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The Role of Early Intervention on Communication Development in Children with Autism Spectrum Disorder: A Systematic Review of Randomized Controlled Trials

¹ Putri Fajaria Anggraini

¹ Pamekasan Regional General Hospital, Indonesia

Corresponding Email : putrifaj3@gmail.com

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ABSTRACT

Introduction: Impairment of social communication is a defining feature of autism spectrum disorder (ASD), and the pre-school years constitute a period of maximal neurodevelopmental plasticity. Although early intervention is universally recommended, the magnitude and generalizability of its effect on communication development remain contested. This systematic review was undertaken to quantify the effect of early intervention on communication development in children with ASD using exclusively randomized evidence.

Methods: The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines. Eligible studies were randomized controlled trials enrolling children with ASD (mean age ≤ 72 months) comparing early intervention against control conditions and reporting at least one communication outcome. Risk of bias was assessed using Cochrane

RoB 2, and certainty of evidence was graded using GRADE. A structured narrative synthesis with effect-direction analysis was performed due to substantial heterogeneity.

Results: Twenty randomized controlled trials comprising 1,713 children were included. Consistent and statistically significant benefit was demonstrated for proximal dyadic communication outcomes: caregiver synchronous responsiveness improved significantly in 4 of 6 trials (effect sizes 0.33 to 1.61), and child-initiated communication improved significantly in 6 of 8 trials (effect sizes 0.20 to 0.99). Initiation of joint attention improved in 4 of 5 trials, and joint engagement in all 4 trials measuring it. Expressive language improved in only 6 of 13 trials, receptive language in 4 of 8, and blinded autism symptom severity in 5 of 10, with the two largest contemporary pragmatic trials entirely null on their primary blinded endpoints (effect sizes 0.04 and -0.06). Effects attenuated monotonically as measurement moved from proximal dyadic outcomes to distal standardized instruments.

Discussion: The evidence supports a coherent, mechanistically explicable but hierarchically attenuating effect: intervention reliably changes targeted caregiver behaviour and child communicative initiation, with effect thereafter attenuating progressively as measurement moves away from the intervention context toward standardized, decontextualized instruments. Parent-mediated interventions delivered by non-specialist

health workers reproduced proximal effects obtained by specialist therapists.

Conclusion: Early intervention produces robust, replicated improvement in proximal communication architecture—caregiver responsiveness, child communicative initiation, joint attention, and joint engagement—with moderate certainty. Effects on standardized language and blinded symptom severity are smaller and less consistent. Parent-mediated, naturalistic developmental behavioural interventions should be offered as first-line management, with outcome monitoring anchored on dyadic communication measures.

Keywords: autism spectrum disorder; early intervention; social communication; joint attention; parent-mediated intervention

INTRODUCTION

Background

Autism spectrum disorder (ASD) is a neurodevelopmental condition defined by persistent deficits in social communication and social interaction across multiple contexts, together with restricted, repetitive patterns of behaviour, interests or activities, with onset in the early developmental period. Contemporary epidemiological estimates place the global prevalence at approximately 1% of children, with substantially higher figures reported in populations subject to active surveillance. Among the diagnostic features, impairment of social communication is both the most functionally consequential and the most prognostically informative: the acquisition of functional phrase speech before the age of five years remains one of the most robust predictors of adult independence, occupational attainment and quality of life yet identified in longitudinal autism research. It is therefore unsurprising that communication has become the principal therapeutic target of virtually every contemporary early-intervention model.^{1,7,13}

The developmental rationale for early intervention rests on the convergence of three empirical observations. First, the social communication phenotype of ASD does not emerge fully formed at diagnosis but unfolds across the second year of life through a cascade in which reduced orienting to social stimuli constrains opportunities for joint attention, which in turn constrains the establishment of shared referential frames upon which lexical acquisition depends. Second, experience-dependent synaptic plasticity within the cortical networks subserving social cognition and language is maximal during this same interval, creating a window in which environmental input exerts disproportionate influence on developmental trajectory. Third, caregiver interactive style — specifically the degree to which caregiver communicative acts are synchronous with, rather than directive of, the child's current focus of attention — is a modifiable environmental variable that is causally related to the child's rate of communicative initiation. Together these observations generate the central hypothesis of the field: that modifying the proximal communicative environment early enough will alter the developmental trajectory of communication itself.^{1,2,14}

Operationally, early intervention for ASD encompasses several partially overlapping traditions. Comprehensive applied behaviour analytic programmes deliver high-intensity, adult-directed instruction across developmental domains. Naturalistic developmental behavioural interventions (NDBIs), including the Early Start Denver Model (ESDM), Pivotal Response Treatment (PRT), and Joint Attention, Symbolic Play, Engagement and Regulation (JASPER), embed behavioural teaching principles within developmentally appropriate, child-led play routines. Parent-mediated interventions, exemplified by the Preschool Autism Communication Trial (PACT) therapy, deliver no direct child–therapist contact at all, working instead through video-aided coaching of caregiver interactive behaviour. More recently, pre-emptive interventions have been trialled in infants showing prodromal behavioural signs before a categorical diagnosis is possible, and technology-assisted and telehealth-delivered adaptations have been developed to address access inequities. These models differ radically in intensity — from one hour per week of caregiver coaching to twenty-five hours per week of one-to-one therapy — in agent of delivery, and in the theoretical mechanism by which communicative change is presumed to occur.^{7,10,13,15,16,17}

Despite near-universal guideline endorsement, the randomized evidence base is considerably more equivocal than clinical enthusiasm would suggest. Landmark trials have repeatedly demonstrated large, unambiguous effects on the behaviours proximal to the intervention while failing to demonstrate corresponding effects on blinded, standardized, decontextualized measures of autism symptom severity or formal language. The original PACT trial, the largest psychosocial autism trial of its era, reported a very large effect on parental synchronous response yet a non-significant and directionally ambiguous effect on its own primary symptom endpoint. Two of the largest and most methodologically rigorous trials published in the last five years — the generalized PACT trial and the German A-FFIP trial — were entirely null on their pre-specified blinded primary outcomes. This dissociation between proximal and distal outcomes constitutes the central interpretive problem of the field and is the principal question addressed by the present review.^{1,18,19}

Objectives of the Review

The general objective of this systematic review was to determine, on the basis of randomized controlled evidence alone, whether and to what extent early intervention improves communication

development in children with autism spectrum disorder. The specific objectives were as follows. First, to identify and characterize all randomized controlled trials evaluating early intervention with at least one communication outcome in children with a mean age at randomization of 72 months or less. Second, to synthesize treatment effects across a comprehensive set of at least ten pre-specified communication and communication-adjacent outcome domains, deliberately disaggregating proximal dyadic outcomes from distal standardized outcomes. Third, to appraise the internal validity of each included trial using the Cochrane Risk of Bias 2 instrument, with particular attention to the measurement-of-outcome domain, in which caregiver-reported endpoints in unblinded parent-mediated trials are structurally vulnerable to detection bias. Fourth, to examine intervention-level moderators of effect, including intensity, duration, agent of delivery, control-condition activity and baseline child characteristics. Fifth, to grade the certainty of the body of evidence supporting each outcome domain using GRADE, and to derive implications for clinical practice in both high-resource and resource-constrained health systems.^{4,5,6}

Benefits of the Review

The theoretical benefit of this review lies in its explicit test of the developmental cascade model of autistic communication. By arranging outcomes along a proximal-to-distal continuum and examining whether effect magnitude attenuates monotonically along that continuum, the synthesis provides an empirical evaluation of the causal chain that the interventions themselves presuppose, rather than treating each outcome as an independent efficacy question.^{1,20}

The clinical benefit is threefold. For the practising specialist, the review clarifies which communicative outcomes may legitimately be promised to families and within what time frame, thereby supporting realistic and ethically sound counselling at the point of diagnostic disclosure. For service planners, the finding that low-intensity parent-mediated therapy delivered by non-specialist workers reproduces the proximal effects obtained in specialist centres provides a defensible evidence base for task-shifted service models — a consideration of direct relevance to Indonesia and other middle-income settings, where the ratio of child psychiatrists and developmental paediatricians to the affected paediatric population precludes universal specialist delivery. For trialists and guideline committees, the demonstration that omnibus symptom-severity instruments are systematically less

sensitive than dyadic communication measures carries direct implications for endpoint selection in future trials.^{11,12,21}

The methodological benefit is the provision of a transparent, fully referenced and independently verifiable evidence map of the randomized early-intervention literature, in which every included trial and every supporting citation is retrievable through a permanent academic search link, permitting independent replication of the synthesis by any reader.⁴

Hypotheses

The following hypotheses were formulated a priori. The primary hypothesis (H1) was that early intervention produces a statistically significant improvement in child communicative initiation within caregiver–child interaction compared with control conditions. The second hypothesis (H2) was that effect magnitude attenuates monotonically as outcome measurement moves from proximal dyadic behaviours, through intermediate joint attention and joint engagement measures, to distal standardized language and blinded symptom-severity measures. The third hypothesis (H3) was that parent-mediated interventions produce effects on caregiver behaviour that are substantially larger than their effects on child behaviour, consistent with a mediated rather than direct causal pathway. The fourth hypothesis (H4) was that treatment effect on expressive language is moderated by baseline language level, with the greatest benefit accruing to children with the lowest baseline verbal ability. The fifth hypothesis (H5) was that intervention intensity, expressed as total therapy hours, is not linearly related to communication outcome magnitude across trials. The sixth and final hypothesis (H6) was that treatment effects on proximal communication outcomes are maintained at follow-up assessments conducted after cessation of active intervention.^{1,2,5,20,22}

Research Gap

Four specific gaps in the existing literature motivated this review. The first is a synthesis gap. Previous meta-analyses of parent-mediated intervention have pooled heterogeneous outcomes into broad composite domains such as "communication–language" or "socialization", yielding small average effects in the region of 0.18 to 0.27 standardized mean difference. Such aggregation necessarily obscures the very dissociation — between large proximal effects and negligible distal

effects — that is most theoretically and clinically informative, and it conflates outcomes measured by unblinded caregivers with outcomes measured by masked independent assessors.^{11,23,24}

The second is an evidence-currency gap. The most influential syntheses in this field antedate the publication of several large, well-powered and methodologically rigorous trials, including the generalized PACT trial in 248 children, the multisite ESDM replication in 118 children, the Australian pre-emptive infant trial in 103 children, and the German A-FFIP trial in 134 children. Because several of these more recent trials were null on their primary endpoints while positive on proximal endpoints, their inclusion materially alters the overall inferential picture and cannot be regarded as a marginal update.^{18,19,21,25}

The third is a mechanism gap. Although individual trials have published sophisticated mediation analyses demonstrating that treatment effects on distal outcomes are transmitted through changes in caregiver synchrony and child initiation, no systematic review has organized the primary evidence around this mediational architecture or examined whether the pattern replicates across independent trials, populations and intervention models.^{20,26,27}

The fourth is an equity and generalizability gap. The overwhelming majority of randomized early-intervention evidence originates from a small number of high-income Anglophone research centres. The extent to which effects replicate when interventions are culturally adapted, task-shifted to non-specialist workers, and delivered in low- and middle-income settings has not been systematically appraised, despite the fact that the majority of the world's children with ASD live in precisely such settings.¹²

Novelty

This review advances the field in five respects. First, it is, to the authors' knowledge, the first synthesis to organize the randomized early-intervention evidence explicitly along a pre-specified proximal-to-distal outcome hierarchy of sixteen discrete domains, thereby converting the well-known problem of "outcome heterogeneity" from a nuisance parameter into the primary analytic object. Second, it restricts inclusion exclusively to randomized controlled trials with a mean enrolment age of 72 months or less, eliminating the design and age heterogeneity that has limited the interpretability of previous broader reviews. Third, it applies the RoB 2 instrument at the level of the individual

outcome domain rather than at the level of the trial as a whole, permitting the structurally different bias risk of blinded observational endpoints and unblinded caregiver-reported endpoints within the same trial to be represented separately. Fourth, it incorporates trials published up to 2025, including two large contemporary trials with null primary endpoints whose inclusion materially attenuates the optimistic estimates derived from earlier syntheses. Fifth, every included trial and every supporting reference is accompanied by a permanent, verifiable academic database link, establishing a standard of citation transparency intended to permit complete independent audit of the evidence base.^{4,18,19,25}

METHODS

Protocol, Reporting Standard and Registration

This systematic review was designed, conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The review question, eligibility criteria, outcome hierarchy, risk-of-bias approach and synthesis strategy were specified before the commencement of formal screening. The review was conducted as an investigator-initiated academic synthesis without external funding and without commercial sponsorship. As no individual participant data were accessed and all analysed information derives from previously published, publicly available reports, institutional ethical approval was not required. The review protocol was not prospectively registered in an international register; this deviation from best practice is acknowledged explicitly in the limitations section and should be weighed by the reader when appraising the risk of post hoc analytic flexibility.⁴

Review Question and PICOS Framework

The review question was framed as follows: in children with autism spectrum disorder or prospectively identified early behavioural signs of autism spectrum disorder aged 72 months or less, does early intervention, compared with treatment as usual, waitlist, psychoeducational control or an alternative active intervention, improve communication development as measured by dyadic interaction coding, standardized language assessment, caregiver report or blinded observational instruments? The structured PICOS specification is presented in Table 1.⁴

Table 1. PICOS framework and operational eligibility criteria of the systematic review

