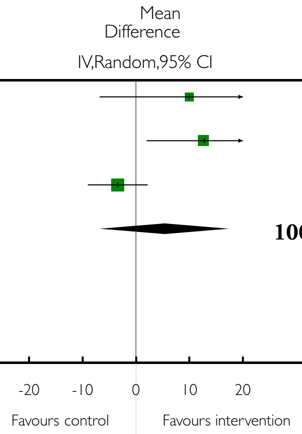
Outcome: 2 Communication (reported)

| Study or subgroup | Intervention N | Intervention Mean(SD) | Control N | Control Mean(SD) | Weight | Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|
| Aldred 2004 | 14 | 71 (24.82) | 14 | 60.93 (20.26) | 24.4 % | 10.07 [ -6.71, 26.85 ] |
| Dawson 2010 | 24 | 82.1 (21.8) | 24 | 69.4 (15.8) | 33.7 % | 12.70 [ 1.93, 23.47 ] |
| Green 2010 | 77 | 64.3 (17.7) | 75 | 67.7 (17.5) | 41.9 % | -3.40 [ -9.00, 2.20 ] |
| **Total (95% CI)** | **115** | | **113** | | **100.0 %** | **5.31 [ -6.77, 17.39 ]** |

Heterogeneity: $Tau^2 = 82.49$; $Chi^2 = 8.02$, df = 2 (P = 0.02); $I^2 = 75\%$

Test for overall effect: Z = 0.86 (P = 0.39)

Test for subgroup differences: Not applicable



## Analysis 1.3. Comparison 1 Child communication and social development, Outcome 3 Language - Expression (direct or independent assessment).

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 1 Child communication and social development

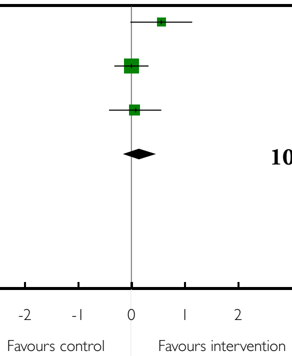
Outcome: 3 Language – Expression (direct or independent assessment)

| Study or subgroup | Intervention N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Dawson 2010 | 24 | 36.6 (13.6) | 24 | 30 (9.2) | | 22.0 % | 0.56 [ -0.02, 1.14 ] |
| Green 2010 | 77 | 20 (11.2) | 75 | 20 (11.3) | | 49.8 % | 0.0 [ -0.32, 0.32 ] |
| Siller 2012 | 34 | 19.35 (10.72) | 30 | 18.57 (11.25) | | 28.2 % | 0.07 [ -0.42, 0.56 ] |
| **Total (95% CI)** | **135** | | **129** | | | **100.0 %** | **0.14 [ -0.16, 0.45 ]** |

Heterogeneity: Tau$^2$ = 0.02; Chi$^2$ = 2.80, df = 2 (P = 0.25); I$^2$ =29%

Test for overall effect: Z = 0.92 (P = 0.36)

Test for subgroup differences: Not applicable



## Analysis 1.4. Comparison 1 Child communication and social development, Outcome 4 Language - Expression (reported).

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 1 Child communication and social development

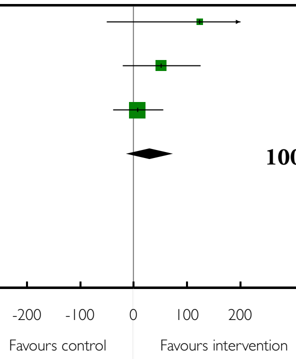
Outcome: 4 Language – Expression (reported)

| Study or subgroup | Intervention | | Control | | Mean Difference | Weight | Mean Difference |
|---|---|---|---|---|---|---|---|
| | N | Mean(SD) | N | Mean(SD) | IV,Random,95% CI | | IV,Random,95% CI |
| Aldred 2004 | 14 | 314 (230.98) | 14 | 189.5 (237.81) | | 6.3 % | 124.50 [ -49.16, 298.16 ] |
| Drew 2002 | 12 | 96.6 (118.8) | 12 | 44 (50.2) | | 31.4 % | 52.60 [ -20.37, 125.57 ] |
| Green 2010 | 77 | 171.9 (150.7) | 75 | 163.8 (144.3) | | 62.3 % | 8.10 [ -38.80, 55.00 ] |
| **Total (95% CI)** | **103** | | **101** | | | **100.0 %** | **29.44 [ -14.99, 73.86 ]** |

Heterogeneity: $Tau^2 = 252.11$; $Chi^2 = 2.31$, df = 2 ($P = 0.32$); $I^2 = 13\%$

Test for overall effect: $Z = 1.30$ ($P = 0.19$)

Test for subgroup differences: Not applicable



## Analysis 1.5. Comparison 1 Child communication and social development, Outcome 5 Language - Comprehension (direct or independent assessment).

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 1 Child communication and social development

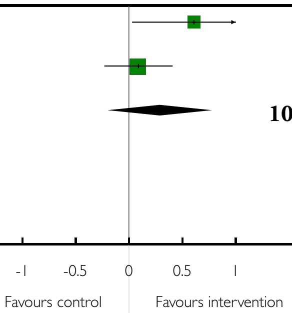
Outcome: 5 Language – Comprehension (direct or independent assessment)

| Study or subgroup | Intervention N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Dawson 2010 | 24 | 40 (16.3) | 24 | 31.5 (10.6) | | 38.5 % | 0.61 [ 0.03, 1.19 ] |
| Green 2010 | 77 | 21.5 (13) | 75 | 20.3 (12.8) | | 61.5 % | 0.09 [ -0.23, 0.41 ] |
| **Total (95% CI)** | **101** | | **99** | | | **100.0 %** | **0.29 [ -0.20, 0.78 ]** |

Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 2.33$, df = 1 (P = 0.13); $I^2 = 57\%$

Test for overall effect: Z = 1.16 (P = 0.25)

Test for subgroup differences: Not applicable



## Analysis 1.6. Comparison 1 Child communication and social development, Outcome 6 Language - Comprehension (reported).

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 1 Child communication and social development

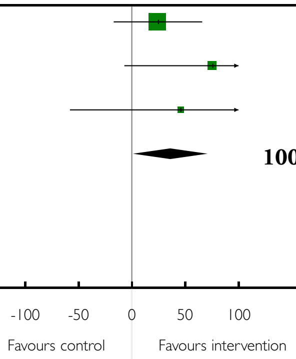
Outcome: 6 Language – Comprehension (reported)

| Study or subgroup | Intervention N | Mean(SD) | Control N | Mean(SD) | Mean Difference IV,Random,95% CI | Weight | Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Green 2010 | 77 | 233.7 (129.6) | 75 | 209 (131.3) | | 71.0 % | 24.70 [ -16.78, 66.18 ] |
| Drew 2002 | 12 | 176.1 (121.9) | 12 | 100.3 (80.2) | | 17.9 % | 75.80 [ -6.76, 158.36 ] |
| Aldred 2004 | 14 | 265.43 (134.56) | 14 | 219.14 (147.89) | | 11.1 % | 46.29 [ -58.45, 151.03 ] |
| **Total (95% CI)** | **103** | | **101** | | | **100.0 %** | **36.26 [ 1.31, 71.20 ]** |

Heterogeneity: Tau$^2$ = 0.0; Chi$^2$ = 1.21, df = 2 (P = 0.54); I$^2$ =0.0%

Test for overall effect: Z = 2.03 (P = 0.042)

Test for subgroup differences: Not applicable



## Analysis 1.7. Comparison 1 Child communication and social development, Outcome 7 Parent-child interaction (Shared or joint attention time).

