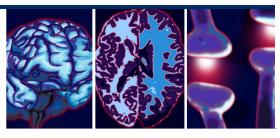
REVIEW

Early comprehensive behaviorally based interventions for children with autism spectrum disorders:



a summary of findings from recent reviews and meta-analyses

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Practice points

- Evidence from recently published meta-analyses, systematic reviews and empirical studies supports previous conclusions that, for children with autism spectrum disorders, early intensive comprehensive interventions, largely based on applied behavior analysis principles, are generally more effective in improving cognitive, language and, to some extent, adaptive behavior skills than standard care or 'eclectic' interventions.
- There is growing evidence for the effectiveness of other early comprehensive programs, such as the Early Start Denver Model, a developmental/behavioral and relationship-based approach, and Learning Experiences and Alternative Program for Preschoolers and their Parents, an incidental teaching approach implemented in school settings.
- There are currently no published comparative studies of the relative effectiveness of different empirically based interventions of equivalent quality and intensity.
- Very few studies have investigated the long-term effectiveness (e.g., after >4 years) of any of the early comprehensive interventions discussed in this paper and there are no follow-up studies in adulthood. Thus, it is currently unknown whether early comprehensive interventions do in fact result in a significantly reduced need for special services in adulthood and there is currently no evidence to support such claims.
- Within and across all early comprehensive interventions, large individual differences are reported and much more research is needed into child, family and intervention factors that moderate treatment progress and outcomes.
- There is great variability in the access to and the quality of early comprehensive provisions as currently implemented and this needs to be considered when making decisions regarding specialist educational programs.
- 'Eclectic' approaches to early interventions for autism spectrum disorders are highly variable, often poorly defined and have poor evidence of effectiveness. It is thus essential to systematically describe the components of these programs and formally monitor their outcomes.

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SUMMARY This paper examines current evidence for the effectiveness of early intensive behavioral interventions and other comprehensive preschool, behaviorally and/or developmentally based programs for young children with autism spectrum disorders (ASD). Data are based on recently published systematic reviews and meta-analyses. Individual differences in response to treatment and current evidence on predictors of outcome are examined. The limited research findings available on the long-term outcomes (>4 years after the start of treatment) of young children with ASD who received such interventions are also summarized. Finally, this review discusses challenges in the implementation of evidence-based early comprehensive interventions for ASD and highlights future priorities in this field.

Given the multiple and complex developmental and behavioral challenges associated with autism spectrum disorders (ASD), much recent research has focused on the effectiveness of early comprehensive interventions for preschool children with ASD. Typically, these programs aim to improve functioning and decrease problems across multiple domains, are based on behavioral and/or developmental theoretical frameworks and principles, are in most cases intensive (>15 h/week) and of long duration (≥1 year), and are recommended to commence in the child's first 2–3 years of life [1].

Earlier claims of 'recovery' or 'being indistinguishable from peers' (i.e., [2]) have led to heated debate and uncertainty for many families, researchers and educational/health professionals regarding the comparative effectiveness of these and other early intervention programs. However, the quality, composition, implementation, evaluation and evidence base of such interventions is very variable. In an attempt to evaluate treatment effects, a number of reviews and metaanalyses have been published in recent years, but the findings from the studies included in these are sometimes conflicting or inconclusive. The aim of the present paper is fourfold. First, to summarize current knowledge about the relative effectiveness of early comprehensive interventions based on recently published systematic reviews and meta-analyses (2005-2012). These reviews mainly include empirical studies published in the period up to and including 2007, and hence, additional data from randomized or quasi-experimental controlled trials not included in existing meta-analyses/reviews and published in English language peer-reviewed journals from 2008 onwards have been incorporated. Second, factors related to treatment outcomes are discussed. Third, in order to examine evidence on the long-term effectiveness of such programs, data from the very few studies that report on the longer-term progress of young children with

ASD are summarized. Finally, the implications of the existing evidence for intervention services and autism treatment research more generally are discussed.

Methodology

Recent reviews, systematic reviews and metaanalyses published from 2005 to July 2012 were identified in a search of PsycINFO, PubMed, MEDLINE, ERIC, CINAHL and Google Scholar databases. Only recently published reviews were included, as the aim of this paper was to synthesize the most recent empirical evidence available. The following search terms were used: 'autis*' and 'intervention* or treatment* or program*' and 'review or meta-analysis'. Reviews of targeted interventions focusing on specific areas (e.g., social skills, play, communication and behavior problems) were excluded. Only reviews or meta-analyses of outcome studies of comprehensive behaviorally or developmentally based interventions for young children with ASD (<6 years at the start of treatment) published in the English language in peer-reviewed journals were included.