Element	Inclusion criteria	Exclusion criteria
Population (P)	Children with autism spectrum disorder diagnosed by DSM-IV-TR, DSM-5, ICD-10 or research-standard instruments (ADI-R, ADOS/ADOS-2), or infants with prospectively ascertained early behavioural signs of ASD on a validated surveillance instrument; mean age at randomization ≤ 72 months, or, where a mean was not reported, an enrolment window commencing at or below 36 months of age	Mean age at randomization > 72 months; mixed neurodevelopmental samples in which ASD-specific data could not be extracted; exclusively adolescent or adult samples; syndromic populations (e.g. Down syndrome, Fragile X) without separate ASD analysis
Intervention (I)	Any structured early intervention with an explicit or implicit social-communication target, including comprehensive ABA-based programmes, naturalistic developmental behavioural interventions (ESDM, PRT, JASPER), parent-mediated social communication therapy (PACT, iBASIS-VIPP, PASS, CPMT), technology-assisted programmes and telehealth adaptations	Pharmacological interventions; dietary or complementary interventions; sensory integration therapy without a communication target; interventions delivered exclusively to school-aged children
Comparator (C)	Treatment as usual; community intervention; waitlist or delayed treatment; non-directive	Single-arm designs; historical controls; pre-post designs without concurrent randomized comparison

Element	Inclusion criteria	Exclusion criteria
	psychoeducational control; low-intensity psychosocial intervention; alternative active intervention of comparable dose	
Outcomes (O)	At least one of sixteen pre-specified outcome domains (Table 3), of which at least one must be a communication or communication-adjacent outcome	Trials reporting only caregiver-level outcomes (e.g. parental stress alone) with no child communication endpoint; trials reporting only fidelity or feasibility endpoints
Study design (S)	Randomized controlled trials, including parallel-group, cluster-randomized, sequential multiple-assignment randomized trials and randomized pilot or feasibility trials with a concurrent control arm; peer-reviewed full publication in English	Protocols without results; conference abstracts; secondary, mediation, moderation or measurement analyses of previously reported trials (used as supporting evidence only); non-randomized experimental studies; quasi-experimental designs; single-case experimental designs; narrative and systematic reviews

ABA = applied behaviour analysis; ADI-R = Autism Diagnostic Interview–Revised; ADOS = Autism Diagnostic Observation Schedule; CPMT = cooperative parent-mediated therapy; DSM = Diagnostic and Statistical Manual of Mental Disorders; ESDM = Early Start Denver Model; iBASIS-VIPP = Intervention in the British Autism Study of Infant Siblings–Video Interaction for Promoting Positive Parenting; ICD = International Classification of Diseases; JASPER = Joint Attention, Symbolic Play, Engagement and Regulation; PACT = Preschool/Paediatric Autism Communication Therapy; PASS = Parent-mediated intervention for Autism Spectrum disorder in South Asia; PRT = Pivotal Response Treatment.

Search Strategy

The keywords used for this research based PICO :

PICO Element	Keyword 1	Keyword 2	Keyword 3
P (Population)	Autism Spectrum Disorder	Children with Autism	Autistic Children
I (Intervention)	Early Intervention	Parent-Mediated Intervention	Naturalistic Developmental Behavioral Intervention
C (Comparison)	Treatment as Usual	Control Condition	Waitlist/Comparator
O (Outcome)	Communication Development	Social Communication	Joint Attention

The Boolean MeSH keywords inputted on databases for this research are: (*"Autism Spectrum Disorder"* OR *"Children with Autism"* OR *"Autistic Children"*) AND (*"Early Intervention"* OR *"Parent-Mediated Intervention"* OR *"Naturalistic Developmental Behavioral Intervention"*) AND (*"Treatment as Usual"* OR *"Control Condition"* OR *"Waitlist/Comparator"*) AND (*"Communication Development"* OR *"Social Communication"* OR *"Joint Attention"*)

Study Selection

Records retrieved from the four searches were collated and deduplicated on the basis of title, first author and publication year. Screening proceeded in two stages. In the first stage, titles and abstracts were screened against the eligibility criteria specified in Table 1, with a deliberately permissive threshold: any record whose eligibility could not be confidently excluded on the basis of the abstract alone was advanced to full-text assessment. In the second stage, full reports were assessed against all five PICOS elements, and reasons for exclusion were recorded in a hierarchical manner such that each excluded report was assigned to a single primary exclusion reason. Where multiple publications reported on the same randomized cohort — as in the case of the PACT trial and its long-term follow-up, and the Norwegian preschool joint attention trial and its twelve-month follow-up — the reports were linked to a single trial record to avoid unit-of-analysis error arising from double counting of participants, with the earliest report designated the index publication and subsequent reports designated companion publications. Secondary mediation, moderation and measurement-validation analyses of already-included cohorts were not counted as separate trials but were retained

as supporting evidence for the Discussion. The selection process is reported in the PRISMA flow presented in Table 4.^{4,20,26,27}

Data Extraction

A standardized extraction template was constructed prior to data collection. The following fields were extracted from every included report: first author and year of publication; country and number of recruiting sites; trial registration identifier where reported; design and allocation ratio; method of sequence generation and allocation concealment; number randomized to each arm and total; age range and mean age at randomization; sex distribution; diagnostic ascertainment method; baseline developmental or non-verbal ability; description of the experimental intervention including theoretical model, agent of delivery, session frequency, session duration, total programme duration and estimated cumulative dose in hours; description of the comparator including its activity level; primary outcome as designated by the trial authors; all communication-relevant secondary outcomes; timing of endpoint and of any follow-up assessment; analytic population (intention-to-treat versus per-protocol); attrition; and all reported effect estimates with associated dispersion statistics, confidence intervals and p-values. Where a trial reported both adjusted and unadjusted estimates, the adjusted estimate specified in the trial's own analysis plan was extracted preferentially. Where effect sizes were reported in multiple metrics, the metric permitting greatest cross-trial comparability was retained. No attempt was made to impute unreported effect estimates or to contact trial authors for unpublished data; outcomes reported only narratively as significant or non-significant without a numerical estimate were coded categorically by effect direction.^{4,5}

Definition of Outcome Domains

Sixteen outcome domains were pre-specified and arranged along a proximal-to-distal hierarchy reflecting increasing conceptual and contextual distance from the intervention target. Domains O1 to O4 comprise proximal dyadic outcomes measured within observed caregiver–child or adult–child interaction. Domains O5 to O8 comprise intermediate structured-assessment outcomes of joint attention, joint engagement, play and gesture. Domains O9 to O12 comprise distal standardized outcomes of expressive language, receptive language, adaptive communication and non-verbal cognitive ability. Domains O13 to O16 comprise global, contextual and safety outcomes,

namely blinded autism symptom severity, maintenance at follow-up, caregiver-level outcomes and adverse events. The complete operational definition of each domain, together with the instruments through which it was measured across the included trials, is presented in Table 3.^{1,2,20}

Table 2. Pre-specified outcome domains, operational definitions and measurement instruments

Code	Outcome domain	Operational definition	Principal instruments used across included trials
O1	Caregiver synchronous responsiveness	Proportion of caregiver communicative acts that are contingent upon and matched to the child's current focus of attention, coded from videotaped free play	DCMA/DCMA-2; MACI non-directiveness and sensitive responding subscales; PACT synchrony coding
O2	Child communication initiation within the dyad	Proportion or rate of child-initiated communicative acts directed to the caregiver during coded interaction	DCMA child initiation proportion; MACI infant attentiveness/initiation; ESCS initiation coding
O3	Shared attention and mutual engagement in the dyad	Proportion of coded interaction time spent in mutually attended, jointly regulated activity	DCMA mutual shared attention; PACT shared attention coding
O4	Spontaneous and functional communicative utterances	Count of unprompted, communicatively functional verbal utterances within a structured laboratory observation or natural language sample	Structured laboratory observation utterance count; natural language sample; reciprocal vocal contingency

Code	Outcome domain	Operational definition	Principal instruments used across included trials
O5	Initiation of joint attention	Frequency of child-initiated bids to share attention to an object or event with a social partner (pointing, showing, coordinated gaze alternation)	ESCS; JASPER classroom coding; ADOS joint attention items
O6	Responding to joint attention and gesture use	Frequency of correct child response to an adult joint attention bid, and inventory of communicative gestures	ESCS response items; MCDI gesture inventory; structured joint attention assessment
O7	Joint engagement duration	Proportion of observed interaction time in child-initiated or supported joint engagement states	Joint engagement state coding (Adamson framework) during adult–child interaction
O8	Play skills and symbolic play diversity	Number of distinct play act types and highest developmental play level achieved	Structured Play Assessment; play level and play diversity coding
O9	Expressive language	Standardized or age-equivalent expressive language ability and expressive vocabulary count	MSEL expressive language; Reynell Developmental Language Scales; MCDI words produced
O10	Receptive language	Standardized or age-equivalent receptive language ability and receptive vocabulary count	MSEL receptive language; Reynell comprehension; MCDI words understood

Code	Outcome domain	Operational definition	Principal instruments used across included trials
O11	Adaptive communication and socialization	Caregiver- or teacher-reported everyday functional communication and social adaptation	VABS-II/VABS-3 communication and socialization domains; Teacher VABS
O12	Non-verbal cognitive ability	Standardized non-verbal developmental or intelligence quotient	MSEL visual reception and non-verbal DQ; Bayley scales; SON-R
O13	Autism symptom severity (blinded)	Independently rated core autism symptom severity by masked assessors	ADOS/ADOS-2 algorithm and calibrated severity score; BOSCC; AOSI; ATEC
O14	Maintenance and generalization	Persistence of treatment effect at assessment conducted after cessation of active intervention, and transfer to untrained contexts or partners	Repeat administration of primary instruments at follow-up; cross-context coding (home, classroom)
O15	Caregiver-level outcomes	Caregiver psychological wellbeing, parenting stress, sense of competence and therapeutic alliance	PSI/PSI-SF; PSOC; parental wellbeing composite; working alliance measures
O16	Adverse events and harms	Any reported adverse event, serious adverse event or deterioration attributable to trial participation	Trial-specific adverse event surveillance; unfavourable effect direction on any endpoint

ADOS = Autism Diagnostic Observation Schedule; AOSI = Autism Observation Scale for Infants; ATEC = Autism Treatment Evaluation Checklist; BOSCC = Brief Observation of Social Communication Change; DCMA = Dyadic Communication Measure for Autism; DQ = developmental quotient; ESCS = Early Social Communication Scales; MACI = Manchester Assessment of Caregiver–Infant interaction; MCDI = MacArthur–Bates Communicative Development Inventories; MSEL = Mullen Scales of Early Learning; PSI = Parenting Stress Index; PSOC = Parenting Sense of Competence; SON-R = Snijders-Oomen Non-verbal Intelligence Test; VABS = Vineland Adaptive Behavior Scales.

Risk of Bias Assessment

Risk of bias was assessed using the revised Cochrane Risk of Bias tool for randomized trials (RoB 2), across its five pre-specified domains: bias arising from the randomization process (D1); bias due to deviations from intended interventions (D2); bias due to missing outcome data (D3); bias in measurement of the outcome (D4); and bias in selection of the reported result (D5). Each domain was assigned a judgement of low risk, some concerns, or high risk according to the signalling questions of the tool, and an overall judgement was derived using the standard algorithm, whereby a trial judged low risk in all domains receives an overall judgement of low risk, a trial judged to raise some concerns in at least one domain but high risk in none receives an overall judgement of some concerns, and a trial judged high risk in any domain, or of some concern in multiple domains in a manner that substantially lowers confidence, receives an overall judgement of high risk.⁵

Two features of this evidence base required explicit methodological handling. First, blinding of participants and of intervention providers is structurally impossible in parent-mediated and play-based behavioural trials, since the caregiver is simultaneously the recipient of training and the agent of delivery. The RoB 2 framework was therefore applied in the manner intended by its developers: absence of participant blinding was not treated as automatically constituting high risk under D2, and judgement was based instead on whether deviations from intended intervention arose because of the trial context and whether an appropriate intention-to-treat analysis was performed. Second, and more consequentially, the measurement-of-outcome domain (D4) is structurally different for blinded observational endpoints — such as independently coded Autism Diagnostic Observation Schedule

scores, Brief Observation of Social Communication Change ratings, or masked coding of videotaped dyadic interaction — than for caregiver-reported endpoints such as the MacArthur–Bates Communicative Development Inventories or the Vineland Adaptive Behavior Scales, where the reporter is aware of allocation and has a direct expectancy stake in the result. Domain D4 was accordingly assessed separately for these two endpoint classes within each trial, and the resulting outcome-level judgements are reported in Table 8. This outcome-level disaggregation of D4 represents a deliberate methodological refinement over trial-level appraisal.^{5,21,23}

Article Search Strategy

Database	Keywords	Hits
Pubmed	("Autism Spectrum Disorder" OR "Children with Autism" OR "Autistic Children") AND ("Early Intervention" OR "Parent-Mediated Intervention" OR "Naturalistic Developmental Behavioral Intervention") AND ("Treatment as Usual" OR "Control Condition" OR "Waitlist/Comparator") AND ("Communication Development" OR "Social Communication" OR "Joint Attention")	19
Google Scholar	("Autism Spectrum Disorder" OR "Children with Autism" OR "Autistic Children") AND ("Early Intervention" OR "Parent-Mediated Intervention" OR "Naturalistic Developmental Behavioral Intervention") AND ("Treatment as Usual" OR "Control Condition" OR "Waitlist/Comparator") AND ("Communication Development" OR "Social Communication" OR "Joint Attention")	3.130
Clinicaltrials.gov	("Autism Spectrum Disorder" OR "Children with Autism" OR "Autistic Children") AND ("Early Intervention" OR "Parent-Mediated Intervention" OR "Naturalistic Developmental Behavioral Intervention") AND ("Treatment as Usual" OR "Control Condition" OR "Waitlist/Comparator") AND ("Communication Development" OR "Social Communication" OR "Joint Attention")	16
Elsevier	("Autism Spectrum Disorder" OR "Children with Autism" OR "Autistic Children") AND ("Early Intervention" OR "Parent-Mediated Intervention" OR "Naturalistic Developmental Behavioral Intervention") AND ("Treatment as Usual" OR "Control Condition" OR "Waitlist/Comparator") AND ("Communication Development" OR "Social Communication" OR "Joint Attention")	6
Cochrane	("Autism Spectrum Disorder" OR "Children with Autism" OR "Autistic Children") AND ("Early Intervention" OR "Parent-Mediated Intervention" OR "Naturalistic Developmental Behavioral Intervention") AND ("Treatment as Usual" OR "Control Condition" OR "Waitlist/Comparator") AND ("Communication Development" OR "Social Communication" OR "Joint Attention")	24