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 1 Child communication and social development

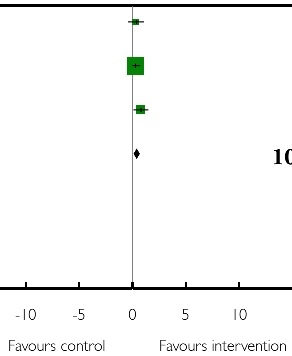
Outcome: 7 Parent-child interaction (Shared or joint attention time)

| Study or subgroup | Intervention<br>N | Mean(SD) | Control<br>N | Mean(SD) | Std. Mean Difference<br>IV,Random,95% CI | Weight | Std. Mean Difference<br>IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Aldred 2004 | 14 | 88.6 (8.7) | 14 | 80.3 (30.1) | | 13.1 % | 0.36 [ -0.38, 1.11 ] |
| Green 2010 | 77 | 64 (25.7) | 75 | 55.6 (25.7) | | 71.7 % | 0.33 [ 0.01, 0.65 ] |
| Kasari 2010 | 19 | 42.85 (19.96) | 16 | 27.87 (14.01) | | 15.1 % | 0.84 [ 0.14, 1.53 ] |
| **Total (95% CI)** | **110** | | **105** | | | **100.0 %** | **0.41 [ 0.14, 0.68 ]** |

Heterogeneity: Tau$^2$ = 0.0; Chi$^2$ = 1.72, df = 2 (P = 0.42); I$^2$ =0.0%

Test for overall effect: Z = 2.95 (P = 0.0032)

Test for subgroup differences: Not applicable



## Analysis 1.8. Comparison 1 Child communication and social development, Outcome 8 Child initiations (coding of parent child interactions).

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 1 Child communication and social development

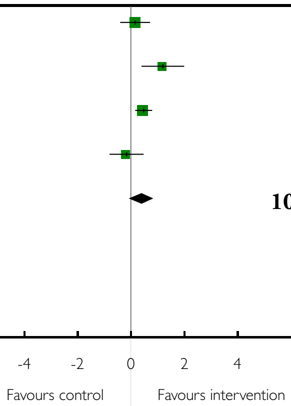
Outcome: 8 Child initiations (coding of parent child interactions)

| Study or subgroup | Intervention<br>N | Mean(SD) | Control<br>N | Mean(SD) | Std. Mean Difference<br>IV,Random,95% CI | Weight | Std. Mean Difference<br>IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Carter 2011 | 24 | 10.33 (9.82) | 25 | 8.68 (9.26) | | 25.2 % | 0.17 [ -0.39, 0.73 ] |
| Casenhiser 2011 | 16 | 1.84 (0.549) | 13 | 1.23 (0.43) | | 17.7 % | 1.19 [ 0.38, 1.99 ] |
| Green 2010 | 77 | 34.9 (19.7) | 75 | 26 (17.5) | | 34.6 % | 0.47 [ 0.15, 0.80 ] |
| Kasari 2010 | 19 | 3.11 (3.41) | 19 | 3.77 (3.76) | | 22.5 % | -0.18 [ -0.82, 0.46 ] |
| **Total (95% CI)** | **136** | | **132** | | | **100.0 %** | **0.38 [ -0.07, 0.82 ]** |

Heterogeneity: Tau$^2$ = 0.12; Chi$^2$ = 7.72, df = 3 (P = 0.05); I$^2$ =61%

Test for overall effect: Z = 1.67 (P = 0.095)

Test for subgroup differences: Not applicable



## Analysis 1.9. Comparison 1 Child communication and social development, Outcome 9 Autism severity.

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 1 Child communication and social development

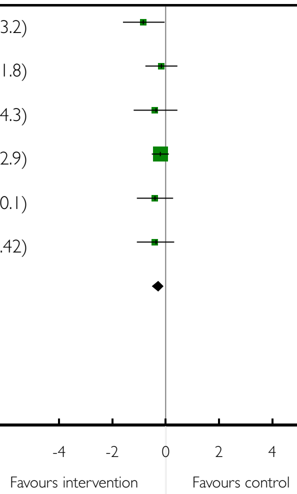
Outcome: 9 Autism severity

| Study or subgroup | Intervention N | Intervention Mean(SD) | Control N | Control Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Aldred 2004 | 14 | 7.7 (3.8) | 14 | 10.7 (3.2) | | 8.2 % | -0.83 [ -1.61, -0.05 ] |
| Dawson 2010 | 24 | 7 (1.9) | 21 | 7.3 (1.8) | | 14.4 % | -0.16 [ -0.75, 0.43 ] |
| Drew 2002 | 12 | 18.3 (4.9) | 12 | 20.1 (4.3) | | 7.6 % | -0.38 [ -1.19, 0.43 ] |
| Green 2010 | 77 | 9.2 (3) | 75 | 9.8 (2.9) | | 48.8 % | -0.20 [ -0.52, 0.12 ] |
| Jocelyn 1998 | 16 | 48.5 (18.4) | 19 | 56.5 (20.1) | | 11.0 % | -0.40 [ -1.08, 0.27 ] |
| Pajareya 2011 | 16 | 34.5 (6.01) | 16 | 37.13 (7.42) | | 10.1 % | -0.38 [ -1.08, 0.32 ] |
| **Total (95% CI)** | **159** | | **157** | | | **100.0 %** | **-0.30 [ -0.52, -0.08 ]** |

Heterogeneity: Tau$^2$ = 0.0; Chi$^2$ = 2.54, df = 5 (P = 0.77); I$^2$ =0.0%

Test for overall effect: Z = 2.65 (P = 0.0081)

Test for subgroup differences: Not applicable



## Analysis 1.10. Comparison 1 Child communication and social development, Outcome 10 Adaptive behaviour.

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 1 Child communication and social development