In order to identify any additional recent empirical studies not included in the reviews listed in Tables 1 & 2 (which included original studies published up to 2007), the databases above were searched again from 2007 to July 2012 using the following search terms: 'intervention or treatment' and 'outcome* or progress or trial or effectiveness or evaluation' and 'autis*'. Only randomized controlled trials (RCTs) or quasi-experimental comparison studies of comprehensive, intensive (>15 h/week), early behavioral/developmental interventions with more than ten participants were included in this update. Nine such studies were identified and these are summarized in Table 3.

Finally, a further search of the same databases, but with no restrictions on publication date, was conducted to identify studies that reported on outcomes 4 years or more after the start of treatment. This timeframe was chosen because most published studies typically report outcomes 1–3 years after the start of the intervention. The following search terms were used: 'outcome* or progress or trial or effectiveness', 'longitudinal or long-term or follow-up' and 'autis*'. The characteristics and findings of the five studies that were identified are summarized in Table 4.

Findings

Summary of findings from reviews & meta-analyses published 2005–2012

Fifteen meta-analyses and/or reviews published in peer-reviewed journals since 2005 were identified. Nine were meta-analyses (one was a reanalysis of the included studies' original participant data [3]), three were systematic reviews and three were descriptive reviews (of which one was an overview of five of the eight meta-analyses presented in this paper [4]). Their methodologies, scope, number and type of included studies, inclusion criteria, quality evaluation and conclusions vary widely and are summarized in Table 1. Table 2 summarizes the reviews' findings by domain of functioning, conclusions regarding the relative effectiveness of early intensive behavioral interventions (EIBI) versus other interventions, and the overall quality of the research studies included, based on judgments of the original authors.

The number of studies included in each of the meta-analyses/reviews was variable, from four [5] to over 100 [6]. The main focus of most was on the efficacy or effectiveness of EIBI compared with treatment as usual/standard care, less intensive behavioral approaches or 'eclectic' interventions. Two included evaluations of the Early Start Denver Model (ESDM) [7,8], a comprehensive manualized early intervention for infants and young preschoolers with ASD integrating developmental, applied behavioral analytic and relationshipbased approaches. Three included studies that evaluated Treatment and Education of Autistic and Related Communication Handicapped Children (TEACCH) [8-11], a structured, community-based teaching approach emphasizing the need for visual supports, and one was an 'umbrella' review of systematic reviews of a wide range of psychosocial interventions [12], including those based on behavioral principles. With the exception of Virués-Ortega, who analyzed clinicor university-directed (efficacy) and parentmanaged (effectiveness) intervention outcomes separately [9], all other reviews and meta-analyses analyzed empirical studies of clinic-/universitydirected and parent-/community-managed programs together, and thus, it is difficult to separately report on the efficacy versus effectiveness of these programs. All meta-analyses and reviews included children who were younger than 10 years of age at the start of treatment, with the majority of participants being under 6 years. All reported on IQ and/or adaptive behavior outcomes, 12 reported on language outcomes [8,11,13–17] and two reported on overall autism severity or associated problem behaviors [6,12].

Overall, the early comprehensive interventions evaluated were reported to result in improved outcomes across different domains of functioning. Gains tend to be greater in intellectual/cognitive functioning, and moderate or small in language and adaptive behavior; however, findings are mixed, with some reviews reporting large effect sizes for language and/or adaptive behavior and others showing smaller changes in these domains (Table 2) [10,15,17].

All but one of the reviews included in Tables 1 & 2 concluded that EIBI is an effective comprehensive approach for many young children with ASD and that it is more likely to lead to better intellectual, language and/or adaptive behavioral outcomes compared with nonspecific 'eclectic' provisions or other, less intensive interventions [3,4,6-11,13-15]. The only exception reported no advantages of EIBI versus 'eclectic' treatment [5], but this included only four empirical studies and is likely to have reached erroneous conclusions due to misinterpretation of findings of one of the included studies (see [4]). Although EIBI is now considered to meet criteria for 'well-established' treatment [11,16,18], in most cases, comparison of 'eclectic' or 'standard care' interventions were of much lower quality and/or intensity, and/or were poorly described. Moreover, the inadequate quality of much of the empirical research was one of the most consistent findings of the reviews/ meta-analyses, with many of the included studies rated as 'poor' or 'weak' using a range of grading methods and criteria (Table 2). This was highlighted by most review authors as the main reason for being unable to make conclusive recommendations for any specific intervention. A further limitation is that none of the empirical studies directly compared different early, comprehensive, behavioral or developmental models of similar quality and intensity, and few examined individual differences and factors related to