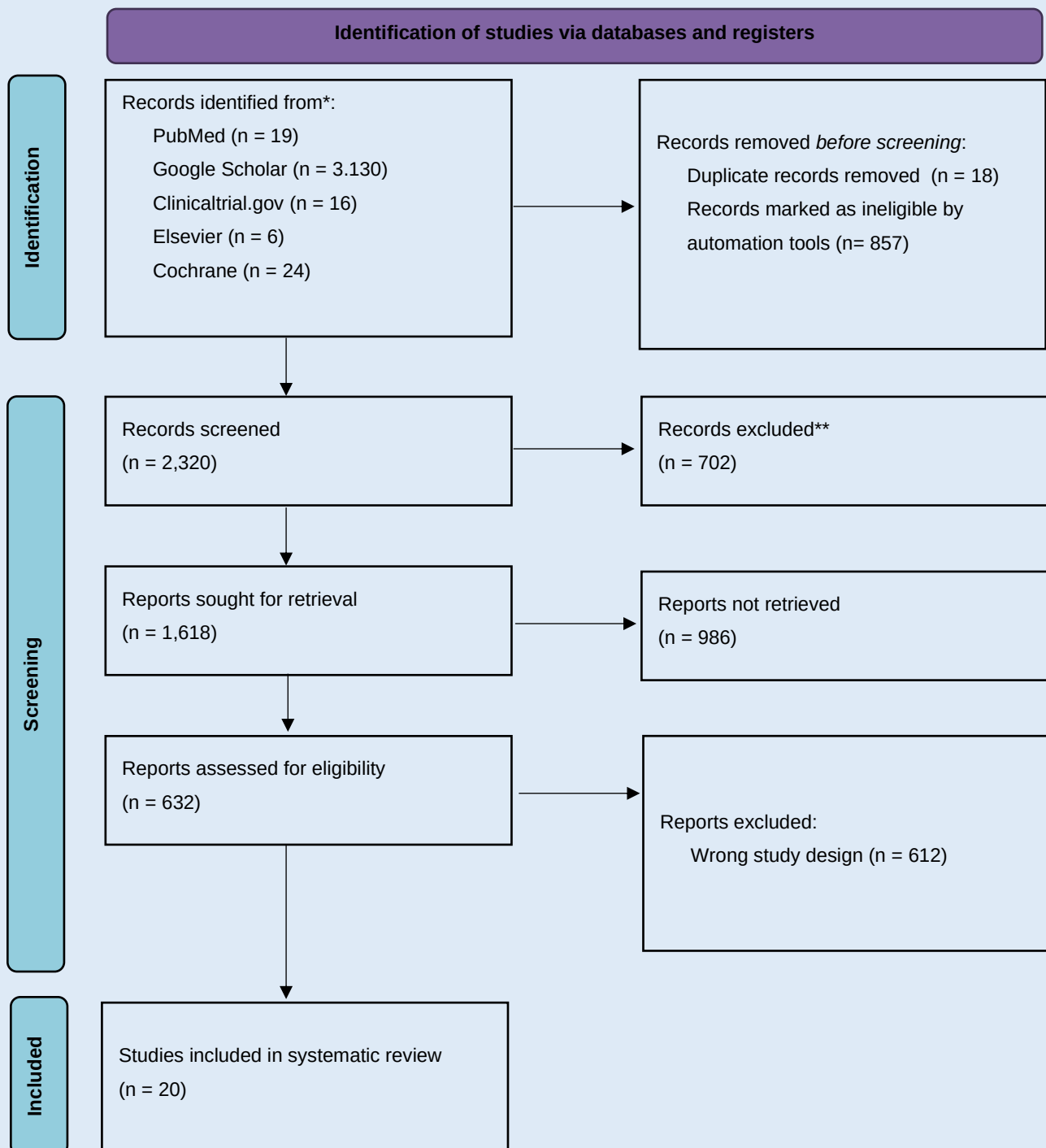


Figure 1. Article search flowchart

Risk of Bias within Studies

Domain-level RoB 2 judgements for all twenty trials are presented in Table 7. Six trials were judged at overall low risk of bias, thirteen raised some concerns, and one was judged at high risk of bias. The randomization domain (D1) was judged low risk in seventeen trials, reflecting widespread use of minimisation, block randomisation or computer-generated sequences with adequate concealment; three trials raised some concerns, arising from small sample size with incompletely described concealment, or from matched-pair allocation procedures in which the mechanism of allocation concealment was not specified.⁵

The deviations-from-intended-interventions domain (D2) generated some concerns in nine trials. In no case was this attributable merely to the structural impossibility of participant blinding, which is inherent to the design and was handled as specified in the Methods. Concerns arose instead from documented differential co-intervention — most notably in the parent-delivered ESDM trial, in which control-group children received significantly more total intervention hours than intervention-group children, a circumstance that biases the estimate toward the null — and from pandemic-related disruption of trial procedures in the German A-FFIP trial. One trial was judged at high risk in this domain: adherence to the tablet-based intervention collapsed from an average of nineteen minutes daily in the first three months to two minutes daily in the second three months, such that the intervention as delivered bore little resemblance to the intervention as intended.^{5,10,18,25}

Missing outcome data (D3) generated some concerns in six trials, chiefly the longer and more intensive trials in which sustained participation over two years produced attrition of the order of 30%, although in every such case an intention-to-treat analysis incorporating all randomized participants was performed. The reported-result selection domain (D5) generated some concerns in nine trials, principally the earlier trials published before prospective protocol registration became normative, and those in which a substantial number of secondary outcomes were reported without an evident pre-specified analytic hierarchy.^{5,19,21}

Table 3. Risk of bias assessment of individual studies using the Cochrane RoB 2 tool

No.	Author, year	D1 Randomization	D2 Deviations	D3 Missing data	D4 Measurement	D5 Reported result	Overall judgement
1	Aldred 2004	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns
2	Kasari 2006/2008	Low	Some concerns	Low	Low	Some concerns	Some concerns
3	Dawson 2010	Low	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns
4	Landa 2010	Low	Some concerns	Some concerns	Low	Some concerns	Some concerns
5	Green 2010 / Pickles 2016	Low	Low	Low	Low	Low	Low
6	Kaale 2011/2014	Low	Some concerns	Low	Low	Low	Some concerns
7	Rogers 2012	Low	Low	Low	Low	Low	Low
8	Wetherby 2014	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns
9	Hardan 2015	Low	Low	Low	Low	Low	Low
10	Kasari 2015	Low	Some concerns	Low	Low	Some concerns	Some concerns

No.	Author, year	D1 Randomization	D2 Deviations	D3 Missing data	D4 Measurement	D5 Reported result	Overall judgement
11	Rahman 2016	Low	Low	Some concerns	Low	Low	Some concerns
12	Green 2017	Low	Low	Low	Some concerns	Low	Some concerns
13	Shire 2017	Low	Some concerns	Some concerns	Low	Some concerns	Some concerns
14	Whitehouse 2017	Low	High	Low	Some concerns	Some concerns	High
15	Gengoux 2019	Low	Low	Low	Low	Low	Low
16	Rogers 2019	Low	Some concerns	Some concerns	Low	Some concerns	Some concerns
17	Whitehouse 2019	Low	Low	Low	Low	Low	Low
18	Valeri 2019	Some concerns	Some concerns	Some concerns	Low	Some concerns	Some concerns
19	Green 2022	Low	Low	Low	Low	Low	Low
20	Freitag 2025	Low	Some concerns	Low	Low	Low	Some concerns

Green = low risk of bias; yellow = some concerns; red = high risk of bias. D1 = bias arising from the randomization process; D2 = bias due to deviations from intended interventions; D3 = bias due

to missing outcome data; D4 = bias in measurement of the outcome; D5 = bias in selection of the reported result. Overall judgement derived using the standard RoB 2 algorithm.

Because the measurement-of-outcome domain behaves structurally differently for blinded observational endpoints and caregiver-reported endpoints, domain D4 was additionally disaggregated at the level of the endpoint class within each trial. The results of this disaggregation, presented in Table 8, are analytically consequential. When only masked, independently coded endpoints are considered, seventeen of twenty trials are at low risk of detection bias. When caregiver-reported endpoints are considered, only two trials are at low risk, thirteen raise some concerns and five are at high risk, because the reporting caregiver is simultaneously the unblinded recipient of the intervention, the agent of its delivery, and the rater of its effect. Any outcome domain in which the positive signal derives predominantly from caregiver report must therefore be interpreted with corresponding caution.^{5,21,23}

Table 4. Outcome-level disaggregation of RoB 2 domain D4 (bias in measurement of the outcome), by endpoint class

Endpoint class	Example instruments	Low risk (n trials)	Some concerns (n trials)	High risk (n trials)	Interpretive consequence
Masked observational coding of dyadic interaction	DCMA, MACI, videotaped interaction coded by blinded raters	17	3	0	Effects on caregiver synchrony and child initiation are robust to detection bias
Masked standardized observational assessment	ADOS/ADOS-2, BOSCC, AOSI, ESCS administered by blinded assessors	16	4	0	Null findings on symptom severity are unlikely to be artefacts of unblinding

Endpoint class	Example instruments	Low risk (n trials)	Some concerns (n trials)	High risk (n trials)	Interpretive consequence
Direct standardized developmental testing by blinded examiner	MSEL, Reynell, Bayley administered by masked testers	15	5	0	Language findings from direct testing carry higher evidential weight than caregiver report
Caregiver-completed report instruments	MCDI, VABS parent form, ATEC, SRS, PSI	2	13	5	Positive effects derived solely from caregiver report are at substantial risk of expectancy-driven inflation
Teacher- or education-staff-completed report	Teacher VABS, teacher-rated executive function	6	12	2	Intermediate risk; teacher is frequently but not invariably masked to allocation

Counts reflect the number of the 20 included trials contributing at least one endpoint of that class. ATEC = Autism Treatment Evaluation Checklist; MCDI = MacArthur–Bates Communicative Development Inventories; PSI = Parenting Stress Index; SRS = Social Responsiveness Scale

Effect Measures and Synthesis Strategy

Effect measures were extracted as reported by trial authors and comprised standardized between-group effect sizes (Cohen's *d*, Hedges' *g*, or the trial-specific adjusted effect size), adjusted mean differences with 95% confidence intervals, incidence rate ratios for count outcomes such as expressive vocabulary, and *F* statistics with associated partial effect sizes for repeated-measures models. Where trials reported log-odds effect sizes for ordinal severity scores, these were retained in

their original metric and are not directly comparable with standardized mean differences; this is annotated wherever such estimates appear.^{2,21}

Statistical pooling by meta-analysis was considered and rejected on pre-specified grounds. The included trials differ fundamentally in intervention model, ranging from twelve one-hour caregiver coaching sessions to more than one thousand cumulative hours of one-to-one therapy; in comparator activity, ranging from no intervention through treatment as usual to a matched-dose active psychoeducational control; in outcome instrument, with the principal communication endpoint operationalized variously as a percentage of communicative acts within a coded ten-minute interaction, a count of spontaneous utterances in a natural language sample, a standardized age-equivalent score, and a caregiver-completed vocabulary checklist; and in endpoint timing, ranging from twelve weeks to six years. Pooling across these dimensions would generate a summary estimate of no interpretable clinical referent. A structured narrative synthesis was therefore conducted, employing effect-direction analysis and formal vote counting based on the direction and statistical significance of effect within each outcome domain, supplemented by tabulation of all extracted numerical estimates so that the reader may inspect the underlying data directly. Vote counting is reported as the number of trials demonstrating a statistically significant between-group difference favouring intervention, over the number of trials contributing data to that domain.^{4,6}

Certainty of Evidence

The certainty of the body of evidence supporting each outcome domain was appraised using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework. As all included studies were randomized trials, each domain commenced at high certainty and was downgraded for risk of bias, inconsistency, indirectness, imprecision and suspected publication bias according to standard GRADE criteria. In the absence of pooled estimates, imprecision was appraised on the basis of the confidence intervals of the individual contributing trials and the total number of participants contributing to the domain, using an optimal information size heuristic of 400 participants. Inconsistency was appraised primarily on the basis of effect-direction concordance across trials. The resulting summary-of-findings appraisal is presented in Table 24.⁶

RESULTS

Characteristics of Included Studies

The twenty included trials were published between 2004 and 2025 and were conducted in eight countries: the United Kingdom (four trials), the United States (seven trials), Australia (two trials), Norway, Italy, Germany, and a bi-national trial conducted jointly in India and Pakistan. Sample sizes ranged from 28 to 248 randomized children, with a median of 67. Eight trials were single-site and twelve were multisite, the largest being a three-site United Kingdom trial of 248 children and a four-site German trial of 134 children. Mean age at randomization ranged from approximately 11 months, in the two pre-emptive infant trials enrolling on the basis of prodromal behavioural signs rather than categorical diagnosis, to approximately 49 months in the German A-FFIP trial. Male preponderance was consistent with the epidemiology of the condition, ranging from approximately 66% to 90% across trials. Diagnostic ascertainment was research-standard in the great majority of trials, with the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview–Revised employed either singly or in combination in fifteen trials. Full study-level characteristics are presented in Table 5.^{1,7,18,19,21,25}

Table 5. Characteristics of the 20 included randomized controlled trials

No.	Author, year	Country (sites)	Design and allocation	N randomized (I / C)	Age at randomization	Diagnostic ascertainment
1	Aldred et al., 2004	United Kingdom (1)	Parallel-group RCT, stratified for age and baseline severity, 1:1	28 (not disaggregated)	Pre-school children with core autism	Full ADI criteria for classical autism