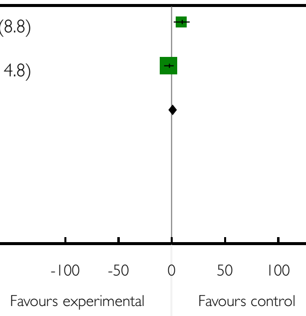
Outcome: 10 Adaptive behaviour

| Study or subgroup | Intervention N | Mean(SD) | Control N | Mean(SD) | Mean Difference IV,Fixed,95% CI | Weight | Mean Difference IV,Fixed,95% CI |
|---|---|---|---|---|---|---|---|
| Dawson 2010 | 24 | 68.7 (15.9) | 21 | 59.1 (8.8) | | 29.4 % | 9.60 [ 2.21, 16.99 ] |
| Green 2010 | 77 | 60.3 (15.2) | 75 | 62.8 (14.8) | | 70.6 % | -2.50 [ -7.27, 2.27 ] |
| **Total (95% CI)** | **101** | | **96** | | | **100.0 %** | **1.06 [ -2.95, 5.06 ]** |

Heterogeneity: $\text{Chi}^2 = 7.27$, df = 1 (P = 0.01); $I^2$ =86%

Test for overall effect: Z = 0.52 (P = 0.61)

Test for subgroup differences: Not applicable



## Analysis 2.1. Comparison 2 Parent outcomes, Outcome 1 Parents' level of stress.

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 2 Parent outcomes

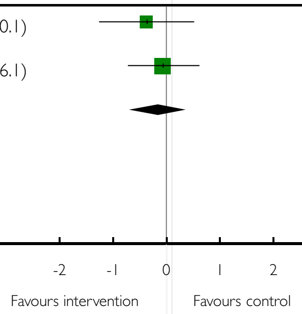
Outcome: 1 Parents' level of stress

| Study or subgroup | Intervention N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Drew 2002 | 10 | 104.3 (20) | 10 | 112.1 (20.1) | | 36.1 % | -0.37 [ -1.26, 0.51 ] |
| Jocelyn 1998 | 16 | 5.9 (7) | 19 | 6.3 (6.1) | | 63.9 % | -0.06 [ -0.73, 0.61 ] |
| **Total (95% CI)** | **26** | | **29** | | | **100.0 %** | **-0.17 [ -0.70, 0.36 ]** |

Heterogeneity: $\text{Tau}^2 = 0.0$; $\text{Chi}^2 = 0.31$, df = 1 (P = 0.58); $I^2$ =0.0%

Test for overall effect: Z = 0.64 (P = 0.52)

Test for subgroup differences: Not applicable



## Analysis 2.2. Comparison 2 Parent outcomes, Outcome 2 Parent-child interaction (parent synchrony).

Review: Parent-mediated early intervention for young children with autism spectrum disorders (ASD)

Comparison: 2 Parent outcomes

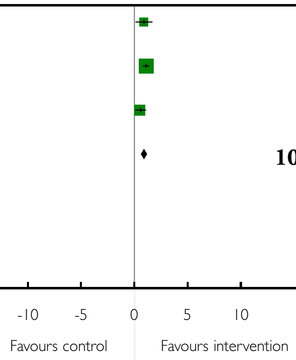
Outcome: 2 Parent-child interaction (parent synchrony)

| Study or subgroup | Intervention N | Mean(SD) | Control N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Aldred 2004 | 14 | 65.1 (14.3) | 14 | 49.5 (18.9) | | 15.7 % | 0.90 [ 0.12, 1.69 ] |
| Green 2010 | 77 | 51.3 (19.6) | 75 | 32.6 (14) | | 52.3 % | 1.09 [ 0.75, 1.43 ] |
| Siller 2012 | 34 | 0.73 (0.21) | 30 | 0.61 (0.2) | | 32.0 % | 0.58 [ 0.08, 1.08 ] |
| **Total (95% CI)** | **125** | | **119** | | | **100.0 %** | **0.90 [ 0.56, 1.23 ]** |

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 2.75$, df = 2 (P = 0.25); $I^2 = 27\%$

Test for overall effect: Z = 5.26 (P < 0.00001)

Test for subgroup differences: Not applicable



# ADDITIONAL TABLES

### Table 1. Table showing changes to methods described in the protocol

| Section of the review | Issues | What was done |
|---|---|---|
| **Measurement of treatment effect** | No relevant categorical data encountered | No analysis using categorical data was done |
| **Unit of analysis** | No cluster randomised trials were identified | No analysis was done |
| | | Wong 2010 presented a cross-over design. Information from this study was used only in the narrative synthesis as the measures used in the study, the way in which results were reported and the theoretical background prohibited its inclusion in the meta-analysis. Thus the study did not present any "unit of analysis" issue (see Appendix |

**Table 1. Table showing changes to methods described in the protocol** *(Continued)*

| | | |
|---|---|---|
| | | 2 and Characteristics of included studies sections). Only data in the first part of the study, before participants swapped groups, was used in the discussions. |
| | Studies with multiple treatment groups | Two studies had multiple treatment groups and a control group. Roberts 2011 had a non-randomised control group, so the two treatment conditions were compared (home based treated as the experimental intervention group, and centre-based treated as the control group). Data from this study were included only in the narrative synthesis as the measures used in the study and the study methods prohibited its inclusion in the meta-analysis (see Appendix 2 and Characteristics of included studies sections) . Tonge 2006/Tonge 2012 also had 2 treatment arms, with hypothesised greater effects for the treatment with dedicated skills training versus a parent education-only group. Therefore for this review, the 2 treatment arms were compared with the latter arm as the control<br>In future revisions of this review, it is likely that there will be more examples of comparison of multiple-treatment groups. In that case the authors will first examine studies that compare with no treatment, waiting-list or treatment as usual, and then examine studies with other treatment controls, so as to interpret the latter in light of the evidence for the former group of studies |

**Table 2. Sensitivity analyses**

| **Analysis** | **Sequence generation** | **Allocation concealment** | **Blinding of outcome (detection bias)** | **Attrition** |
|---|---|---|---|---|
| Joint language (direct assessment) Analysis 1.1 | Not applicable | Not done (only 1 study had low risk) | Not applicable | Not applicable |
| Communication (reported) Analysis 1.2 | Not applicable | Not done (only 1 study had low risk) | Not applicable | Not applicable |
| Language - expression (direct assessment) Analysis 1.3 | Not applicable | Not done (only 1 study had low risk) | Not applicable | Not applicable |
| Language - expression (reported) Analysis 1.4 | Not applicable | Not done (only 1 study had low risk) | No difference | Not applicable |

**Table 2. Sensitivity analyses** *(Continued)*

| | | | | |
|---|---|---|---|---|
| Language - comprehension (direct assessment) Analysis 1.5 | Not done as there were only 2 studies | | | |
| Language - comprehension (reported) Analysis 1.6 | Not applicable | Not done (only 1 study had low risk) | There was a difference $ | Not applicable |
| Parent-child interaction (shared or joint attention time) Analysis 1.7 | Not applicable | Not done (only 1 study had low risk) | Not applicable | Not applicable |
| Child initiations (coding of parent-child interactions) Analysis 1.8 | Not applicable | Not done (only 1 study had low risk) | Not applicable | No difference |
| Autism severity Analysis 1.9 | Not applicable | There was a difference * | No difference | No difference |
| Parents' level of stress Analysis 2.1 | Not done as there were only two studies | | | |
| Parent-child interaction (parent synchrony) Analysis 2.2 | Not applicable | Not done (only 1 study had low risk) | Not applicable | Not applicable |

$ New effect estimate mean difference 27.63 (95% CI -10.94 to 66.20) P value > 0.05.