Author (year)	Type of review/meta-analysis methods	Search strategy/databases searched	Criteria for inclusion in the review/meta-analysis
())			
Meta-analys	es		
Kuppens and Onghena (2012)	SMA of five previously published meta- analyses (standardized mean difference <i>d</i> for dependent or independent groups applied with <i>g</i> ; four-step SMA carried out)	EIBI studies from the five selected meta-analyses [5,10,15–17]	Group comparison/longitudinal design; children <10 years of age at start of treatment; interventions addressed at least one of intellectual, language or adaptive skills; 18 studies initially met criteria, but three excluded due to weak quality
Peters- Scheffer <i>et al.</i> (2011)	MIX; ESs were <i>d</i> ; publication bias and heterogeneity attested with funnel plots, adjusted rank correlations, Galbraith plots and Tau-squared measures	Three search strategies: computerized search in MEDLINE, PsycInfo and ERIC (using terms 'behavioral treatment or behavioral intervention' and 'autism or pervasive developmental disorder'); manual search of 12 disability, autism and behaviorally focused journals; inspection of references lists of recent EIBI publications	Interventions addressed core ASD impairments using ABA; had a pre–post test control group; children had diagnosis of ASD, autistic disorder or PDD-NOS according to DSM or ICD, and were <10 years of age at start of treatment; means and SDs were available for IQ, language or adaptive behavior; study was in peer-reviewed English-language journal published between 1980 and 2009
Eldevik <i>et al.</i> (2010)	Systematic review and reanalysis of included studies' original participant data (Jacobson and Truax [63] reliable change statistical approach was employed for reanalysis)	Computerized search in PsycInfo, ERIC and PubMed up to March 2008 (using terms 'behavior analytic or behavioral or early or intervention' and 'autism or pervasive developmental disorder'); reference lists of studies obtained from this search manually searched for disability, autism and behaviorally focused journals; inspection of references lists of recent EIBI publications	Participants in treatment group had received EIBI that adhered to common elements described by [64]; there was a comparison or control group; there were adequate intake and outcome data; the study reported on outcome after at least 2 years of intervention; data were not reported in earlier papers of the same research group
Makrygianni and Reed (2010)	Meta-analysis (standardized weighted mean gain as index of ES used pre–post treatment and between-group difference calculations and extreme ES excluded; homogeneity Q statistic analyses carried out)	Computerized search of databases (not specified); manual search of citations of reviews and included studies, and expert recommendations between March 2006 and December 2007	Studies were in peer-reviewed journals; at least one treatment group's intervention was using ABA methods; included children with diagnosis of autism, ASD, autistic disorder or PDD/PDD-NOS; children were <54 months old at treatment onset; quantitative data on at least one domain of intellectual, language or adaptive behavior functioning were provided; studies had moderate-to-high methodological quality based on criteria by [65]

Abb. Applied Denavior analysis, Abc.: Adaptive Denavior composite, Abi. Applied Denavior an intervention, AD-A. Addisin Diagnostic Interview-NewSed, ADOS. Addisin Diagnostic Observation Schedule; AMED: Allied and Complementary Medicine Database; APA: American Psychological Association; AS: Aperger's syndrome; ASD: Autism spectrum disorder; CBT: Cognitive behavioral therapy; CINAHL: Cumulative Index to Nursing and Allied Health Literature; *d*: Cohen's *d* effect size; DIR: Developmental, individual difference, Relationship-based model; EIBI: Early intensive behavioral intervention; ERIC: Education Resources Information Center; ES: Effect size; *g*: Hedge's *g*; HFA: High functioning autism; ICD: WHO International Classification of Diseases; MeSH: Medical Subject Headings; MIX: Meta-analysis with interactive explanations; PDD: Pervasive developmental disorder; PDD-NOS: Pervasive developmental disorder not otherwise specified; PECS: Picture Exchange Communication System; PRT: Pivotal response training; RCT: Randomized controlled trial; SD: Standard deviation; SMA: Sequential meta-analysis; SS: Standard score; TAU: Treatment as usual; TEACCH: Treatment and Education of Autistic and Related Communication Handicapped Children; UCLA: University of California, Los Angeles; VABS: Vineland Adaptive Behavior Scales; YAP: Young Autism Project.