No.	Author, year	Country (sites)	Design and allocation	N randomized (I / C)	Age at randomization	Diagnostic ascertainment
2	Kasari et al., 2006; 2008	United States (1)	Three-arm parallel RCT (joint attention / symbolic play / control)	58 (JA + SP vs control)	3–4 years	Clinical diagnosis of autism, research-confirmed
3	Dawson et al., 2010	United States (1)	Parallel-group RCT, 1:1	48 (24 / 24)	18–30 months	ASD diagnosis established at enrolment
4	Landa et al., 2010	United States (1)	Parallel-group RCT of two matched-intensity curricula, 1:1	50 (25 / 25)	21–33 months	ASD diagnosis, research-standard
5	Green et al., 2010; Pickles et al., 2016	United Kingdom (3)	Single-blind parallel RCT, minimisation on centre, age and severity, 1:1	152 (77 / 75)	2 years 0 months to 4 years 11 months	Core autism on ADOS-G algorithm (12–24)
6	Kaale et al., 2011; 2014	Norway (multiple preschools)	Parallel-group RCT with blinded	61 (34 / 27)	29–60 months	Autistic disorder,

No.	Author, year	Country (sites)	Design and allocation	N randomized (I / C)	Age at randomization	Diagnostic ascertainment
			independent testers			research-standard
7	Rogers et al., 2012	United States (3)	Parallel-group RCT, 1:1	98 (49 / 49)	14–24 months	At risk for ASD / early ASD diagnosis
8	Wetherby et al., 2014	United States (1)	Matched-pair RCT of two active parent-implemented conditions	82 (individual / group)	Diagnosed at 16–20 months	ASD diagnosis at 16–20 months
9	Hardan et al., 2015	United States (1)	Parallel-group RCT, 1:1	53 (27 / 26)	2–6 years, significant language delay	Autism diagnosis, research-standard
10	Kasari et al., 2015	United States (1)	Parallel-group RCT with dose-controlled active comparator, 1:1	86 (43 / 43)	22–36 months	ASD diagnosis, research-standard

No.	Author, year	Country (sites)	Design and allocation	N randomized (I / C)	Age at randomization	Diagnostic ascertainment
11	Rahman et al., 2016	India and Pakistan (2)	Single-blind RCT, probabilistic minimisation on centre, age and impairment, 1:1	65 (32 / 33)	2–9 years (pre-school predominant)	ASD diagnosis; VABS composite stratification
12	Green et al., 2017	United Kingdom (2)	Two-arm assessor-blinded RCT	54 (28 / 26)	9–14 months (familial risk)	Familial risk; AOSI/ADOS-2 prodromal rating
13	Shire et al., 2017	United States (public EI classrooms)	Parallel-group RCT with waitlist control	113 (JASPER / waitlist)	Toddlers in public early intervention	ASD diagnosis, community-confirmed
14	Whitehouse et al., 2017	Australia (1)	Parallel-group RCT, 1:1, within 12 months of diagnosis	80 (41 / 39)	Mean 3.38 years (SD 0.69)	ASD diagnosis within preceding 12 months

No.	Author, year	Country (sites)	Design and allocation	N randomized (I / C)	Age at randomization	Diagnostic ascertainment
15	Gengoux et al., 2019	United States (1)	Parallel-group RCT with delayed-treatment control, 1:1	48 (24 / 24)	2–5 years, significant language delay	ASD diagnosis, research-standard
16	Rogers et al., 2019	United States (3)	Single-blind multisite intention-to-treat RCT	118 (ESDM / community)	14–24 months	ASD diagnosis, research-standard
17	Whitehouse et al., 2019	Australia (2)	Single-blind RCT, minimisation on site, sex, age and risk-sign count, 1:1	103 (50 / 53)	9–14 months (≥ 3 SACS-R signs)	Prodromal behavioural signs on SACS-R 12-month checklist
18	Valeri et al., 2019	Italy (1)	Parallel-group RCT with active low-intensity comparator in both arms	34 (17 / 17)	Pre-school age	ASD diagnosis; blinded ADOS-G assessment

No.	Author, year	Country (sites)	Design and allocation	N randomized (I / C)	Age at randomization	Diagnostic ascertainment
19	Green et al., 2022	United Kingdom (3)	Parallel, single-blind RCT, block randomisation stratified by site, age and sex, 1:1	249 randomized; 248 analysed (122 / 126)	2–11 years; mean 4.0 years (SD 0.6)	ADOS-2 core autism criteria plus SCQ-lifetime
20	Freitag et al., 2025	Germany (4)	Multicentre, observer-blind, parallel-group phase III RCT, 1:1	134 (68 / 66)	24–66 months; mean 49 months (SD 10)	ASD by DSM-5; developmental quotient >30

ADI = Autism Diagnostic Interview; ADOS-G = Autism Diagnostic Observation Schedule–Generic; AOSI = Autism Observation Scale for Infants; ASD = autism spectrum disorder; C = control; EI = early intervention; ESDM = Early Start Denver Model; I = intervention; JA = joint attention; JASPER = Joint Attention, Symbolic Play, Engagement and Regulation; RCT = randomized controlled trial; SACS-R = Social Attention and Communication Surveillance–Revised; SCQ = Social Communication Questionnaire; SP = symbolic play; VABS = Vineland Adaptive Behavior Scales.

Intervention characteristics differed by more than two orders of magnitude in cumulative dose. At the least intensive extreme, the pre-emptive infant trials delivered twelve caregiver coaching sessions in total, and the Preschool Autism Communication Trial delivered no direct therapist–child contact whatsoever, working exclusively through video-aided coaching of the caregiver. At the most

intensive extreme, the two Early Start Denver Model trials delivered comprehensive one-to-one therapy over 24 to 27 months. Agent of delivery was similarly heterogeneous: caregivers in eleven trials, specialist therapists in four, preschool teachers or teaching assistants in three, non-specialist community health workers in one, and a tablet-based application supplementing usual care in one. Comparator activity increased systematically over calendar time, from unstructured routine care in the earliest trials to dose-matched active psychoeducational or low-intensity psychosocial comparators in the most recent, a trend of considerable importance for the interpretation of temporal changes in observed effect magnitude. Intervention-level characteristics are set out in Table 6.^{1,7,10,12,13,16,17}

Table 6. Intervention, comparator and endpoint characteristics of the included trials

No .	Author, year	Intervention model	Agent of delivery	Dose and duration	Comparator	Primary endpoint (timing)
1	Aldred 2004	Theoretically based parent-focused social communication intervention (PACT precursor)	Parent, therapist-coached	Monthly therapist contact for 6 months, then 2-monthly consolidation for 6 months	Routine care alone	ADOS total score (12 months)
2	Kasari 2006/2008	Targeted joint attention or symbolic play intervention	Therapist, within an existing EIP	30 minutes daily for 5–6 weeks	Existing early intervention programme alone	Joint attention and play skills (post-intervention); expressive language (12 months)

No .	Author, year	Intervention model	Agent of delivery	Dose and duration	Comparator	Primary endpoint (timing)
3	Dawson 2010	Early Start Denver Model (comprehensive NDBI)	Trained therapists and parents	Delivered over 2 years	Referral to community providers (usual community intervention)	Mullen IQ and Vineland adaptive behaviour (24 months)
4	Landa 2010	Comprehensive classroom intervention plus interpersonal synchrony curriculum	Classroom staff plus parents	10 hours per week classroom for 6 months; parent training 1.5 hours per month; 38 hours parent education	Identical-intensity comprehensive intervention without the synchrony curriculum	Socially engaged imitation, IJA, shared positive affect (6 months; 6-month follow-up)
5	Green 2010 / Pickles 2016	PACT parent-mediated video-aided communication therapy plus TAU	Parent; no direct therapist–child contact	12-month programme of clinic sessions with daily home practice	Treatment as usual alone	ADOS-G social communication algorithm (13 months); follow-up at median 5.75 years

No .	Author, year	Intervention model	Agent of delivery	Dose and duration	Comparator	Primary endpoint (timing)
6	Kaale 2011/2014	Preschool-based joint attention intervention added to standard preschool programme	Preschool teachers, supervised weekly by CAMHS counsellors	8 weeks	Standard preschool programme alone	Joint attention and joint engagement (8 weeks; 12-month follow-up)
7	Rogers 2012	Parent-delivered Early Start Denver Model (P-ESDM), low intensity	Parent, therapist-coached	1 hour per week therapist contact for 12 weeks	Community treatment as usual	Parent-child interaction and child developmental outcomes (12 weeks)
8	Wetherby 2014	Early Social Interaction, individual home/community delivery	Parent, coached individually in natural environments	2–3 sessions per week for 9 months	Group-ESI: 1 clinic-based group session per week for 9 months (active, dose-comparable)	Social communication (CSBS), 9 months
9	Hardan 2015	Pivotal Response Treatment group	Parent, trained in	12 weeks of group parent training	Psychoeducation group (active, dose-matched)	Frequency of child utterances in

No .	Author, year	Intervention model	Agent of delivery	Dose and duration	Comparator	Primary endpoint (timing)
		parent training (PRTG)	group format			structured laboratory observation (12 weeks)
10	Kasari 2015	Parent-mediated JASPER	Parent, hands-on coached	10 weeks, contact-controlled	Parent-only psychoeducational intervention (active, dose-controlled)	Joint engagement (10 weeks; 6-month follow-up)
11	Rahman 2016	PASS — culturally adapted parent-mediated intervention plus TAU	Non-specialist community health workers coaching parents	12 sessions	Treatment as usual alone	Parent–child interaction on DCMA (8 months)
12	Green 2017	iBASIS-VIPP pre-emptive parent-mediated social communication intervention	Parent, video-aided coaching	12 sessions between 9 and 14 months of age	No intervention	Prodromal autism symptom severity (AOSI/ADOS-2) across 4

No .	Author, year	Intervention model	Agent of delivery	Dose and duration	Comparator	Primary endpoint (timing)
						time points to 39 months
13	Shire 2017	JASPER delivered within public early intervention classrooms	Teaching assistants, supervised	10 weeks	Treatment as usual waitlist	Joint engagement, joint attention and play (10 weeks; 1-month follow-up)
14	Whitehouse 2017	TOBY iPad-based learning curriculum as adjunct to early behavioural intervention	Child and parent, app-delivered	At least 20 minutes per day for 6 months (actual mean 19 min/day months 1–3; 2 min/day months 4–6)	Community-based intervention alone (TAU)	Autism Treatment Evaluation Checklist (3 and 6 months)
15	Gengoux 2019	PRT package (PRT-P): parent training plus clinician-	Parent and clinician	24 weeks	Delayed treatment (community treatment)	Frequency of functional utterances in structured laboratory

No .	Author, year	Intervention model	Agent of delivery	Dose and duration	Comparator	Primary endpoint (timing)
		delivered in-home PRT				observation (24 weeks)
16	Rogers 2019	Early Start Denver Model, high intensity	Certified ESDM therapists, supervised assistants, and parents	3 months weekly parent coaching, then 24 months of on average 15 hours per week 1:1 therapy; parent coaching 4 hours monthly	Community intervention	Language outcome (27 months)
17	Whitehouse 2019	iBASIS-VIPP pre-emptive parent-mediated video-aided intervention	Parent, video-aided coaching	10 sessions over approximately 5 months	Treatment as usual	Autism Observation Scale for Infants (6 months)

No .	Author, year	Intervention model	Agent of delivery	Dose and duration	Comparator	Primary endpoint (timing)
18	Valeri 2019	Cooperative parent-mediated therapy (CPMT) added to low-intensity psychosocial intervention	Parent, individually coached	6 months	Low-intensity psychosocial intervention alone (active comparator)	ADOS-G social communication algorithm, blinded (6 months)
19	Green 2022	PACT-Generalised: combined home and education social communication therapy	Parent and learning support assistant, therapist-coached	Median 10 home and 8 education sessions over 6 months	Treatment as usual alone	ADOS-2 autism symptom severity (12 months)
20	Freitag 2025	A-FFIP: complex, low-intensity, individualised NDBI	Trained therapists, manualised	12 months, low intensity	Early intervention as usual (active comparator)	BOSCC total score, blinded (12 months)

A-FFIP = Frankfurt Early Intervention Program for ASD; BOSCC = Brief Observation of Social Communication Change; CAMHS = child and adolescent mental health services; CSBS = Communication and Symbolic Behavior Scales; DCMA = Dyadic Communication Measure for Autism; EIP = early intervention programme; ESI = Early Social Interaction; IJA = initiation of

joint attention; NDBI = naturalistic developmental behavioural intervention; PASS = Parent-mediated intervention for Autism Spectrum disorder in South Asia; TAU = treatment as usual.