* New effect estimate standardised mean difference -0.20 (95% CI -0.52 to 0.12).

**Table 3. Principal meta-analyses table**

| **Outcome** | | **Study ID (measure)** | **Intervention group** | | **Control group** | |
|---|---|---|---|---|---|---|
| | | | **n** | **Follow-up mean (SD)** | **n** | **Follow-up mean (SD)** |
| **Child communication and social development** | **Language - joint (direct assessment)** | Jocelyn 1998 (EIDP/PSDP) | 16 | 30.2 (15.0) | 19 | 21.9 (9.6) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | Casenhiser 2011 (PLS/CASL) | 16 | 0.72 (0.39) | 13 | 0.64 (0.32) |
| | **Communication (reported)** | Green 2010 (Teacher VABS) | 77 | 64·3 (17·7) | 75 | 67·7 (17·5) |
| | | Aldred 2004 (VABS) ¤ | 14 | 71.0 (24.82) | 14 | 60.93(20.26) |
| | | Dawson 2010 (VABS) ^^ | 24 | 82.1 (21.8) | 24 | 69.4 (15.8) |
| | **Language - expression (direct** | Green 2010 (PLS) | 77 | 20·0 (11·2) | 75 | 20·0 (11·3) |
| | | Dawson 2010 (MSEL) ^^ | 24 | 36.6 (13.6) | 24 | 30.0 (9.2) |
| | | Siller 2012 (MSEL) ¶¶ | 34 | 19.35 (10.72) | 30 | 18.57 (11.25) |
| | **Language - expression (re-** | Green 2010 (MCDI) $ | 77 | 171·9 (150·7) | 75 | 163.8 (144·3) |
| | | Aldred 2004 (MCDI) | 14 | 314.00 (230.98) | 14 | 189.50 (237.81) |
| | | Drew 2002 (MCDI) | 12 | 96.6 (118.8) | 12 | 44.0 (50.2) |
| | **Language - compre-** | Green 2010 (PLS) | 77 | 21·5 (13·0) | 75 | 20·3 (12·8) |
| | | Dawson 2010 (MSEL) ^^ | 24 | 40.0 (16.3) | 24 | 31.5 (10.6) |
| | **Language - com-** | Green 2010 (MCDI) $ | 77 | 233·7 (129·6) | 75 | 209·0 (131·3) |
| | | Aldred 2004 (MCDI) | 14 | 265.43 (134.56) | 14 | 219.14 (147.89) |
| | | Drew 2002 (MCDI) | 12 | 176.1 (121.9) | 12 | 100.3 (80.2) |
| | **Parent-child interaction** | Green 2010 (shared attention time) | 77 | 64·0% (25·7) | 75 | 55·6% (25·7) |

**Table 3. Principal meta-analyses table** *(Continued)*

| | | | | | | |
|---|---|---|---|---|---|---|
| | | Kasari 2010 (Joint engagement) * | 19 | 42.85 (19.96) | 16 | 27.87 (14.01) |
| | | Aldred 2004 (Parent Shared Attention) | 14 | 88.60 (8.70) | 14 | 80.30 (30.10) |
| | **Child initiations (coding of parent-child interactions)** | Green 2010 (Parent-child interaction: child initiations) | 77 | 34·9% (19·7) | 75 | 26·0% (17·5) |
| | | Carter 2011 (Frequency of initiating joint attention ESCS) ** | 24 | 10.33 (9.82) | 25 | 8.68 (9.26) |
| | | Kasari 2010 (Frequency of joint attention initiations) | 19 | 3.11 (3.41) | 19 | 3.77 (3.76) |
| | | Casenhiser 2011 (Initiation of Joint Attention - mCBRS)* | 16 | 1.84 (0.549) | 13 | 1.23 (0.430) |
| **Child problem behaviour** | **Severity of autism characteristics** | Dawson 2010 (ADOS severity) ^^ | 24 | 7.0 (1.9) | 24 | 7.3 (1.8) |
| | | Jocelyn 1998 (Autism behaviour checklist) | 16 | 48.5 (18.4) | 19 | 56.5 (20.1) |
| | | Pajareya 2011 (CARS) | 16 | 34.50 (6.01) | 16 | 37.13 (7.42) |
| | | Drew 2002 Reciprocal social interaction (ADI-R) | 12 | 18.3 (4.9) | 12 | 20.1 (4.3) |

**Table 3. Principal meta-analyses table** *(Continued)*

| | | | | | | |
|---|---|---|---|---|---|---|
| | | Green 2010 (Social-communication algorithm ADOS) | 77 | 9·2 (3·0) | 75 | 9·8 (2·9) |
| | | Aldred 2004 (Social-communication algorithm ADOS) | 14 | 7.70 (3.80) | 14 | 10.70 (3.20) |
| **Child ability** | **Adaptive behaviour** | Dawson 2010 (VABS) | 24 | 68.7 (15.9) | 21 | 59.1 (8.8) |
| | | Green 2010 (VABS) | 77 | 60.3 (15.2) | 75 | 62.8 (14.8) |
| **Parental** | **Parent stress** | | | | | |
| | | Jocelyn (Mothers Stress on the Stress-Arousal Checklist) | 16 | 5.9 (7.0) | 19 | 6.3 (6.1) |
| | **Parent-child interaction (parent synchrony)** | Green 2010 (Parent synchrony) | 77 | 51·3% (19·6) | 75 | 32·6% (14·0) |
| | | Aldred 2004 (Parent synchrony) | 14 | 65.10 (14.30) | 14 | 49.50 (18.90) |
| | | Siller 2012 (Maternal synchronisation) ¶ | 34 | 0.73 (0.21) | 30 | 0.61 (0.20) |

**Notes:** ^^ second-year outcome, $^{\$}$ raw score , ¤ age equivalents in months was provided in the article but was transformed to standardised scores from individual data, ¶¶ time 3 values were extracted from the article, * coded child-parent free play, ¶ only time 2 values were available in the study,** outcome data collected at time 3 (9 months into study)

ADI-R: Autism Diagnostic Interview-Revised; ADOS: Autism Diagnostic Observation Schedule; CARS: Childhood Autism Rating Scale; CASL: Comprehensive Assessment of Spoken Language; EIDP: Early Intervention Developmental Profile; MCDI: MacArthur Communicative Development Inventory; MSEL: Mullen Scales of Early Learning; PLS: Preschool Language Scales; PSDP: Preschool Developmental Profile; SD: standard deviation; VABS: Vineland Adaptive Behaviour Scales.