Research studies included; n (number of RCTs and non-RCTs)	Time period in which included studies were published	Information on participants	Type(s) of interventions included	Ref.
15 (12 group comparison; three no control group)	1987–2007	263 children with autism, ASD or PDD-NOS; age at start of treatment: <10 years	EIBI and comparison groups ('eclectic'/standard provisions, less-intensive EIBI, parent-directed EIBI); no further information on interventions provided	[14]
11 (one RCT; ten pre–post test control group design)	1997–2007	312 children with ASD, autistic disorder or PDD-NOS; age at start of treatment: 33.6–65.7 months; 66% male, 10.5% female, 23.8% not reported; intake IQ: 27.5–76.5	EIBI groups received 12.5–38.6 h/week ranging from 10 months to >2 years; control groups consisted of less intensive EIBI (<10 h/week), 'eclectic' treatment, parent-directed ABA or standard provisions (i.e., nursery). No further information on interventions provided	[15]
16 (11 with comparison [of the same intensity] or control group [less intensive or TAU])	1987–2007	453 participants (309 in EIBI, 39 in comparison and 105 in control groups); mean age at start of treatment: 38.5 months (SD: 11.5); mean intake IQ: 55.3 (SD: 17.5; range: 17–120); mean Vineland ABC SS: 61.3 (SD: 11.5; range: 26–113)	EIBI (clinic, home/parent directed; half of children in EIBI received >36 h of intervention/week); comparison and control treatments only defined as different interventions of similar or lower intensity or TAU	[3]
14	1984–2007	322 children with autism, ASD or PDD/PDD-NOS; intake age: 26.6–53 months; intake IQ: 27–83; intake adaptive behavior SS range: 50.7–70.5	Intervention groups were those that received EIBI, based on ABA methods/YAP; control groups were 'eclectic' in nature (no further information provided); duration of interventions: 8–58 months	[17]

Author

Table 1. Meta-analyses and systematic reviews of comprehensive behavioral/developmental interventions for young children with autism spectrum disorders published between 2005 and July 2012: summary of reviews' characteristics, methods, participants and interventions (cont.).

Criteria for inclusion in the

Type of review/meta-analysis methods Search strategy/databases searched

(year)	Type of review/meta-analysis methods	Search strategy/databases searched	review/meta-analysis
Meta-analys	es (cont.)		
Virués- Ortega (2010)	Meta-analysis (inverse variance-weighted random effects meta-analysis; ES calculated as the difference in outcome progression between treatment and control groups divided by pretest SD pooled across groups; ES also calculated for pre–post test outcomes; all ES corrected for small sample bias; homogeneity assessed with I ² statistic; publication and small study effects assessed by extended Egger's test)	Search in MEDLINE, PsycInfo and Cochrane Clinical Trials databases (using terms 'behavior/behavioral control/ therapy/intervention/treatment' and 'autism/autistic/developmental or pervasive') for studies published between 1985 and April 2009; no language restrictions; references list of selected review articles also searched manually	Original, peer-reviewed and published studies; at least one of the groups implemented ABA according to key components of behavior analytic interventions; interventions were comprehensive; interventions were at least 10 h/week for at least 45 weeks; there were more than five participants with a formal diagnosis based on DSM, ADI-R [66] and/or ADOS [67]; standardized pre–post treatment outcome mean and SD scores were reported
Spreckley and Boyd (2009)	Systematic review/meta-analysis (fixed effect model calculating pooled data for treatment effect across studies; ES, standardized mean differences and 95% CI reported; I ² statistic employed for homogeneity testing)	Cochrane, MEDLINE, Embase, Psychinfo, CINAHL and AMED databases were searched up to November 2007 (using MeSH or keywords: 'autism or autistic or Asperger or child development disorder' and 'behavior therapy or early behavioral treatment' and 'cognition outcomes or rehabilitation or child health outcomes')	RCTs, quasi-randomized or controlled trials; participants were 1.5–6 years old with ASD or PDD; intervention focused on applied behavior interventions delivered to parents/ caregivers and children directly; reported adequate cognitive, language or adaptive behavior outcomes; obtained scores of 6 or more in the 9-point Physiotherapy Evidence Database Scale of quality assessment
Eldevik <i>et al.</i> (2009)	Meta-analysis (using <i>g</i> ES; individual study and overall EIBI ESs against comparison/control groups computed; tests of homogeneity and publication bias also carried out using Q-statistic, I ² , funnel plots, and trip and fill method)	PsycInfo, PubMed, and ERIC databases searched up to March 2008 (using terms 'behavior analytic, behavioral, early, intervention' and 'autism and/or PDD'); reference lists of selected papers also searched manually	Children with independent diagnoses of autism or PDD-NOS; a cognitive or adaptive behavior measure was used and reported at intake and follow-up; duration of intervention was 12–36 months; not a case study and published in a peer-reviewed journal; included comparison or control group
Reichow and Wolery (2009)	Comprehensive synthesis and meta- analysis (standardized mean change and standardized mean difference <i>d</i> ; <i>g</i> ES metrics with small sample correction factor; individual study and mean ESs; tests of homogeneity and publication bias using Q- and I ² statistics, funnel plots, and trip and fill method; analyses of moderator analyses)	Electronic database search; review of reference lists from review articles and reports; hand search of selected journals; expert contact (no further details provided)	ElBI based on [2,64,80] or other comprehensive ABIs for ASD; participants had diagnosis of AS, ASD, PDD or PDD-NOS, and were <84 months old at intake; mean ElBI duration was >12 months; at least one child outcome was reported; pre–post or quasi- experimental multiple-group designs were employed; published in a peer-reviewed journal
Ospina <i>et al.</i> (2008)	Systematic review and meta-analysis of behavioral and developmental interventions (sensory motor, social skills and other integrated programs also included but not presented here)	22 electronic databases were searched up to May 2007 for peer-reviewed literature, abstracts and dissertations; experts were contacted; complete search strategy is in the online appendix of the original study	RCTs, controlled clinical trials or cohort studies with comparison groups; published in English; reported data on the effectiveness of behavioral or developmental interventions for ASD
ABA: Applied be	havior analysis: ABC: Adaptive behavior composite: A	ABI: Applied behavioral intervention: ADI-R: Autism Di	agnostic Interview-Revised; ADOS: Autism Diagnostic