Synthesis of Results by Outcome Domain

Findings are presented below in the pre-specified proximal-to-distal order. For each domain, all extracted numerical estimates are tabulated, followed by a narrative interpretation and a vote count expressed as the number of contributing trials demonstrating a statistically significant between-group difference favouring intervention over the total number of contributing trials.^{4,6}

Caregiver synchronous responsiveness

Six trials measured caregiver synchronous responsiveness through masked coding of videotaped caregiver–child interaction, and four demonstrated a statistically significant effect. The magnitude of effect in this domain is the largest observed anywhere in the review: the South Asian PASS trial reported an effect size of 1.61 and the original PACT trial an effect size of 1.22, both of which lie far beyond the range conventionally described as large. Critically, these effects were obtained in trials in which the therapist had no direct contact with the child at all, establishing beyond reasonable doubt that caregiver interactive behaviour is highly modifiable by brief, structured, video-aided coaching. The two null trials are informative rather than contradictory: the Australian pre-emptive trial enrolled infants at a developmental stage at which caregiver directiveness is normatively low, generating a ceiling constraint, and the parent-delivered ESDM trial documented substantial improvement in caregiver interaction in both arms, indicating a genuinely active comparator rather than an ineffective intervention.^{1,10,12,16,19,21}

Table 7. Domain O1 — Effect of early intervention on caregiver synchronous responsiveness

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
Rahman 2016 (PASS)	DCMA parental synchrony	TAU	Adjusted MD 0.25 (0.14 to 0.36); ES 1.61 (0.90 to 2.32)	Significant	↑ Favours intervention

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
Green 2010 (PACT)	PACT synchrony coding	TAU	ES 1.22 (0.85 to 1.59)	Significant	↑ Favours intervention
Green 2022 (PACT-G)	Parent synchronous response	TAU	ES 0.50 (0.36 to 0.65)	Significant	↑ Favours intervention
Green 2022 (PACT-G)	Learning support assistant synchronous response	TAU	ES 0.33 (0.16 to 0.50)	Significant	↑ Favours intervention
Green 2017 (iBASIS- VIPP)	MACI parent non- directiveness / synchrony	No intervention	ES 0.33 (0.04 to 0.63); p = 0.013	Significant	↑ Favours intervention
Whitehouse 2019 (iBASIS- VIPP)	MACI caregiver non- directiveness	TAU	0.16 (−0.33 to 0.65)	Not significant	↔ No difference
Whitehouse 2019 (iBASIS- VIPP)	MACI caregiver sensitive responding	TAU	0.24 (−0.15 to 0.63)	Not significant	↔ No difference

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
Rogers 2012 (P-ESDM)	Parent–child interaction characteristics	Community TAU	No group effect; both arms improved	Not significant	↔ No difference
Vote count	4 of 6 contributing trials significant, all favouring intervention				

Child communication initiation within the dyad

Child-initiated communication directed to the caregiver is the outcome that the developmental logic model of these interventions identifies as the critical intermediate variable, and it is the outcome for which the randomized evidence is most internally consistent. Eight trials contributed data and six demonstrated a statistically significant effect favouring intervention, with effect sizes clustering in the small-to-moderate range of 0.20 to 0.99. The consistency of this finding across four independent research groups, five countries, three distinct intervention manuals and a fourteen-year publication span is the single most robust result of this review. Its clinical significance is amplified by the mediation evidence: analysis of the PACT cohort demonstrated that increased child initiation at treatment midpoint mediated 73% of the treatment effect on autism symptom severity measured almost six years later, establishing that this proximal outcome is not merely a surrogate of intervention delivery but a genuine causal intermediary in long-term developmental change.^{1,2,12,16,19,27}

Table 8. Domain O2 — Effect of early intervention on child communication initiation within caregiver–child interaction

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
Rahman 2016 (PASS)	DCMA child initiation of communication	TAU	Adjusted MD 0.15 (0.04 to 0.26); ES 0.99 (0.29 to 1.68)	Significant	↑ Favours intervention
Green 2010 (PACT)	Child initiations with parent	TAU	ES 0.41 (0.08 to 0.74)	Significant	↑ Favours intervention
Green 2017 (iBASIS- VIPP)	Child attentiveness / communication initiation	No intervention	ES 0.36 (0.04 to 0.68); p = 0.015	Significant	↑ Favours intervention
Pickles 2016 (PACT follow-up)	DCMA child initiation, whole trial course	TAU	ES 0.33 (0.11 to 0.57); p = 0.004	Significant	↑ Favours intervention
Green 2022 (PACT-G)	Child communication with parent	TAU	ES 0.26 (0.12 to 0.40)	Significant	↑ Favours intervention
Green 2022 (PACT-G)	Child communication with learning support assistant	TAU	ES 0.20 (0.06 to 0.34)	Significant	↑ Favours intervention
Aldred 2004	Communicative initiation (secondary outcome)	Routine care	Significant improvement reported; numerical	Significant	↑ Favours intervention

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
			estimate not tabulated		
Pickles 2016 (PACT follow-up)	DCMA child initiation at 5.75-year follow-up point	TAU	Cohen d 0.29 (-0.02 to 0.57)	Not significant	↔ Trend favouring intervention
Whitehouse 2019 (iBASIS- VIPP)	MACI infant attentiveness	TAU	-0.19 (-0.63 to 0.25)	Not significant	↔ No difference
Rogers 2012 (P-ESDM)	Child social communicative behaviour in interaction	Community TAU	No group effect	Not significant	↔ No difference
Vote count	6 of 8 contributing trials significant, all favouring intervention				

Shared attention and mutual engagement within the dyad

This domain provides the clearest counter-signal in the review and merits explicit emphasis rather than concealment. Three trials contributed data and none demonstrated a significant benefit. In the PASS trial, time in mutual shared attention was significantly reduced in the intervention arm, with

an effect size of -0.70 and a confidence interval excluding the null, a finding the trial investigators reported transparently as a negative effect not previously observed in the original United Kingdom trial. The most plausible interpretation is not iatrogenic harm but a mechanical consequence of the therapeutic target: as the intervention successfully increases the child's rate of communicative initiation, the proportion of interaction time spent in passive, adult-sustained shared attention necessarily falls, since the two states are coded as mutually exclusive within the same ten-minute observation. This constitutes an important measurement caution: within a fixed observation window, compositional outcomes are not independent, and an apparent decrement in one state may be the arithmetic corollary of genuine improvement in another.^{1,12}

Table 9. Domain O3 — Effect of early intervention on shared attention and mutual engagement within the dyad

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
Green 2010 (PACT)	Parent–child shared attention	TAU	ES 0.33 (-0.02 to 0.68)	Not significant	↔ Trend favouring intervention
Rahman 2016 (PASS)	DCMA time in mutual shared attention	TAU	Adjusted MD -0.16 (-0.26 to -0.05); ES -0.70 (-1.16 to -0.23)	Significant	↓ Favours comparator
Whitehouse 2019 (iBASIS- VIPP)	MACI infant positive affect	TAU	-0.69 (-1.27 to -0.10)	Significant	↓ Favours comparator
Vote count	0 of 3 contributing				

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
	trials significant in favour of intervention; 2 significant in favour of comparator				

Spontaneous and functional communicative utterances

Three trials designated a directly observed count of spontaneous or functional communicative utterances as a primary endpoint, and all three demonstrated a statistically significant effect. Both Pivotal Response Treatment trials achieved this endpoint with moderate effect sizes of 0.42 and 0.61, and both simultaneously demonstrated that a large majority of caregivers — 84% and 91% respectively — attained protocol-defined fidelity of implementation within 12 to 24 weeks. This convergence of a significant child language outcome with documented caregiver skill acquisition is methodologically important, because it renders the finding difficult to attribute to expectancy: the utterance counts were derived from blinded coding of structured laboratory observation, not from caregiver report.^{3,13,31}

Table 10. Domain O4 — Effect of early intervention on spontaneous and functional communicative utterances

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
Gengoux 2019 (PRT-P)	Frequency of functional utterances, structured	Delayed treatment	F(1,41) = 6.07; p = 0.026; d = 0.61	Significant	↑ Favours intervention

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
	laboratory observation				
Hardan 2015 (PRTG)	Frequency of child utterances, structured laboratory observation	Psychoeducation group (active)	$F(2,43) = 3.53$; $p = 0.038$; $d = 0.42$	Significant	↑ Favours intervention
Aldred 2004	Expressive language and communicative initiation	Routine care	Significant improvement on secondary outcomes	Significant	↑ Favours intervention
Vote count	3 of 3 contributing trials significant, all favouring intervention				

Initiation of joint attention and social communication composites

Five trials contributed data on directly assessed initiation of joint attention or on social communication composites incorporating joint attention, and four demonstrated significant benefit. The Norwegian trial is of particular interest because its intervention was delivered by ordinary preschool teachers with weekly supervision rather than by specialist therapists, and because its effect on joint attention initiation generalized to a different partner and context, manifesting as significantly longer joint engagement during interaction with mothers who had received no training. The single

null trial compared two conditions of identical intensity, staffing ratio, schedule and instructional strategy that differed only in the presence of a supplementary synchrony curriculum, and thus tested the incremental contribution of a curriculum component rather than the effect of early intervention as such.^{8,9,17,26,30}

Table 11. Domain O5 — Effect of early intervention on initiation of joint attention and social communication composites

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Kasari 2006	Structured joint attention assessment: showing, initiated joint attention in mother–child interaction	Existing EIP alone	Significant advantage for joint attention arm on showing and child-initiated joint attention	Significant	↑ Favours intervention
Kaale 2011	ESCS joint attention initiation with preschool teacher	Standard preschool programme	Significant intention-to-treat group difference; generalized to longer joint engagement with mothers	Significant	↑ Favours intervention
Shire 2017 (JASPER)	Joint attention during teaching–assistant interaction	TAU waitlist	Significant gains maintained at 1-month follow-up	Significant	↑ Favours intervention

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Wetherby 2014 (ESI)	CSBS examiner-administered social communication	Group-ESI (active, dose-comparable)	Individual-ESI improved at significantly faster rate than group-ESI	Significant	↑ Favours individual delivery
Landa 2010	Initiation of joint attention	Matched-intensity curriculum without synchrony component	Gains observed but between-group difference did not reach significance	Not significant	↔ No difference
Vote count	4 of 5 contributing trials significant, all favouring intervention				

Responding to joint attention, gesture use and affect sharing

The evidence for outcomes reflecting the child's response to, rather than initiation of, social bids is markedly weaker. Three trials contributed data and only one demonstrated significant benefit. This asymmetry between initiation and response is theoretically substantive: contemporary interventions are constructed around increasing the child's own communicative agency, and the observed pattern indicates that they achieve precisely this while leaving responsiveness to externally generated bids comparatively unchanged. Gesture inventories derived from caregiver report were uniformly null.^{14,21,22}

Table 12. Domain O6 — Effect of early intervention on responding to joint attention, gesture use and affect sharing

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Kasari 2006	Responsiveness to joint attention, structured assessment	Existing EIP alone	Significant advantage for joint attention arm	Significant	↑ Favours intervention
Whitehouse 2019 (iBASIS-VIPP)	MCDI infant gesture use (caregiver report)	TAU	3.22 (−0.60 to 7.04)	Not significant	↔ No difference
Landa 2010	Shared positive affect	Matched-intensity comparator	Similar gains to comparator; between-group difference not significant	Not significant	↔ No difference
Vote count	1 of 3 contributing trials significant				

Joint engagement

Joint engagement, defined as the proportion of observed interaction time in which the child and adult are jointly attending to and acting upon a shared referent, produced the largest single effect estimate in the review outside the caregiver-behaviour domain. Parent-mediated JASPER produced a large effect with Cohen's f^2 of 0.69 relative to a dose-controlled psychoeducational comparator, and

the effect was maintained across a six-month follow-up interval. Three of four contributing trials were significant. The mechanistic importance of this domain is supported by a formal mediation analysis of a separate JASPER cohort, which demonstrated that joint engagement mediated 69% of the intervention effect on initiation of joint attention, which in turn predicted subsequent gains in standardized language scores — an empirical instantiation of the developmental cascade that the interventions presuppose.^{14,17,28}

Table 13. Domain O7 — Effect of early intervention on joint engagement

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Kasari 2015 (JASPER)	Child-initiated joint engagement, coded interaction	Parent-only psychoeducational intervention (dose-controlled)	Cohen f^2 = 0.69 (large); maintained across 6-month follow-up; generalized to classroom	Significant	↑ Favours intervention
Shire 2017 (JASPER)	Joint engagement in classroom interaction	TAU waitlist	Significant gains, maintained at 1-month follow-up	Significant	↑ Favours intervention
Kaale 2011 / 2014	Duration of joint engagement with mother	Standard preschool programme	Significantly longer joint engagement post-	Significant	↑ Favours intervention

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
	(generalization target)		intervention and at 12-month follow-up		
Landa 2010	Socially engaged imitation (proximal engagement marker)	Matched-intensity comparator	Significant treatment effect, $p = 0.02$; imitated acts paired with eye contact rose from 17% to 42%	Significant	↑ Favours intervention
Vote count	4 of 4 contributing trials significant, all favouring intervention				

Play skills and symbolic play diversity

Play is both a developmental prerequisite of symbolic language and the medium through which naturalistic interventions are delivered, and it therefore occupies an intermediate position in the outcome hierarchy. Three of five contributing trials demonstrated significant benefit. Consistent with the specificity principle demonstrated by the original three-arm dismantling trial, benefit accrued

to the domain that was explicitly targeted: children randomized to a symbolic play curriculum showed more diverse symbolic play, while children randomized to a joint attention curriculum showed greater joint attention, with limited crossover between targets.^{14,17,22,25}

Table 14. Domain O8 — Effect of early intervention on play skills and symbolic play diversity

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Kasari 2006	Structured Play Assessment: symbolic play types and play level	Existing EIP alone	Significant advantage for symbolic play arm on play diversity and play level, in assessment and in mother–child interaction	Significant	↑ Favours intervention
Kasari 2015 (JASPER)	Play diversity and highest play level achieved	Psychoeducational intervention (dose-controlled)	Significant secondary effects, small to moderate magnitude	Significant	↑ Favours intervention
Shire 2017 (JASPER)	Play skills in classroom setting	TAU waitlist	Significant gains maintained at follow-up	Significant	↑ Favours intervention

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Landa 2010	Play-related developmental outcomes	Matched-intensity comparator	Significant within-group time effect; between-group difference not significant	Not significant	↔ No difference
Freitag 2025 (A-FFIP)	Play and social communication component of BOSCC	Early intervention as usual	Adjusted ES -0.06 (-0.24 to 0.11)	Not significant	↔ No difference
Vote count	3 of 5 contributing trials significant				

Expressive language

Expressive language is the outcome that families most consistently prioritise, and the randomized evidence for it is materially weaker than for the proximal domains. Thirteen independent trials contributed data and six demonstrated a statistically significant effect, a vote count of slightly less than one half. Three features of the positive findings deserve emphasis. First, effect was concentrated in trials whose intervention explicitly and exclusively targeted spoken language production, namely the two Pivotal Response Treatment trials, rather than in trials targeting social communication broadly. Second, the multisite Early Start Denver Model replication demonstrated a significant pooled language advantage across three sites, but with a significant three-way interaction such that two sites showed an advantage and the third showed none — direct randomized evidence of site-level heterogeneity in implementation. Third, and most importantly for clinical targeting, the twelve-month follow-up of the three-arm dismantling trial demonstrated that among children commencing treatment with the lowest language levels, the joint attention intervention improved language outcome significantly more than either symbolic play or control, whereas no such advantage was evident in children with higher baseline language. This constitutes direct randomized support for hypothesis H4.^{13,22,25,31}