**Table 4. Definition of abbreviations used in the principal meta-analyses table and direction of scales**

| IMPROVEMENT INDICATED BY INCREASING SCORE | IMPROVEMENT INDICATED BY DECREASING SCORE |
|---|---|
| Comprehensive Assessment of Spoken Language, quotients (CASL)<br>Early Intervention Developmental Profile (EIDP)<br>Early Social Communication Scales (ESCS)<br>MacArthur Communicative Development Inventory (MCDI)<br>Modified Child Behaviour Rating Scales (mCRBS)<br>Mullen Scales of Early Learning (MSEL)<br>Parent child Free Play Procedures (PCFP)<br>Preschool developmental profile (PSDP)<br>Preschool Language Scale (PLS) IV<br>Vineland Adaptive Behavior Scales II (VABS) | Autism Behaviour Checklist (ABC)<br>Autism Diagnostic Interview - Revised (ADI - R)<br>Autism Diagnostic Observation Schedule (ADOS)<br>Parenting Stress Index (PSI) (Short form)<br>Childhood Autism Rating Scale (CARS)<br>Stress-Arousal Checklist (SACL) |

**Table 5. Numerical data from studies not included in meta-analyses**

| Outcomes | Study ID | Intervention group (at follow up) | Control group (at follow up) | Comments |
|---|---|---|---|---|
| **Language development (comprehension and expression)** | Smith 2000 | RDLS (total): 61.33 (SD 31.88)<br>RDLS (comprehension): 33.00 (SD 16.86)<br>RDLS (expressive): 36.23 (SD 21.19)<br>VABS (communication): 60.77 (SD 17.26) | RDLS (total): 87.40 (SD 46.21)<br>RDLS (comprehension): 42.87 (SD 22.29)<br>RDLS (expressive): 44.53 (SD 23.48)<br>VABS (communication): 67.87 (SD 30.08) | Statistically significant difference was reported in favour of the intensive therapist-delivered control group, only on directly assessed total language score |
| | Roberts 2011 | RDLS (comprehension standard score): 2.6<br>(SD 8.4)<br>RDLS (expression standard score): 2.8<br>(SD 7.5)<br>VABS (communication): 68.4 (SD 15.6) | RDLS (comprehension standard score): 10.5 (SD 17.4)<br>RDLS (expression standard score): 7.0 (SD 15.1)<br>VABS (communication): 76.1 (SD 17.1) | Significant difference in favour of the centre-based control group over the home-based group reported for language comprehension (not expression or reported communication) |
| | Tonge 2012 | RDLS (comprehension): PEBM 14.06 (SD 19.67)<br>RDLS (expressive): 17.17 (SD 17.07)<br>VABS (communication): PEBM 71.71 (SD 19.83) | RDLS (comprehension): PEAC 5.45 (SD 12.29)<br>RDLS (expressive: PEAC 8.19<br>(SD 13.65)<br>VABS (communication) :<br>PEAC 58.03 (SD 15.71) | Analyses conducted by the authors suggest that differences between groups at baseline could have accounted for observed differences at follow-up |

**Table 5. Numerical data from studies not included in meta-analyses** *(Continued)*

| | | | | |
|---|---|---|---|---|
| **Social communication skills** | Roberts 2011 | VABS (social): Home-based 66.4 (SD 7.7) | VABS (social): Centre-based 72.6 (SD 11.2) | Significant difference in favour of the centre-based control group over the home-based group |
| | Silva 2009 | PDDBI (language and social): 56.7 (SD 9.7) | PDDBI (language and social): 47.6 (SD 12.1) | Blinded teacher evaluations indicated that children treated with massage made significant classroom improvement in social and language skills |
| | Smith 2000 | VABS (social): 68.92 (SD 16.94) | VABS (social): 66.33 (SD 24.78) | No difference between groups |
| | Tonge 2012 | VABS (social): PEBM 73.31 (SD 16.59) | VABS (social): PEAC 63.03 (SD 15.53) | Significant difference in favour of the PEBM group |
| **Parents'level of stress** | Tonge: 2006 | GHQ (total): PEBM 17.06 (SD 7.59) | GHQ (total): PEAC 16.70 (SD 10.51) | No difference between groups |
| | Roberts 2011 | PSI: Home-based 92.7 (SD 20.9) | PSI: Centre-based 98.2 (SD 20.1) | No difference between groups |
| | Rickards 2007 | QRS-F | QRS-F | No significant difference between groups in family levels of resources and stress |
| | Aldred 2004 | PSI | PSI | Co-varying for baseline scores, there was no significant difference between the groups in change in total PSI score (F = 0.29, P value = 0.597) |
| **Developmental/ intellectual gains** | Tonge 2012 | PEP-R DQ: PEBM - 72.18 (SD 24.77) | PEP-R DQ: PEAC - 53.94 (SD 23.80) | No difference between groups |
| | Smith 2000 | IQ: 49.67 (SD 19.74) | IQ: 66.49 (SD 24.08) | Authors reported that the intensive therapist-delivered control group outperformed the parent-mediated group at the end of the study |
| | Rickards 2007 | IQ: 57.2 (SD 21.9) | IQ: 48.6 (SD 17.5) | The authors reported that there was non-significant |

**Table 5. Numerical data from studies not included in meta-analyses** *(Continued)*

| | | | | |
|---|---|---|---|---|
| | | | | trend in favour of intervention |
| **Adaptive behaviour** | Rickards 2007 | VABS (composite): 64.3 (SD 20.4) | VABS (composite): 59.2 (SD 19.7) | The authors reported that there was significant main effect in favour of intervention |
| | Smith 2000 | VABS (composite): 58.50 (SD 16.58) | VABS (composite): 61.19 (SD 29.72) | No observed difference between treatment and control groups on adaptive functioning at the end of the study |
| **Restricted and repetitive behaviour (autism severity included)** | Tonge 2012 | CARS: PEBM 35.86 (SD 6.14),<br>DBC - ASA: PEBM 20.77 (SD 9.05) | CARS: PEAC 40.06 (SD 5.44) DBC - ASA: PEAC 23.90 (SD 8.23) | No difference between groups |
| | Silva 2009 | ABC: 33.9 (SD 18.6) | ABC: 59.4 (SD 35.4) | Blinded teacher evaluations indicated that children treated with massage made significant classroom reduction in autism characteristics |
| **Maladaptive behaviour** | Smith 2000 | CBC (withdrawal): 55.0 (SD 4.40)<br>CBC (social problems): 59.43<br>(SD 8.02)<br>CBC (aggression): 55.71 (SD 5.53) | CBC (withdrawal): 61.89 (SD 7.04)<br>CBC (social problems): 59.78<br>(SD 9.59)<br>CBC (aggression): 60.0 (SD 10.81) | No significant differences reported by teachers between groups on this domain |
| | Roberts 2011 | DBC total: Home-based 52.9<br>(SD 29.3) | DBC total: Centre-based 55.7<br>(SD 19.5) | There were no statistically significant differences between the 2 groups |
| | Rickards 2007 | PBCL: 13.7 (SD 8.3) | PBCL: 21.2 (SD 6.7) | The authors reported that there was non-significant trend in favour of intervention |
| | Tonge 2012 | DBC - TBPS: PEBM 53.29 (SD 24.36) | DBC - TBPS: PEAC 57.61 (SD 19.72), | No difference between groups |
| **Parents'confidence in coping with child's disability and behaviour problems** | Nefdt 2010 | - | - | Significant differences between the intervention group and control group; parents ap- |