ABA: Applied behavior analysis; ABC: Adaptive behavior composite; ABI: Applied behavioral intervention; ADI-R: Autism Diagnostic Interview-Revised; ADOS: Autism Diagnostic Observation Schedule; AMED: Allied and Complementary Medicine Database; APA: American Psychological Association; AS: Aperger's syndrome; ASD: Autism spectrum disorder; CBT: Cognitive behavioral therapy; CINAHL: Cumulative Index to Nursing and Allied Health Literature; *d*: Cohen's *d* effect size; DIR: Developmental, individual difference, Relationship-based model; EIBI: Early intensive behavioral intervention; ERIC: Education Resources Information Center; ES: Effect size; *g*: Hedge's *g*; HFA: High functioning autism; ICD: WHO International Classification of Diseases; MeSH: Medical Subject Headings; MIX: Meta-analysis with interactive explanations; PDD: Pervasive developmental disorder; PDD-NOS: Pervasive developmental disorder not otherwise specified; PECS: Picture Exchange Communication System; PRT: Pivotal response training; RCT: Randomized controlled trial; SD: Standard deviation; SDA: Sequential meta-analysis; SS: Standard score; TAU: Treatment as usual; TEACCH: Treatment and Education of Autistic and Related Communication Handicapped Children; UCLA: University of California, Los Angeles; VABS: Vineland Adaptive Behavior Scales; YAP: Young Autism Project.

Research studies included; n (number of RCTs and non-RCTs)	Time period in which included studies were published	Information on participants	Type(s) of interventions included	Ref.
22 (13 studies with control groups, six of which with random or quasi-random assignment; three with no control groups)	1987–2008	323 participants with autism, ASD, PDD-NOS; intake age: 22.6–66.3 months; intake IQ: 15–76.5	EIBI (13 UCLA model/nine broader definition of more 'general' or other ABA programs such as PRT); clinic based or parent managed); control groups were 'eclectic'; TEACCH, special education classes, low-intensity EIBI (<10 h/week), sensory integration therapy, typically developing children; intensity was 12–45 h/week and duration was 48–407 weeks	[9]
Four (two RCTs; two quasi-randomized)	2000–2007	101 participants with ASD or PDD; intake age: <6 years; mean mental intake age: 50 months;	ABA at home (two studies) or kindergarten/school settings (two studies) for 12–48 months; intensity was 28–39 h/week (one study dropped to 18 h/week after school start); ABA delivered by student therapists or teachers/teacher aides who were trained and supervised; comparison groups received 'eclectic' treatment at kindergarten/school or parent-directed ABA for 5–31 h/week	[5]
Nine (eight quasi-experimental controlled trials; one RCT)	1987–2007	297 children (153 in EIBI; 105 in control and 39 in comparison groups); intake age: 30.9–66.3 months; intake IQ: 27.3–65.2; intake Vineland ABC: 47.5–71.9	EIBI (clinic directed; parent directed in community setting; home or school settings) for from less than 10 to 40 h/week for 12–36 months; comparison groups received minimal or 'eclectic' treatment (including PECS, TEACCH, local education classes and special school classes) with similar or lower intensity	[10]
13 (two RCTs; 11 quasi- experimental); six prospective multiple-group comparisons; one prospective pre-post design; three retrospective multiple-group comparisons; one retrospective pre-post design)	1987–2007	373 children with autism, ASD, PDD or PDD-NOS; intake IQ: 28–83; adaptive behavior at intake typically 2–3 SD below mean	67% of children received 18.7–40 h/week of EIBI for 12–48 months; most EIBI groups were clinic coordinated and 64% of EIBI programs were based on training to supervisors using the UCLA YAP training model; parents provided some EIBI in 11 studies; 122 participants (33%) were in non-EIBI comparison groups (receiving TAU/'eclectic' interventions)	[16]
101 (55 RCTs; 32 controlled clinical trials; four prospective cohort studies; ten retrospective cohort studies); 13 contributed data to a meta-analysis	1977–2007	Individual data presented for each included study, but no summary information presented	12 evaluated ABA (discrete trial training and UCLA/Lovaas models); 12 evaluated 'contemporary ABA' (contemporary discrete trial, incidental teaching, PRT and CBT); 12 evaluated developmental approaches (DIR and DIR-based interventions, imitative interaction, incidental teaching and more than words)	[6]