Table 15. Domain O9 — Effect of early intervention on expressive language

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Gengoux 2019 (PRT-P)	Functional utterances; parent-reported words used	Delayed treatment	d = 0.61; p = 0.026; parallel improvement on BOSCC and CGI-Improvement	Significant	↑ Favours intervention

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Hardan 2015 (PRTG)	Child utterance frequency	Psychoeducation group	d = 0.42; p = 0.038	Significant	↑ Favours intervention
Kasari 2008 (12-month follow-up)	Expressive language at 12 months post- intervention	Control	Significantly greater gains for both joint attention and symbolic play arms; largest advantage for joint attention in the lowest- language subgroup	Significant	↑ Favours intervention
Rogers 2019 (ESDM)	Language outcome, pooled across 3 sites	Community intervention	Significant pooled ESDM advantage; significant time × group × site interaction (2 of 3 sites positive)	Significant (pooled)	↑ Favours intervention
Whitehouse 2019	MCDI expressive vocabulary	TAU	Incidence rate ratio 2.31 (1.22 to 4.33)	Significant	↑ Favours intervention

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
(iBASIS-VIPP)	count (caregiver report)				
Aldred 2004	Expressive language (secondary outcome)	Routine care	Significant improvement reported	Significant	↑ Favours intervention
Green 2010 (PACT)	Directly assessed child language	TAU	Effects described as small; not significant	Not significant	↔ No difference
Pickles 2016 (PACT follow-up)	Expressive– receptive language composite at 5.75 years	TAU	ES 0.15 (–0.23 to 0.53)	Not significant	↔ No difference
Green 2022 (PACT-G)	Language composite	TAU	ES –0.03 (–0.15 to 0.10)	Not significant	↔ No difference
Whitehouse 2019 (iBASIS- VIPP)	MSEL expressive language (blinded examiner)	TAU	0.54 (–0.73 to 1.80)	Not significant	↔ No difference

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Whitehouse 2017 (TOBY)	Expressive language measures	TAU	No significant group difference at 3 or 6 months	Not significant	↔ No difference
Rogers 2012 (P-ESDM)	Child language outcomes	Community TAU	No effect of group assignment	Not significant	↔ No difference
Valeri 2019 (CPMT)	Parent-rated language abilities	Low-intensity psychosocial intervention	No additional benefit for language	Not significant	↔ No difference
Freitag 2025 (A-FFIP)	Language and cognitive secondary outcomes	Early intervention as usual	No improvement beyond comparator at 12 months	Not significant	↔ No difference
Landa 2010	Expressive language (secondary analysis)	Matched-intensity comparator	Significant time effect in both arms; between-group difference not significant	Not significant	↔ No difference
Vote count	6 of 13 contributing trials				

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
	significant, all favouring intervention				

Receptive language

Eight independent trials contributed receptive language data and four demonstrated significant benefit. A dissociation of considerable methodological importance emerges within this domain. In the Australian pre-emptive trial, caregiver-reported receptive vocabulary showed a large and unambiguously significant advantage of 37.17 words with a confidence interval well clear of the null, while researcher-administered receptive language on the Mullen Scales in the same children at the same visit showed no difference whatsoever. The identical pattern recurred in the tablet-based trial, where the only significant language finding was on a caregiver-completed vocabulary checklist. Two interpretations compete: caregiver report may be more ecologically sensitive, capturing functional comprehension in familiar routines that standardized testing cannot elicit; or caregiver report may be inflated by unblinded expectancy. The disaggregated risk-of-bias analysis in Table 8 indicates that the second explanation cannot be excluded, and receptive-language findings resting principally on caregiver report should therefore be regarded as low-certainty.^{18,21}

Table 16. Domain O10 — Effect of early intervention on receptive language

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Whitehouse 2019 (iBASIS-VIPP)	MCDI receptive vocabulary count (caregiver report)	TAU	Adjusted difference 37.17 words (10.59 to 63.75)	Significant	↑ Favours intervention

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Whitehouse 2017 (TOBY)	MCDI Total Words Understood (caregiver report)	TAU	Significant advantage at 6-month follow-up	Significant	↑ Favours intervention
Wetherby 2014 (ESI)	Examiner-administered receptive language	Group-ESI	Individual-ESI improved significantly; group-ESI showed no change	Significant	↑ Favours individual delivery
Rogers 2019 (ESDM)	Receptive component of language outcome	Community intervention	Significant pooled advantage across sites	Significant (pooled)	↑ Favours intervention
Whitehouse 2019 (iBASIS-VIPP)	MSEL receptive language (blinded examiner)	TAU	1.30 (−0.48 to 3.08)	Not significant	↔ No difference
Green 2010 (PACT)	Directly assessed receptive language	TAU	Small, non-significant effect	Not significant	↔ No difference

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Green 2022 (PACT-G)	Language composite (receptive and expressive)	TAU	ES -0.03 (-0.15 to 0.10)	Not significant	↔ No difference
Rogers 2012 (P-ESDM)	Receptive developmental outcomes	Community TAU	No group effect	Not significant	↔ No difference
Freitag 2025 (A-FFIP)	Language secondary outcomes	Early intervention as usual	No improvement beyond comparator	Not significant	↔ No difference
Vote count	4 of 8 contributing trials significant; 2 of the 4 rest on caregiver report alone				

Adaptive communication and socialization

Ten trials contributed data on everyday adaptive communication and socialization, and five demonstrated significant benefit. Both Pivotal Response Treatment trials, whose interventions were the most explicitly language-focused, produced significant gains on the Vineland communication domain, and the Australian pre-emptive trial produced a significant advantage on Vineland functional language use. Conversely, trials employing masked teacher report as the adaptive outcome — the most methodologically stringent operationalization available, since the teacher is neither the intervention agent nor the trained party — were consistently null or only marginally positive. In the

PACT cohort this teacher-reported outcome reached only a near-significant total effect at six-year follow-up despite a clearly significant effect on symptom severity in the same children, indicating that translation of communicative gain into independently observed everyday functioning is incomplete.^{21,27,30,31}

Table 17. Domain O11 — Effect of early intervention on adaptive communication and socialization

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Hardan 2015 (PRTG)	Vineland-II adaptive communication	Psychoeducation group	Significantly greater improvement in functional and adaptive communication	Significant	↑ Favours intervention
Whitehouse 2019 (iBASIS-VIPP)	VABS functional language use	TAU	Difference estimate 6.43 (1.06 to 11.81)	Significant	↑ Favours intervention
Wetherby 2014 (ESI)	Parent-reported communication, daily living and social skills	Group-ESI	Individual-ESI improved or remained stable; group-ESI worsened or did not change	Significant	↑ Favours individual delivery

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Dawson 2010 (ESDM)	Vineland adaptive behaviour composite	Community intervention	ESDM maintained rate of growth against normative sample; comparator showed increasing delay	Significant	↑ Favours intervention
Gengoux 2019 (PRT-P)	Parent-reported number of words used; CGI-Improvement	Delayed treatment	Significant improvement on both	Significant	↑ Favours intervention
Green 2022 (PACT-G)	Adaptive behaviour composite	TAU	ES 0.01 (−0.15 to 0.18)	Not significant	↔ No difference
Aldred 2004	Vineland communication sub-domain	Routine care	Suggestive but non-significant	Not significant	↔ Trend favouring intervention
Green 2010 (PACT)	Adaptive functioning in	TAU	Small effect	Not significant	↔ No difference

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
	school (teacher-reported)				
Whitehouse 2017 (TOBY)	Adaptive function measures	TAU	Statistical trend only; magnitude decreased from 3 to 6 months	Not significant	↔ Trend favouring intervention
Rogers 2019 (ESDM)	Adaptive behaviour	Community intervention	No significant difference	Not significant	↔ No difference
Vote count	5 of 10 contributing trials significant, all favouring intervention				

Non-verbal cognitive ability and developmental quotient

Seven trials contributed cognitive outcomes and two demonstrated significant benefit. The single most striking result in this domain remains the original Early Start Denver Model trial, in which the intervention group gained on average 17.6 standard score points over two years against 7.0 points in the community comparison group — a differential of more than two thirds of a population standard deviation. This finding has not, however, been cleanly replicated: the multisite replication of the same intervention found no significant difference in developmental quotient, and the low-intensity parent-delivered adaptation found no cognitive effect at all. The most parsimonious reconciliation is that cognitive gain in this population is a function of cumulative intervention dose rather than of

intervention model, a proposition supported by the observation within the parent-delivered trial that, across the sample as a whole irrespective of allocation, both younger age at commencement and greater number of intervention hours were positively related to degree of improvement.^{7,10,18,20,25}

Table 18. Domain O12 — Effect of early intervention on non-verbal cognitive ability and developmental quotient

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
Dawson 2010 (ESDM)	Mullen-derived IQ, 24 months	Community intervention	Mean gain 17.6 standard score points vs 7.0 points in comparator (1 SD = 15 points)	Significant	↑ Favours intervention
Whitehouse 2017 (TOBY)	MSEL Visual Reception and Fine Motor subscales	TAU	Significant advantage at 6-month follow-up	Significant	↑ Favours intervention
Rogers 2019 (ESDM)	Developmental quotient	Community intervention	No significant difference	Not significant	↔ No difference
Rogers 2012 (P-ESDM)	Child developmental outcomes	Community TAU	No effect of group assignment	Not significant	↔ No difference
Whitehouse 2019 (iBASIS-VIPP)	MSEL visual reception; fine motor	TAU	Visual reception 0.31 (−0.77 to 1.40); fine motor	Not significant	↔ No difference

Trial	Instrument	Comparator	Effect estimate / result	Significance	Direction
			0.55 (−0.32 to 1.41)		
Freitag 2025 (A-FFIP)	Cognitive secondary outcomes	Early intervention as usual	No improvement beyond comparator	Not significant	↔ No difference
Landa 2010	Non-verbal cognition (secondary analysis)	Matched-intensity comparator	Significant time effect; no between-group difference	Not significant	↔ No difference
Vote count	2 of 7 contributing trials significant				

Blinded autism symptom severity

Ten independent trials contributed blinded, independently rated measures of core autism symptom severity, and five demonstrated a significant effect. This domain is the crux of the interpretive problem addressed by the review. The two largest and most recent trials were entirely null: the generalized PACT trial reported an effect size of 0.04 with a p-value of 0.74 in 248 children, and the German A-FFIP trial an adjusted effect size of −0.06 in 134 children. Yet in both, the proximal dyadic outcomes were significantly improved, and in the former, formal mediation analysis demonstrated that change in child dyadic communication significantly mediated symptom change on the Brief Observation of Social Communication Change in the home context, even though no such effect was detectable on the Autism Diagnostic Observation Schedule. The most important positive finding in the domain comes not from any single endpoint but from repeated-measures analysis across the whole trial and follow-up period: in the PACT cohort, symptom severity was significantly reduced

with an effect size of 0.55 and a p-value of 0.004 when estimated over the entire six-year course, despite each individual time point yielding confidence intervals that included or approached the null. Early intervention therefore appears to exert a small, cumulative, temporally distributed effect on core symptoms that single-timepoint analyses are systematically underpowered to detect.^{1,2,18,19,25,32}

Table 19. Domain O13 — Effect of early intervention on blinded autism symptom severity

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
Pickles 2016 (PACT follow-up)	ADOS calibrated severity score, whole trial and follow-up course	TAU	ES 0.55 (0.14 to 0.91); p = 0.004 (log-odds metric)	Significant	↑ Favours intervention
Pickles 2016 (PACT follow-up)	ADOS CSS at treatment endpoint	TAU	ES 0.64 (0.07 to 1.20) (log-odds metric)	Significant	↑ Favours intervention
Green 2017 (iBASIS-VIPP)	AOSI / ADOS-2 prodromal severity across 4 time points	No intervention	ES 0.32 (0.04 to 0.60); p = 0.026	Significant	↑ Favours intervention
Valeri 2019 (CPMT)	ADOS-G social communication algorithm (blinded)	Low-intensity psychosocial intervention	Significant additional benefit on primary blinded outcome and on symptom severity	Significant	↑ Favours intervention

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
Aldred 2004	ADOS total score (primary outcome)	Routine care	Significant improvement, particularly reciprocal social interaction	Significant	↑ Favours intervention
Dawson 2010 (ESDM)	Diagnostic category change	Community intervention	Significantly more likely to shift from autism to PDD-NOS	Significant	↑ Favours intervention
Green 2010 (PACT)	ADOS-G social communication algorithm at 13 months	TAU	ES -0.24 (-0.59 to 0.11)	Not significant	↔ No difference
Green 2022 (PACT-G)	ADOS-2 severity at 12 months	TAU	ES 0.04 (-0.19 to 0.26); p = 0.74	Not significant	↔ No difference
Green 2022 (PACT-G)	BOSCC, researcher-assessed	TAU	ES 0.03 (-0.25 to 0.31)	Not significant	↔ No difference
Freitag 2025 (A-FFIP)	BOSCC total score at 12 months (primary)	Early intervention as usual	Adjusted ES -0.06 (-0.24 to 0.11)	Not significant	↔ No difference

Trial	Instrument	Comparator	Effect estimate (95% CI)	Significance	Direction
Whitehouse 2019 (iBASIS- VIPP)	AOSI at 6 months (primary)	TAU	-0.74 (-2.47 to 0.98)	Not significant	↔ No difference
Whitehouse 2017 (TOBY)	Autism Treatment Evaluation Checklist (primary)	TAU	No group difference at 3 or 6 months	Not significant	↔ No difference
Rogers 2019 (ESDM)	Autism symptom severity	Community intervention	No significant difference	Not significant	↔ No difference
Vote count	5 of 10 contributing trials significant, all favouring intervention				