**Table 5. Numerical data from studies not included in meta-analyses** *(Continued)*

| | | | | |
|---|---|---|---|---|
| | | | | peared more confident during interactions with their child following the self directed learning programmes (F = 16.37 and P value = 0.001 with an effect size of 1.28) |
| **Any cost information provided by the authors** | Roberts 2011 | - | - | The cost per child was AUD6383. Staff hours were the same for home based and centre based |
| | Rickards 2007 | - | - | Teacher's salary for 1 year plus some expenses for travelling (this travelling estimate was not provided) |

ABC: Autism Behaviour Checklist; BRS: Bayley Behaviour Rating Scale; CARS: Childhood Autism Rating Scale; CBC: Child Behaviour Checklist; DBC: Developmental Behaviour Checklist; DBC-ASA: Developmental Behaviour Checklist Autism Screening Algorithm; DBC-TBPS: Developmental Behaviour Checklist Total Behaviour Problem Score; GHQ: General Health Questionnaire; IQ: intelligence quotient; PBC: Preschool Behaviour Checklist; PEAC: Parent Education and Counselling; PEBM: parent education and behaviour management; PBCL: Preschool Behaviour Checklist; PDDBI: Pervasive Developmental Disorders Behaviour Inventory; PEP-R DQ: Psychoeducational Profile-Revised - Developmental Quotient; PSI: Parenting Stress Index; QRS-F: Questionnaire on Resources and Stress (Friedrich short form); RDLS: Reynell Developmental Language Scales; SD: standard deviation; VABS: Vineland Adaptive Behaviour Scales

# APPENDICES

## Appendix 1. Search strategies

### Ovid MEDLINE (R) search terms

# 1 exp child development disorders, pervasive/
# 2 Developmental Disabilities/
# 3 pervasive development$ disorder$.tw.
# 4 (PDD or PDDs or ASD or ASDs).tw.
# 5 autis$.tw.
# 6 asperger$.tw.
# 7 kanner$.tw.
# 8 childhood schizophrenia.tw.
# 9 Rett$.tw.
#10 or/1-9
#11 Family/

#12 exp Parents/
#13 (parent$ or family or families or mother$ or father$ or maternal$ or paternal$).tw.
#14 (at home or (in adj3 home) or home based or home-based).tw.
#15 Caregivers/
#16 (carer$ or care-giver$ or caregiver$).tw.
#17 or/11-16
#18 10 and 17
#19 exp child/
#20 infant/
#21 (child$ or infant$ or babies or baby or toddler$ or girl$ or boy$ or pre-school$ or preschool$ or nurser$ or kindergarten$ or kinder-garten$).tw.
#22 or/19-21
#23 18 and 22
#24 randomized controlled trial.pt.
#25 controlled clinical trial.pt.
#26 randomi#ed.ab.
#27 placebo$.ab.
#28 drug therapy.fs.
#29 randomly.ab.
#30 trial.ab.
#31 groups.ab.
#32 or/24-31
#33 exp animals/ not humans.sh.
#34 32 not 33
#35 23 and 34

### *EBSCO Host search terms*

(TX (Child development disorders OR pervasive developmental disorder OR PDD OR PDDs OR ASD OR ASDs OR autism OR asperger OR kanner OR childhood schizophrenia OR Rett syndrome)) AND (TX (Family OR families OR Parents OR parent OR mother OR father OR maternal OR paternal AND home OR "in" home OR home based OR home-based OR Caregivers OR carer OR care-giver OR caregiver)) AND (SU (Child OR infant OR children OR babies OR baby OR toddler OR girl OR girls OR boy OR boys OR pre-school OR preschool nursery OR kindergarten)) AND (TX (Randomized controlled trial OR controlled clinical trial OR randomised OR randomized OR placebo drug therapy)) AND (TX (randomly OR trial OR groups NOT animals)). An alert was set up to update the search when new records matching the search was added to the database.

### *ERIC search terms*

((Keywords:Autism OR Keywords:Pervasive and Keywords:Developmental and Keywords:Disorders or Keywords:retts or Keywords: kanner) and (Keywords:randomised and Keywords:controlled and Keywords:trial or Keywords:clinical and Keywords:trial) and (Keywords:parent and Keywords:mediated or Keywords:parent or Keywords:caregiver or Keywords:children or Keywords:toddlers)) Publication Date:2002-2012. An alert was set up to update the search when new records matching the search was added to the database.

### MetaRegister search terms

All - ISRCTN Register (International) - copy of ISRCTN Register, NIH ClinicalTrials.gov Register (International) - subset of randomised trial records, Action Medical Research (UK) - subset from ISRCTN Register, The Wellcome Trust (UK) - subset from ISRCTN Register, Medical Research Council (UK) - subset from ISRCTN Register, UK trials (UK) - subset from ISRCTN Register, UK trials only. Search term was "Autism".

### Scopus search terms

autism spectrum disorders or pervasive developmental disorder or ASD or ASDs or autism or asperger or kanner or childhood schizophrenia or Rett syndrome or child development disorders and parents or caregivers or care-givers or mother or father and Randomized controlled trial or controlled clinical trial or randomised or randomized or placebo drug therapy AND ( LIMIT-TO(PUBYEAR,2012) OR LIMIT-TO(PUBYEAR,2011) OR LIMIT-TO(PUBYEAR,2010) OR LIMIT-TO(PUBYEAR,2009) OR LIMIT-TO(PUBYEAR,2008) OR LIMIT-TO(PUBYEAR,2007) OR LIMIT-TO(PUBYEAR,2006) OR LIMIT-TO(PUBYEAR,2005) OR LIMIT-TO(PUBYEAR,2004) OR LIMIT-TO(PUBYEAR,2003) OR LIMIT-TO(PUBYEAR,2002) ). An alert was set up to update the search when new records matching the search was added to the database.

### CSA Illumina

KW=((Child development disorder*) or (pervasive developmental disorder*) or (autism spectrum disorde*)) or (PDD or PDDs or ASD) or (asperger* or Kanner or rett*) and ((randomi* contro* trial) or (contro* clinical trial) or RCT) and (parent or mother or father) and care*giver. The ERIC database was excluded from the search and an alert was set up to update the search when new records matching the search was added to the database.