	trum disorders published between 200		tal interventions for young children with haracteristics, methods, participants and
Author (year)	Type of review/meta-analysis methods	Search strategy/databases searched	Criteria for inclusion in the review/meta-analysis
Systematic r	eviews		
Reichow (2012)	Descriptive review/overview of five meta-analyses	Meta-analyses published between 2009 and 2010; exact search procedure not specified	Inclusion criteria of the five included meta-analyses varied
Warren <i>et al.</i> (2011)	Systematic review	MEDLINE, PsycInfo and ERIC searched from 2000 to May 2010 (using keywords relating to ASD and therapy-related terms); manual search of reference lists of included articles	Not single case studies; at least ten participants <13 years of age at intake with ASD (or children <2 years at risk for ASD)
Howlin <i>et al.</i> (2009)	Systematic review	MEDLINE, Embase, Cochrane, PsycInfo, CINAHL and ERIC searched between 1985 and May 2007 (using terms 'autism/ autistic/ASD' and 'intervention/early intervention/behavio(u)ral/EIBI/ABA'; manual search of international reviews	Case-control/comparison study of EIBI; UCLA-affiliated or other home-based EIBI largely based on the UCLA model for at least 12 h/week for at least 12 months; at least ten participants <6 years at intake; adequate data on IQ or other standard measures
Eikeseth (2009)	Descriptive review	MEDLINE, ERIC and PsycLit (APA) searched (no details provided); manual search of reference lists from recent intervention outcome publications; personal communication with autism outcome researchers	Published in a peer-reviewed journal; children <6 years at intake; participants received comprehensive psycho-educational interventions; outcome data were reported
Seida <i>et al.</i> (2009)	'Umbrella' systematic review of systematic reviews of effectiveness of a wide range of psychosocial interventions for ASD	Comprehensive search carried out in 25 databases up to May 2007 with no language restrictions (keywords were terms connected with autism, related disorders and psychosocial interventions); manual searches of reference lists and personal collections were also conducted	The review defined a search strategy; participants had autism, AS, HFA, PDD-NOS or suspected but not confirmed autism; the review focused on a psychosocial intervention
Rogers and Vismara (2008)	Descriptive review	Search of PsycInfo (using keywords such as 'autism', 'preschool', 'treatment' and 'intervention') from 1998 to 2006	Studies evaluated comprehensive interventions for children with autism predominantly ≤5 years old; used controlled group designs or single-subject multiple baseline designs with at least three subjects; included outcome data
Observation Sch CBT: Cognitive E Relationship-ba ICD: WHO Interr PDD-NOS: Perva trial; SD: Standar	nedule; AMED: Allied and Complementary Medicine hehavioral therapy; CINAHL: Cumulative Index to Nur- sed model; EIBI: Early intensive behavioral interventic hational Classification of Diseases; MeSH: Medical Sub hisive developmental disorder not otherwise specified d deviation; SMA: Sequential meta-analysis; SS: Stance	Database; APA: American Psychological Association; A sing and Allied Health Literature; d: Cohen's d effect si on; ERIC: Education Resources Information Center; ES: ject Headings; MIX: Meta-analysis with interactive exy d; PECS: Picture Exchange Communication System; PR	Effect size; g: Hedge's g; HFA: High functioning autism; planations; PDD: Pervasive developmental disorder; T: Pivotal response training; RCT: Randomized controlled nt and Education of Autistic and Related Communication