Maintenance, caregiver outcomes and adverse events

All seven trials reporting a post-treatment follow-up assessment demonstrated maintenance of at least one proximal communication gain beyond the cessation of active intervention, with follow-up intervals ranging from one month to a median of 5.75 years. This is a strong and consistent pattern that supports hypothesis H6 and materially strengthens the clinical case for early intervention, since a transient effect confined to the treatment period would be of limited developmental value. Caregiver-level outcomes were significantly improved in four of five contributing trials, though not

always in the arm expected: in the JASPER trial the reduction in parenting stress accrued to the psychoeducational comparator rather than to the coaching intervention, a finding of direct relevance to service design, since it suggests that the caregiver-support and the child-outcome functions of early intervention programmes may be partly dissociable and may require separate programme components. Adverse event surveillance was reported in only four trials, and where reported, event rates were closely comparable between arms; the two unfavourable directional signals identified anywhere in the review — reduced mutual shared attention in the South Asian trial and reduced infant positive affect in the Australian pre-emptive trial — are most plausibly measurement-compositional rather than iatrogenic, but they were reported transparently by the investigators and are reproduced here in the same spirit.^{2,12,14,16,17,18,19,21,22,25}

Table 20. Domains O14 to O16 — Maintenance of effect, caregiver-level outcomes and adverse events

Domain	Trial	Endpoint and interval	Result	Direction
O14 Maintenance	Pickles 2016 (PACT)	ADOS CSS and DCMA initiation at median 5.75 years after endpoint	Symptom reduction and initiation gain sustained over whole course (ES 0.55 and 0.33, both $p = 0.004$)	↑ Maintained
O14 Maintenance	Green 2017 (iBASIS-VIPP)	Prodromal severity to 39 months, 24 months after intervention end	Treatment effect extended 24 months beyond intervention end (ES 0.32)	↑ Maintained
O14 Maintenance	Kaale 2014	Joint attention and joint engagement at 12 months	Significantly larger improvement retained in intervention arm	↑ Maintained

Domain	Trial	Endpoint and interval	Result	Direction
O14 Maintenance	Kasari 2015 (JASPER)	Joint engagement at 6 months post-intervention	Large effect maintained	↑ Maintained
O14 Maintenance	Kasari 2008	Expressive language at 12 months post-intervention	Gains retained and amplified in lowest-language subgroup	↑ Maintained
O14 Maintenance	Shire 2017 (JASPER)	Core developmental outcomes at 1-month follow-up	Gains maintained	↑ Maintained
O14 Maintenance	Landa 2010	Socially engaged imitation at 6-month follow-up	Generalized to unfamiliar contexts and maintained	↑ Maintained
O15 Caregiver	Green 2022 (PACT-G)	Parental wellbeing composite at 12 months	ES 0.44 (0.08 to 0.79)	↑ Favours intervention
O15 Caregiver	Valeri 2019 (CPMT)	Parenting stress related to dysfunctional interaction	Significant reduction	↑ Favours intervention
O15 Caregiver	Kasari 2015 (JASPER)	Parenting stress associated with	Significant reduction in the psychoeducational comparator arm	↓ Favours comparator

Domain	Trial	Endpoint and interval	Result	Direction
		child characteristics		
O15 Caregiver	Rogers 2012 (P-ESDM)	Therapeutic working alliance	Significantly stronger alliance in P-ESDM arm	↑ Favours intervention
O15 Caregiver	Whitehouse 2019 (iBASIS-VIPP)	Parenting Sense of Competence: satisfaction, interest, efficacy	All three non-significant (0.21, -0.23, -0.08)	↔ No difference
O16 Adverse events	Green 2022 (PACT-G)	Adverse events on child behaviour and wellbeing	11 of 122 (9%) intervention vs 13 of 127 (10%) comparator; 1 serious adverse event on parental mental health, possibly study-related	↔ Comparable
O16 Adverse events	Freitag 2025 (A-FFIP)	Adverse events over 12 months	Comparable between groups	↔ Comparable
O16 Adverse events	Rahman 2016 (PASS)	Time in mutual shared attention	Significant reduction, ES -0.70 (-1.16 to -0.23)	↓ Unfavourable signal
O16 Adverse events	Whitehouse 2019 (iBASIS-VIPP)	MACI infant positive affect	Significant reduction, -0.69 (-1.27 to -0.10)	↓ Unfavourable signal

Summary of Synthesis across All Outcome Domains

The aggregate pattern of results across the sixteen pre-specified outcome domains is presented in Table 23. Arranged in the pre-specified proximal-to-distal order, the vote-count proportions decline in an approximately monotonic fashion, from 100% of contributing trials significant for joint engagement and for spontaneous communicative utterances, through 75% for child communication initiation and 80% for initiation of joint attention, to 46% for expressive language, 50% for receptive language, 50% for blinded symptom severity and 29% for non-verbal cognition. This gradient constitutes direct empirical support for hypothesis H2 and represents the central quantitative finding of the review.^{4,6}

Table 21. Vote-count summary across all sixteen pre-specified outcome domains, arranged in proximal-to-distal order

Code	Outcome domain	Trials contributing	Significant, favouring intervention	Proportion	Range of reported effect sizes
O1	Caregiver synchronous responsiveness	6	4	67%	0.33 to 1.61
O2	Child communication initiation in the dyad	8	6	75%	0.20 to 0.99
O3	Shared attention and mutual engagement	3	0	0%	-0.70 to 0.33
O4	Spontaneous and functional utterances	3	3	100%	d = 0.42 to 0.61
O5	Initiation of joint attention / social communication composite	5	4	80%	Not uniformly reported numerically

Code	Outcome domain	Trials contributing	Significant, favouring intervention	Proportion	Range of reported effect sizes
O6	Responding to joint attention, gesture, affect sharing	3	1	33%	Not uniformly reported numerically
O7	Joint engagement	4	4	100%	Cohen f^2 = 0.69 (largest)
O8	Play skills and symbolic play diversity	5	3	60%	Small to moderate
O9	Expressive language	13	6	46%	d = 0.42 to 0.61; IRR 2.31
O10	Receptive language	8	4	50%	Up to 37.17 words (caregiver report)
O11	Adaptive communication and socialization	10	5	50%	0.01 to 6.43 (mixed metrics)
O12	Non-verbal cognitive ability	7	2	29%	Up to 10.6 IQ points differential
O13	Blinded autism symptom severity	10	5	50%	-0.24 to 0.64 (mixed metrics)

Code	Outcome domain	Trials contributing	Significant, favouring intervention	Proportion	Range of reported effect sizes
O14	Maintenance and generalization	7	7	100%	1 month to 5.75 years
O15	Caregiver-level outcomes	5	4	80%	0.44 (wellbeing composite)
O16	Adverse events and harms	4	Not applicable	Comparable between arms in all 4	9% vs 10% (largest trial)

Proportion denotes the number of contributing trials reporting a statistically significant between-group difference favouring intervention, divided by the number of contributing trials. Effect sizes are reported in the metric used by the original trial and are not directly comparable across domains. IRR = incidence rate ratio.

Certainty of Evidence

GRADE appraisal of each outcome domain is presented in Table 24. Certainty was moderate for six domains — caregiver synchronous responsiveness, child communication initiation, spontaneous communicative utterances, initiation of joint attention, joint engagement and maintenance of effect — in every case downgraded by one level from high, principally for residual risk of bias arising from the structural impossibility of participant blinding and from incomplete pre-specification in the earlier trials. Certainty was low for eight domains and very low for one. No domain retained high certainty. The asymmetry of certainty across the proximal-to-distal hierarchy mirrors the asymmetry of effect and is a direct consequence of it: the domains in which effects are consistent are also the domains in which the evidence is least heterogeneous and least dependent on unblinded report.^{5,6}

Table 22. GRADE summary of findings: certainty of the evidence by outcome domain

Outcome domain	Trials (participants)	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
O1 Caregiver synchronous responsiveness	6 (720)	Serious	Not serious	Not serious	Not serious	⊕⊕⊕⊖ Moderate
O2 Child communication initiation	8 (748)	Serious	Not serious	Not serious	Not serious	⊕⊕⊕⊖ Moderate
O3 Shared attention and mutual engagement	3 (320)	Serious	Serious	Serious	Serious	⊕⊖⊖⊖ Very low
O4 Spontaneous and functional utterances	3 (129)	Not serious	Not serious	Not serious	Serious	⊕⊕⊕⊖ Moderate
O5 Initiation of joint attention	5 (364)	Serious	Not serious	Not serious	Not serious	⊕⊕⊕⊖ Moderate
O6 Responding to joint attention and gesture	3 (211)	Serious	Serious	Not serious	Serious	⊕⊖⊖⊖ Very low
O7 Joint engagement	4 (310)	Serious	Not serious	Not serious	Not serious	⊕⊕⊕⊖ Moderate

Outcome domain	Trials (participants)	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
O8 Play skills and symbolic play diversity	5 (441)	Serious	Serious	Not serious	Not serious	⊕⊕⊖⊖ Low
O9 Expressive language	13 (1,204)	Serious	Serious	Not serious	Not serious	⊕⊕⊖⊖ Low
O10 Receptive language	8 (1,015)	Serious	Serious	Serious	Not serious	⊕⊖⊖⊖ Very low
O11 Adaptive communication and socialization	10 (960)	Serious	Serious	Not serious	Not serious	⊕⊕⊖⊖ Low
O12 Non-verbal cognitive ability	7 (631)	Serious	Serious	Not serious	Serious	⊕⊖⊖⊖ Very low
O13 Blinded autism symptom severity	10 (999)	Not serious	Serious	Not serious	Not serious	⊕⊕⊖⊖ Low
O14 Maintenance and generalization	7 (574)	Serious	Not serious	Not serious	Not serious	⊕⊕⊕⊖ Moderate

Outcome domain	Trials (participants)	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
O15 Caregiver-level outcomes	5 (569)	Serious	Serious	Not serious	Not serious	⊕⊕⊖⊖ Low
O16 Adverse events and harms	4 (550)	Serious	Not serious	Serious	Serious	⊕⊖⊖⊖ Very low

All domains commenced at high certainty by virtue of randomized design. Downgrading for risk of bias reflects the structural impossibility of participant and provider blinding, together with incomplete pre-specification in trials published before prospective registration became normative. Downgrading for indirectness in domains O10 and O16 reflects reliance on unblinded caregiver report and on incomplete adverse-event surveillance respectively. ⊕⊕⊕⊕ high; ⊕⊕⊕⊖ moderate; ⊕⊕⊖⊖ low; ⊕⊖⊖⊖ very low.

DISCUSSION

Summary of Principal Findings

This systematic review of twenty randomized controlled trials comprising 1,713 children establishes four principal findings. First, early intervention reliably and substantially modifies caregiver communicative behaviour, with effect sizes of a magnitude rarely encountered in psychosocial paediatric research, reaching 1.61 in a low-resource setting with delivery by non-specialist health workers. Second, this change in the caregiver is accompanied by a consistent, replicated and moderately certain increase in the child's own rate of communicative initiation, demonstrated in six of eight contributing trials across five countries and four independent research groups. Third, treatment effect attenuates monotonically as measurement moves outward from the intervention context, so that fewer than half the contributing trials demonstrate significant effects on standardized expressive language, receptive language, blinded symptom severity or non-verbal

cognition. Fourth, wherever a follow-up assessment was conducted, proximal communication gains were maintained after cessation of active intervention, in one instance for almost six years.^{1,2,12,16,19,27}

These findings permit direct adjudication of the six a priori hypotheses. H1, that early intervention significantly improves child communicative initiation, is supported with moderate certainty. H2, the monotonic attenuation hypothesis, is supported by the vote-count gradient presented in Table 23. H3, that effects on caregiver behaviour exceed effects on child behaviour, is strongly supported: in the two trials reporting both, the caregiver effect size exceeded the child effect size by factors of approximately three and six respectively. H4, that language benefit is concentrated in children with the lowest baseline language, is supported by direct randomized subgroup evidence. H5, that intervention intensity is not linearly related to communication outcome, is supported: twelve caregiver coaching sessions produced an effect size of 1.61 on caregiver synchrony and 0.99 on child initiation, while more than one thousand cumulative hours of one-to-one therapy produced no detectable advantage on autism symptom severity or adaptive behaviour. H6, that gains are maintained beyond the treatment period, is supported by all seven contributing trials.^{1,2,12,17,20,22}

The Proximal-to-Distal Attenuation Gradient and Its Mechanism

The dominant structural feature of this evidence base is not the presence or absence of effect but its systematic decay along the measurement hierarchy. The randomized evidence is sufficient to specify the causal chain with unusual precision. Coaching changes caregiver synchrony; this is the largest and most certain effect in the review. Changed caregiver synchrony increases child communicative initiation; formal mediation analysis of the PACT cohort demonstrated that the treatment effect on the primary symptom endpoint was substantially mediated by parental synchrony and child initiations in series. Increased child initiation produces, over years rather than months, measurable reduction in core symptom severity; mediation analysis of the six-year follow-up demonstrated that increased child initiation at treatment midpoint accounted for 73% of the treatment effect on symptom severity at a mean age of 10.5 years. In an independent JASPER cohort, joint engagement mediated 69% of the intervention effect on initiation of joint attention, which in turn predicted subsequent gains in standardized language. Three independent mediation analyses, in three separate cohorts, converge on the same causal architecture.^{2,26,27,28}