### TRIP database search

area:"Psychiatry" area:"Pediatrics"
Search term: Autism
Interests: Child development disorders or pervasive developmental disorder or PDD or PDDs or ASD or ASDs or autism or asperger or kanner or childhood schizophrenia or Rett syndrome and Randomized controlled trial or controlled clinical trial or randomised or randomized or placebo drug therapy and randomly or trial or groups not animals

### NCBI Pubmed search

("autistic disorder"[MeSH Terms] OR ("autistic"[All Fields] AND "disorder"[All Fields]) OR "autistic disorder"[All Fields] OR "autism"[All Fields]) AND (randomized controlled trial[Publication Type] OR (randomized[Title/Abstract] AND controlled[Title/Abstract] AND trial[Title/Abstract])). An alert was set up to update the search when new records matching the search was added to the database.
Other databases were handsearched for relevant articles.

## Appendix 2. Study characteristics

| Study ID | Age (range or average) | Study location | Control condition | Intervention condition/ theoretical basis | Duration | Intensity (control vs. intervention) | Intervention delivery methods | Outcome measures of interest |
|---|---|---|---|---|---|---|---|---|
| Aldred 2004 | 2-5 years | UK (England) | Routine care - no further details | Routine care plus parent workshops and individual sessions with child present, based on a | 1 year | Intervention more intense | Mixed: mostly 1-to-1 sessions | VABS, MCDI |

(*Continued*)

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|---|---|---|---|---|---|---|---|---|
| | | | | social communication model | | | | |
| Carter 2011 | 20 months | USA | Treatment as usual - no further details | Parent sessions based on a social communication model (Hanen more than words) | 14 weeks | Intervention appeared to be more intense though control conditions were not stated clearly | Mixed: mostly group sessions | ESCS |
| Casenhiser 2011 | 2 to 4 years, 11 months | Canada | A range of therapies were given (ABA, speech, occupational, social skills) | Sessions held with children and parents based on DSP strategies | 1 year | Intervention likely to be more intense compared with control | Unclear how intervention was delivered but likely to have been mixed | PLS/CASL |
| Dawson 2010 | 18-30 months | USA | Assess and monitor group:<br>this used resource manuals/ reading materials, individual and group therapists sessions. It was likely that ABA techniques were also patronised by families<br>as the community has such services available | ESDM group:<br>therapists delivered sessions were held with parents based on ESDM strategies, which are consistent with ABA and based on developmental behavioural principles. Parents documented the hours they spent using strategies with their child | 2 years | It appeared that the intervention was more intense compared to the control | Group sessions held with parents | VABS, MSEL |
| Drew 2002 | 23 months | UK (England) | Locally available | Locally available ser- | 1 year | The intervention was | 1-to-1 sessions held | MCDI, ADI-R |

(*Continued*)

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|---|---|---|---|---|---|---|---|---|
| | | | treatment services for ASD: speech and language therapy, portage home worker input and other paramedical therapy services | vices plus the intervention which was based on psycholinguistic/ social pragmatic strategies | | more intense | with parents at homes with telephone support services in addition | |
| Green 2010 | 2 to 4 years, 11 months | UK (England) | Local services: speech and language therapies | Locally available services plus the PACT intervention which is based on a social communication model | 1 year | Intervention was more intense | 1-to-1 sessions held with parents and children in attendance at clinics | MCDI, ADOS-G |
| Jocelyn 1998 | 24-72 months | Canada | A standard treatment delivered at community daycare centres with support from childcare workers | Daycare centre services in addition to an intervention based on educational model (the Autism Preschool programme) | 12 weeks | Intervention was more intense | 1-to-1 sessions held with parents of children alone at clinics and home sessions with childcare worker | Stress Arousal Checklist, ABC |
| Kasari 2010 | 21-36 months | USA | Locally available services including ABA, school-based instructions, speech therapy, occupational therapies and what | Children in this group received therapist sessions aimed at joint attention/ engagement skills development through | 8 weeks | Intervention was more intense | Appears to be 1-to-1 sessions delivered at home and centre locations | Coding of interactions |

(*Continued*)

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|---|---|---|---|---|---|---|---|---|
| | | | was said to be “miscellaneous” | approaches that incorporates developmental procedures of responsive and facilitative interaction methods<br>as well as aspects of ABA. They also got other interventions that were similar to the ones in the control condition | | | | |
| Nefdt 2010 | Mean age of 38.<br>92 months (SD 14.57) in the treatment group and 38.<br>43 months (SD 11.20) in the control group | USA | Wait list - no further details | Self directed learning programme based on behavioural and social communication approaches | 1 week | Intervention appeared to be more intense though control conditions were not stated clearly | The use of DVDs as modalities for instruction | - |
| Pajareya 2011 | 2-6 years | Thailand | Routine or typical care - no details provided | An intervention based on functional developmental levels model (DIR/Floortime) was directed at parents in sessions attended by parents alone | 12 weeks | Intervention appeared to be more intense though control conditions were not stated clearly | Group sessions held with parents and DVD lectures | CARS |

*(Continued)*

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| Rickards 2007 | 3-5 years | Australia | A centre-based programme | The intervention was a home-based programme delivered in addition to the centre-based programme | 1 year | Intervention was more intense | Unclear but appeared to have been a mixed approach delivered at home and centre locations | PBCL |
| Roberts 2011 | Mean age of 41.5 months (range 26.5 to 59.4) in the home-based group and 43.7 months (range 27.6 to 60.3) in the centre-based group | Australia | This study has 3 groups: w**ait list group,** which was not randomised and participants in this group had routine interventions available locally. **Centre-based group,** which had participants that had a centre-based intervention focused on the development of social play and functional communication skills. **Home-based group** in which participants had a home-based intervention focused on child's behaviour, functional communication skills, social development, attending and play skills, sensory processing issues, self help skills such as independent toileting, visual communication supports, fine and gross motor skills and pre-academic skills. Parents were a key feature in this group | | 40 weeks | The centre-based programme was designed to be more intensive (40 weekly 2-hour sessions) than the home-based programme (20 sessions lasting 2 hour per session delivered over 40 weeks) | Mixed 1-to- and group sessions including centres and home locations for the centre-based and home-based programmes respectively | PBCL |
| Siller 2012 | Mean age for the intervention group was 58.3 months (SD 2. 7) while that for the control group was 55.9 | USA | A structured programme based on an educational model which involved parents and fami- | A home-based parent training programme based on an educational model that focuses on par- | 12 weeks | Intervention was more intense | A home-based programme that was likely to have been delivered on a 1-to-1 basis | Coding of interaction, MSEL |

(*Continued*)