Research studies included; n (number of RCTs and non-RCTs)	Time period in which included studies were published		Type(s) of interventions included	Ref.
Five meta-analyses	2009–2010	See meta-analyses [5,9,10,16,17]	EIBI based on Lovaas UCLA YAP model, Green <i>et al.</i> [64], Maurice <i>et al.</i> [68] or other comprehensive ABIs for ASD	[4]
34 (five RCTs; five non-RCT control trials; five prospective cohorts; two retrospective cohorts; 17 prospective or retrospective case series)	2000–2010	Intake age: 25.1–66.1 months; more information included in full report [101]	Interventions were classified in three categories: EIBI based on UCLA/Lovaas interventions and related approaches with range of ABA and developmental methodologies; comprehensive interventions for children <2 years (i.e., Early Start Denver Model); parent training protocols (typically low intensity) delivered by trained parents in natural settings (including PRT)	[7]
11 (two RCTs; six prospective; three retrospective case–control trials)	1987–2007	Mean number of EIBI study participants: 18 (11–29/study); mean number in comparison groups: 14.7 (range: 10–21); mean intake age: 31–66 months; mean intake IQ: 55.7 (range: 28–83) for EIBI and 53.6 (range: 27–65.2) for comparison group; mean intake VABS SS: 61.2 and 61.5, respectively	EIBI largely based on UCLA YAP model and related multisite replication groups; two studies reported on school-based EIBI and four were community based; comparison groups received less intensive parent- directed EIBI, standard schooling, 'eclectic' education, parent-directed EIBI, autism-specific nursery or generic special education; mean duration of intervention: 27.4 months (range: 14–48); mean EIBI intensity: 29.8 h/week (range: <10–31.5); estimated total time: 3353 h for EIBI group and 1980 h for comparison groups	[13]
25 (one randomized study design; four nonrandom group designs; 11 retrospective studies with comparison group or single-case pre-post experimental studies; nine pre-post or retrospective studies without comparison, or single-case controls)	1984–2007	Descriptive summaries of the included studies are provided, but information on participants is not provided for all studies, making it difficult to extract overall information	20 of the included studies evaluated interventions based on ABA; three evaluated TEACCH; and two the Colorado Health Science model (Denver model)	[8]
30 systematic reviews (15 single-subject; eight RCTs; seven controlled clinical trials)	1996–2007 (over half post-2004)	Provided separately in online appendix by the authors	Communicative therapy, parent-mediated interventions, sensory/motor interventions, behavioral theory interventions, social skills development interventions	[12]
22 (five RCTs)	1998–2006	Descriptive information provided individually for each study by the authors	A range of interventions were evaluated: EIBI following Lovaas/UCLA models; discrete trial- and incidental teaching-focused ABA interventions; 'eclectic' interventions (incorporating TEACCH, sensory motor therapies and others); public school education; PRT; developmentally focused and naturalistic interventions	[11]

original stud			Description of the film
Author (year)	Original authors' evaluation of methodological quality of studies included in review/meta-analysis	Reported cognitive/intellectual and/or educational outcomes	Reported communication/language and/or social outcomes
Meta-analyse	S		
Kuppens and Onghena (2012)	Quality criteria used: Reichow <i>et al.</i> [65] Five studies high quality; ten studies adequate quality	Medium effect for pre–post treatment change ($d = 0.71$); EIBI > comparison ($d = 0.61$). There was enough cumulative evidence for at least a medium ES group difference favoring EIBI	Medium effect for pre–post treatment change ($d = 0.72$). EIBI > comparison ($d = 0.72$). No evidence for at least a medium pre–post treatment benefit was obtained from the SMA, but sufficient evidence was obtained for at least a medium group difference effect favoring EIBI
Peters- Scheffer <i>et al.</i> (2011)	Quality criteria used: Downs and Black [69] Mean quality score: 24.65 out of 32 (SD: 1.29; range: 23–27)	Full-scale IQ improved 11.98 points more in EIBI group than control groups. Nonverbal IQ improved 11.09 points more in EIBI group than control groups. d = -0.2-7.2 (mean: 2; eight out of ten studies reported $d > 1.3$); overall, large and clinically significant d	Children in EIBI improved 13.94 more SS points in receptive and 15.21 more points in expressive language than controls; ESs large and clinically significant. Mean ES was 1.1 for expressive language and 2.9 for receptive language
Eldevik <i>et al.</i> (2010)	No quality evaluation reported, but studies were excluded if: case reports; did not have independent ASD diagnosis or full-scale IQ and adaptive behavior assessments. Some of the included studies had poor methodological quality	Significantly more EIBI children (30%) achieved reliable change in IQ (≥27 points) compared with comparison (2.6%) and control groups (8.7%)	Not examined/reported
Makrygianni and Reed (2010)	Quality criteria used: Reichow <i>et al.</i> [65] Nine studies of low methodological quality; three studies of high methodological quality; and two studies of mixed methodological quality depending on the group examined	ElBI is effective in improving intellectual abilities post-treatment; weighted mean ES was 0.95 (SE: 0.13) for high- methodological-quality studies and 0.91 (SE: 0.079) for low-methodological- quality studies. Group comparison ES was 0.57 for high-quality and 0.73 for low-quality studies	EIBI is effective in improving language abilities post-treatment; weighted mean ESs: 0.99 (SE: 0.13) for high methodological quality studies and 0.90 (SE: 0.15) for low methodological quality studies. Group comparison ESs was medium (0.53) and large (0.97) in high- and low-quality studies, respectively
Virués- Ortega (2010)	Quality criteria used: Downs and Black [69] Range of quality ratings: 1.7–3.9 out of 5. Evidence of publication bias in all outcomes reported, except for daily living, motor functioning and ABC	ABA produced positive effects in all studies that reported general IQ (ES: 1.19). Effects stronger for clinic-based (1.23) than parent-managed programs (1.02). Of the ten studies that reported nonverbal IQ, pooled ES was 0.65 and effects were similar for clinic-based and parent-managed programs	ABA produced positive effects for receptive and expressive language in all studies that reported them. ESs were 1.48 and 1.47, respectively
Spreckley and Boyd (2009)	Quality criteria used: PEDro Scale of Quality Assessment [71] Ratings of 4–8 on an 11-point scale (studies <6 excluded from analyses)	No significant improvement in cognitive outcomes compared with control groups (standardized mean difference between ABI and standard care groups was 0.38)	No significant improvement in language outcomes compared with control groups (standardized mean difference was 0.37 for expressive and 0.29 for receptive language)
Eldevik <i>et al.</i> (2009)	Quality criteria used: Nathan and Gorman [72] Only one included study met the highest level criteria of methodological rigor (no further quality information or ratings are provided); no evidence of publication bias	Overall ES for change in IQ was large (1.10)	Not reported/analyzed