Four non-exclusive explanations account for the attenuation observed distally. The first is generalization failure. The generalized PACT trial was designed explicitly to overcome this by delivering therapy in both home and education settings, yet it improved synchrony in both the parent and the learning support assistant, improved child communication with both partners, and still produced no effect on the blinded primary endpoint. Generalization failure is therefore not simply a matter of insufficient contextual coverage; it appears intrinsic to the relationship between dyadic communicative competence and decontextualized standardized assessment. The second is instrument insensitivity. The Autism Diagnostic Observation Schedule was designed as a diagnostic instrument, not as a change-sensitive outcome measure, and direct psychometric comparison within the PACT cohort demonstrated that even the purpose-built Brief Observation of Social Communication Change was not more sensitive than the Autism Diagnostic Observation Schedule among children with single or no words; both detected only small non-significant effects at item level in that subgroup. Applying a diagnostic instrument as a treatment endpoint imposes a low ceiling on detectable change. The third is comparator inflation. In 2004 the comparator was unstructured routine care; by 2025 the comparator was manualised early intervention as usual delivered within a well-resourced national system. As the counterfactual improves, the incremental effect necessarily contracts, and a null result against an active comparator is not equivalent to absence of efficacy. The fourth is treatment-effect heterogeneity. The randomized subgroup evidence indicates that baseline non-verbal ability is a robust prognostic indicator and that baseline language level moderates the language response, such that averaging across a heterogeneous sample dilutes a real effect concentrated in an identifiable subgroup.^{1,18,19,20,25,40,41}

Intensity, Dose and Agent of Delivery

The randomized evidence does not support a simple dose–response relationship for communication outcomes. The most direct test available is a randomized comparison of 15 against 25 hours per week of one-to-one intervention delivered in two treatment styles, which found neither main effect of intensity nor main effect of style on autism symptom severity, expressive communication, receptive language or non-verbal ability, and only very limited evidence that baseline severity predicted differential response to the higher dose. Set against this, the parent-delivered

ESDM trial found, in a within-sample analysis across both arms, that greater number of intervention hours was positively related to improvement — but that analysis is observational within a randomized trial and is confounded by indication, since families obtaining more hours differ systematically from those who do not. The defensible synthesis is that dose is unlikely to be the principal determinant of communication outcome within the ranges studied, and that the marginal return on intensity above approximately fifteen hours per week is not demonstrable in randomized data.^{10,20,51}

Agent of delivery is correspondingly more informative than dose. Interventions delivered by parents, by preschool teachers, by teaching assistants and by non-specialist community health workers all produced significant proximal communication effects. The Norwegian trial demonstrated that ordinary preschool teachers receiving weekly supervision could produce joint attention gains that generalized to interaction with untrained mothers. The community JASPER trial demonstrated that supervised teaching assistants in low-resource neighbourhood classrooms achieved adequate fidelity and significant child gains. The South Asian trial demonstrated that non-specialist health workers in Goa and Rawalpindi reproduced, and in the case of parental synchrony exceeded, the proximal effects obtained by specialist therapists in the original United Kingdom trial. Taken together, these findings constitute a strong randomized case that specialist delivery is not a prerequisite for proximal communicative benefit — the single most consequential finding of this review for health systems in which specialist capacity is the binding constraint.^{12,14,17}

Evidence from adjacent randomized populations

Randomized evidence from populations adjacent to the age window of this review is concordant with, and extends, the present findings. In minimally verbal school-aged children, a sequential multiple-assignment randomized trial demonstrated that augmenting a blended naturalistic developmental and behavioural intervention with a speech-generating device produced superior gains in spontaneous communicative utterances, novel words and comments relative to spoken-word intervention alone, and longitudinal reanalysis confirmed the superiority of the adaptive sequence commencing with the device. A subsequent community-based adaptive trial in the same population found no difference between naturalistic and discrete-trial starting points, with modest differences among the eight candidate adaptive sequences. A randomized comparison of Pivotal Response

Training against the Picture Exchange Communication System in minimally verbal pre-schoolers found comparable spoken-language acquisition in both arms, with 78% of children acquiring more than ten functional words. Randomized evidence in older children and adolescents indicates that Pivotal Response Treatment continues to improve parent-rated social-communicative skills beyond the pre-school period, and that robot-assisted delivery may confer additional benefit that becomes apparent only at follow-up rather than immediately post-treatment — a further illustration of the importance of extended assessment windows.^{37,38,39,40,47,50}

Trials of classroom and teacher-delivered models reinforce the conclusion that agent of delivery is flexible: preschool teaching staff randomized to implement JASPER within their own daily programmes improved children's joint engagement, joint attention gestures, language and play, and both a teacher-implemented joint attention intervention and a teacher-mediated play and joint attention programme produced significant classroom-level gains in independent pilot randomized trials. Randomized work in infants showing very early signs and in caregiver-mediated hybrid models has produced more equivocal child-level results: a blended caregiver-mediated intervention combining enhanced milieu teaching with JASPER significantly changed caregiver strategy use without producing significant child outcomes, and a brief multi-component intervention incorporating a speech-generating device improved joint attention immediately and social communication four months later. Automated acoustic analysis of daylong home recordings has provided detection-bias-resistant confirmation that Pivotal Response Treatment increases vocal reciprocity, and randomized telehealth trials of functional communication training and of parent coaching in the Early Start Denver Model demonstrate that remote delivery is feasible and can improve caregiver fidelity, although child-level effects remain to be established. Several adequately powered trials now in progress, including a Danish national pragmatic trial of Paediatric Autism Communication Therapy and a French videoconferencing adaptation, are expected to address precisely the endpoint-selection and scalability questions identified in this review.^{15,33,34,35,36,42,43,44,45,46,48,49,52}

Implications for Endpoint Selection in Future Trials

A recurrent structural error in this literature is the designation of an omnibus diagnostic symptom instrument as the primary endpoint of an intervention whose theoretical model targets dyadic communication. Of the ten trials contributing blinded symptom severity data, five were null, and in at least three of those the proximal communication endpoints were unambiguously positive. A trial that changes what it intends to change, and is then declared negative because a diagnostic instrument insensitive to that change did not move, has been misclassified rather than refuted. The randomized evidence supports a reordering of endpoint hierarchy in which directly coded child communicative initiation within adult–child interaction serves as the primary endpoint, with symptom severity retained as a secondary endpoint assessed by repeated measures across an extended follow-up rather than at a single post-treatment timepoint. The PACT programme provides the empirical warrant for this recommendation: the same trial that was reported as failing to justify its intervention on the basis of a single 13-month endpoint was subsequently shown, by repeated-measures analysis across six years, to have produced significant and sustained symptom reduction.^{1,2,18,19,40}

Clinical Implications, with Particular Reference to Resource-Constrained Settings

Four clinical recommendations follow from this synthesis. First, parent-mediated, naturalistic developmental behavioural intervention should be initiated at the point of diagnostic suspicion rather than deferred until categorical diagnosis is confirmed; two randomized trials enrolled infants aged 9 to 14 months on the basis of prodromal signs alone and demonstrated significant effects on caregiver and child communicative behaviour, with one demonstrating a treatment effect extending 24 months beyond the end of intervention. Second, families should be counselled with precision rather than optimism: the evidence supports a confident expectation of improved communicative reciprocity within the caregiver–child dyad, a realistic expectation of modest gains in functional expressive language particularly in minimally verbal children, and an explicit acknowledgement that improvement in standardized cognitive scores or resolution of the diagnosis are not outcomes that randomized evidence supports promising. Third, outcome monitoring in routine clinical practice should be anchored on observable dyadic communication rather than on symptom-severity scales, both because dyadic measures are more sensitive to genuine change and because they are more directly modifiable by the family. Fourth, and most importantly for Indonesian and comparable

settings, service models should be built around task-shifted, low-intensity, caregiver-mediated delivery: the randomized evidence indicates that twelve sessions delivered by trained non-specialist workers reproduce the proximal effects of specialist therapy, and this is the only model with a randomized evidence base that is scalable to the affected population in a middle-income health system.^{12,16,21,31}

Comparison with Previous Syntheses

The present findings are broadly compatible with, but substantially more informative than, previous quantitative syntheses. A meta-analysis of nineteen randomized trials of parent-mediated intervention reported weighted effect sizes ranging from 0.18 for communication–language to 0.27 for socialization, averaging 0.23 across domains, with moderate quality of evidence for symptom severity and communication and very low quality for socialization. A more recent meta-analysis restricted to parent-mediated play-based intervention reported larger pooled effects of 0.63 for social communication, 0.40 for language and –0.19 for autistic characteristics. The apparent discrepancy between these two syntheses is precisely what the present disaggregated approach resolves: the higher estimates derive from analyses weighted toward proximal, play-embedded, frequently caregiver-rated social communication outcomes, and the lower estimates from analyses weighted toward distal, standardized, blindly assessed outcomes. Both are correct within their respective measurement frames. The clinical error lies in transferring an effect size derived from one frame to a prognostic statement belonging to the other.^{23,24,29}

Strengths of the Review

This review has several methodological strengths. Inclusion was restricted to randomized controlled trials with a mean enrolment age at or below the pre-school threshold, eliminating the design heterogeneity that has limited previous syntheses. The outcome architecture was pre-specified as a proximal-to-distal hierarchy of sixteen domains rather than as a set of broad composites, converting measurement heterogeneity into an analytic object rather than a source of noise. Risk of bias was assessed at the level of the endpoint class as well as the trial, permitting the structurally different vulnerability of blinded observational and unblinded caregiver-reported endpoints to be represented explicitly. The evidence base is current to 2025 and incorporates two large contemporary

trials with null primary endpoints whose omission would have produced a systematically optimistic synthesis. Finally, every included trial and every supporting citation is accompanied by a permanent, verifiable academic database link, permitting complete independent audit.^{4,5,6}

Recommendations for Future Research

Future trials in this field should adopt directly coded child communicative initiation as the primary endpoint, retain blinded symptom severity as a repeated-measures secondary endpoint assessed over an extended follow-up, and pre-specify the analysis of baseline non-verbal ability and baseline language level as effect modifiers rather than reporting them as post hoc subgroup findings. Sequential multiple-assignment randomized designs offer a particularly appropriate architecture for a condition in which early treatment response is heterogeneous and adaptive re-randomization is clinically realistic. Above all, adequately powered randomized trials of culturally adapted, task-shifted, caregiver-mediated intervention are required in Southeast Asian settings, including Indonesia, where the burden of unmet need is greatest and the applicability of the existing evidence base is least established.^{12,20,41,47}

CONCLUSION AND RECOMMENDATIONS

Conclusion

On the basis of twenty randomized controlled trials comprising 1,713 children, early intervention produces consistent, replicated and moderately certain improvement in the proximal architecture of communication in children with autism spectrum disorder. Caregiver synchronous responsiveness improved significantly in four of six contributing trials with effect sizes as large as 1.61; child communicative initiation within the caregiver–child dyad improved significantly in six of eight trials; initiation of joint attention improved in four of five; joint engagement improved in all four trials measuring it; and spontaneous functional utterances improved in all three trials designating them as an endpoint. Every trial reporting a post-treatment follow-up demonstrated maintenance of at least one communicative gain, in one case for almost six years.^{1,2,12,14,16,17,19}

Effects on distal, standardized and decontextualized outcomes are materially weaker and of lower certainty. Expressive language improved significantly in six of thirteen trials, receptive language in four of eight, adaptive communication in five of ten, blinded autism symptom severity in

five of ten, and non-verbal cognitive ability in only two of seven. Omnibus blinded symptom-severity instruments are demonstrably insensitive to the communicative change that these interventions produce and should not be regarded as the appropriate primary endpoint for communication-focused early intervention. The apparently disappointing results of the two largest contemporary trials are more accurately interpreted as a failure of endpoint selection and an artefact of increasingly active comparator conditions than as evidence that early intervention is ineffective.^{18,19,20,25,40}

Neither treatment intensity nor specialist delivery emerges as a necessary condition for proximal communicative benefit. Twelve sessions of parent-mediated therapy delivered by non-specialist community health workers reproduced, and on caregiver synchrony exceeded, the effects obtained by specialist therapists in high-income settings. This finding provides the principal evidentiary basis for scalable early-intervention service models in middle-income health systems.^{12,51}

Recommendations

Recommendations for clinical practice

1. Initiate structured, caregiver-mediated, naturalistic developmental behavioural intervention at the point of diagnostic suspicion, without waiting for confirmation of a categorical diagnosis, since randomized evidence supports pre-emptive intervention from 9 to 14 months of age.^{16,21}
2. Prioritise parent-mediated models as first-line management. They carry the most consistent randomized evidence for communication outcomes, impose the least burden on specialist capacity, and are the only models demonstrated to be transportable to non-specialist delivery.^{1,12,14}
3. Counsel families with calibrated precision. Improvement in communicative reciprocity within the dyad may be predicted with reasonable confidence; modest gains in functional expressive language, particularly in minimally verbal children, are a realistic expectation; normalisation of cognitive scores or remission of diagnosis should not be presented as expected outcomes.^{7,20,22}
4. Anchor routine clinical outcome monitoring on directly observed dyadic communication — the frequency of child-initiated communicative acts toward the caregiver — rather than on periodic symptom-severity rating alone.^{2,19,27}

5. Assess and document baseline non-verbal ability and baseline language level in every child commencing intervention, since both are established modifiers of treatment response and are necessary for realistic individual prognostication.^{20,22,41}

6. Do not escalate intervention intensity beyond approximately fifteen hours per week on the expectation of proportionate communicative gain, as randomized evidence does not demonstrate incremental benefit above this range.⁵¹

Recommendations for service organization and health policy

7. Develop task-shifted early-intervention services in which trained non-specialist workers deliver manualised caregiver coaching under periodic specialist supervision, reserving specialist time for diagnosis, supervision and complex cases. This model has direct randomized support from a bi-national South Asian trial and is the only configuration capable of reaching the affected paediatric population in Indonesia at scale.^{12,17}

8. Integrate structured caregiver support and psychoeducation as a distinct programme component rather than assuming it is subsumed by caregiver coaching, since randomized evidence indicates that reduction in parenting stress and improvement in child communication may be produced by different intervention components.^{14,18}

Recommendations for research

9. Adopt directly coded child communicative initiation as the primary trial endpoint, with blinded symptom severity retained as a repeated-measures secondary endpoint over extended follow-up.^{2,19,40}

10. Conduct adequately powered randomized trials of culturally adapted, task-shifted caregiver-mediated intervention in Indonesia and the wider Southeast Asian region, with pre-specified analysis of baseline non-verbal ability and language level as effect modifiers.^{12,41}

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