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| | months (SD 11.9) | | lies of participating children | ent-child interaction | | | | |
| Silva 2009 | 3-6 years | USA | Wait list group | The QST programme, which is a therapy based on massage | 20 weeks | Intervention appeared more intense | Group sessions held in locations not clearly defined | AWP/C, REXSCA/C |
| Smith 2000 | 18-42 months | USA | This study had 2 intervention arms. **Intensive treatment group,** which was based on Lovaas et al manual and a **Parent training group,** which utilised the "parents as therapists" model as parents were the primary targets of the intervention | | 1 year | The intensive treatment group was more intense than the parent training arm of the study | A mix of 1-to-1 and group sessions delivered in home and out of home locations | VABS, RDLS |
| Tonge 2006 and Tonge 2012 | 2.5-5 years | Australia | This study had 3 groups. **Control group,** which used only local services. The **PEAC group,** which received intervention based on an educational model but lacking in any skills training. The **PEBM group,** which was similar to the PEAC group but with the addition of skills training. Both PEAC and PEBM groups were allowed to use locally available services | | 20 weeks | Both interventions (PEAC and PEBM) were more intensive than the contro | It appears to be a 1-to-1 delivered intervention with parents present (but without their children) in the sessions. Location was unclear | DBC-TBPS, RDLS, GHQ, VABS |
| Wong 2010 | 17-36 months | China | Only stated as "no treatment" | This group received an intervention (autism 1-2-3), which is based on behavioural and social-pragmatic models | 2 weeks | It appeared the intervention was more intense | It appears an intervention predominantly delivered at home on a 1-to-1 basis | - |

ABA: applied behavioural analysis; ABC Autism Behaviour Checklist; ADI-R: Autism Diagnostic Interview-Revised; ADOS-G: Autism Diagnostic Observation Schedule; ASD: autism spectrum disorder; AWP/C:Approach/Withdrawal Problems Composite of the Pervasive Developmental Disorders Behavior Inventory ; CARS: Childhood Autism Rating Scale; CASL: Comprehensive Assessment of Spoken Language; DBC-TBPS: Developmental Behaviour Checklist; DSP: Developmental Social Pragmatics; ESCS: Early Social Communication Scales; ESDM: Early Start Denver Model; GHQ: General Health Questionnaire; HMTW: Hanen More Than Words; MCDI: MacArthur Communicative Development Inventory; MSEL: Mullen Scales of Early Learning; PACT: Preschool Autism Communication Trial; PBCL: Preschool Behaviour Checklist; PEAC: parent education and counselling; PEBM: parent education and behaviour management; PLS: Preschool Language Scales; RDLS: Reynell Developmental Language Scales; REXSCA/C:Receptive/Expressive Social Communication Abilities Composite of the Pervasive Developmental Disorders Behavior Inventory; SD: standard deviation; VABS: Vineland Adaptive Behaviour Scales

## Appendix 3. Details of the 2002 search conducted for the original review

In the 2002 search (Diggle 2002), over 15,000 articles were identified; since it was a wide search there were many duplications and a sizeable number of irrelevant articles were located. All databases searched yielded relevant citations, however, the majority originated from PsycINFO, ERIC and MEDLINE. From the initial yield of citations, 68 articles qualified for further inspection based upon their abstract and were formally reviewed. Lead authors of the 68 articles were contacted to determine whether they were aware of any published or unpublished studies that had not been identified through the database searches. Sixty-one authors were approached (via email), eliciting 18 responses. In total one study was added to the list for formal review and one ongoing study recorded. Of the 68 articles five were published in languages other than English including two from Italy, two from Japan and one from Turkey. These articles were translated to a degree necessary to understand the essentials of the study. Nine were unpublished doctoral dissertations, and one an unpublished conference paper. Sixty-six of the 68 articles obtained in full for formal review were excluded from the systematic review, primarily on methodological grounds (N = 55). A handful of these articles used properly constituted control groups in their designs, and of these only five used any random allocation technique. Eight articles were excluded as participants did not have a diagnosis of autism spectrum disorder and one as the intervention did not focus upon parent-mediated early intervention. Of the four articles with random allocation of participants, two used no child-related outcome measures, leaving only two articles which met the specified inclusion criteria for this review. Details of the search and the results can be found in the earlier publication (Diggle 2002).

# WHAT'S NEW

Last assessed as up-to-date: 28 February 2013.

| Date | Event | Description |
|---|---|---|
| 6 February 2012 | Amended | New protocol written prior to updating currently published review: Diggle TJ, McConachie HR. Parent-mediated early intervention for young children with autism spectrum disorder. Cochrane Database of Systematic Reviews 2002, Issue 2. Art. No.: CD003496. DOI: 10.1002/14651858. CD003496 |

# HISTORY

Protocol first published: Issue 1, 2002

Review first published: Issue 4, 2013

| Date | Event | Description |
|---|---|---|
| 12 November 2008 | Amended | Converted to new review format. |
| 29 January 2002 | New citation required and conclusions have changed | Substantive amendment |

# CONTRIBUTIONS OF AUTHORS

Inalegwu Oono and Helen McConachie wrote the revised protocol. Inalegwu Oono was chiefly responsible for searching, data extraction and analysis, with final versions created in consensus with Helen McConachie and Emma Honey. The writing of the review was carried out by Inalegwu Oono and Helen McConachie, with additions by Emma Honey.

# DECLARATIONS OF INTEREST

Helen McConachie - none known.

Inalegwu P Oono - none known.

Emma J Honey - none known.

# SOURCES OF SUPPORT

## Internal sources

- No sources of support supplied

## External sources

- The Nuffield Foundation, UK.

# DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Some of the secondary outcomes such as developmental/intellectual gains, restricted and repetitive behaviours, parents' satisfaction with therapy, or parents' confidence in coping were not reported in the articles in ways that allowed for them to be aggregated systematically. Rather than separately reporting restricted and repetitive behaviours, a number of studies reported a combined measure of overall autism severity and therefore we replaced the secondary outcome 'restricted and repetitive behaviour' with 'severity of autism characteristics' and included it in the Summary of findings for the main comparison. Similarly, due to the wide variation in the theoretical basis of types of intervention, the intensity of intervention and duration of intervention that precludes any logical combination of the studies, we could not carry out statistical analyses aimed at exploring the heterogeneity due to these factors. Furthermore, child IQ could not be investigated as it was usually reported by group mean rather than in ability bands. Given small numbers of studies, we could not conduct analysis based on the average age of child participants.

For the sensitivity analysis based on risk of bias judgements, we only considered studies that had low and unclear risks for bias in the pre-specified domains, as we judged that these levels of risk held few implications for the conclusions.

## NOTES

This review updates the previous review (citation below) on the same topic but is based on a new protocol.

Diggle T J, McConachie H R, Randle V. Parent-mediated early intervention for young children with autism spectrum disorder. Cochrane Database of Systematic Reviews 2003, Issue 1. Art. No.: CD003496. DOI: 10.1002/14651858.CD003496.

## INDEX TERMS

### Medical Subject Headings (MeSH)

*Parent-Child Relations; *Parents; Child Development Disorders, Pervasive [psychology; *therapy]; Communication; Early Intervention (Education) [*methods]; Interpersonal Relations; Randomized Controlled Trials as Topic

### MeSH check words

Child; Child, Preschool; Female; Humans; Infant; Male