ABA: Applied behavior analysis; ABC: Adaptive behavior composite; ABI: Applied behavioral intervention; ASD: Autism spectrum disorder; d: Cohen's d effect size; EIBI: Early intensive behavioral intervention; ES: Effect size; ESDM; Early Start Denver Model; OQAQ: Overview Quality Assessment Questionnaire; PEDro: Physiotherapy Evidence Database; RCT: Randomized controlled trial; SD: Standard deviation; SE: Standard error; SMA: Sequential meta-analysis; SS: Standard score; TAU: Treatment as usual; TEACCH: Treatment and Education of Autistic and Related Communication Handicapped Children; UCLA: University of California, Los Angeles; VABS: Vineland Adaptive Behavior Scales.

Reported adaptive behavior and/or autism symptom severity outcomes	Original authors' summary and conclusions regarding the comparative effectiveness of reviewed interventions	Ref.
Small effect for pre–post treatment change in adaptive behavior ($d = 0.35$; p = 0.104). EIBI > comparison ($d = 0.60$). No evidence was obtained from the SMA for at least a medium pre–post treatment benefit; however, there was sufficient cumulative evidence for at least a medium ES group difference in favor of EIBI. Autism severity not examined/reported	Overall EIBI more effective than comparison programs	[14]
EIBI groups surpassed control groups in ABC by 5.92 points, communication subscale by 10.44, daily living skills by 5.48 and socialization by 4.96. Mean ES was 0.91 for overall ABC (1.3 for Vineland communication and 1.5 for Vineland socialization, but 0.68 for daily living skills). Autism severity was not examined/reported	EIBI group generally outperformed control groups on measures of IQ, communication and adaptive behavior, but group differences were less pronounced for adaptive behavior	[15]
Significantly more EIBI children (20.6%) achieved reliable change of >21 points in VABS [70] compared with comparison (5.7%) and control groups (5.1%). Autism severity was not examined/reported	EIBI resulted in greater gains in IQ and adaptive behavior than comparison programs	[3]
EIBI is effective in improving adaptive behavior; weighted mean ES was 0.42 (SE: 0.15) for high- and 0.47 (SE: 0.11) for low-quality studies. Group comparison ESs in this domain were large (0.97 and 0.66 in high- and low-quality studies, respectively). Autism severity was not examined/reported	ElBIs are more effective than 'eclectic' programs in improving intellectual, language and adaptive behavior abilities	[17]
All studies indicated favorable effects of ABA in VABS communication, daily living and socialization domains. 13 out of 15 studies indicated favorable effects of ABA on the ABC measure, pooled ES was 1.09 for ABC, 1.45 for Vineland communication, 0.62 for daily living skills and 0.95 for socialization. Autism severity was not examined/reported	Author reports that findings are difficult to interpret because of differences in treatment implementation, intensity and fidelity, but concludes that comprehensive ABA interventions produce medium- to-large effects in intellectual functioning, language and adaptive behaviors, and overall, result in better outcomes than controls	[9]
No significant improvement in adaptive behavior outcomes compared with control groups (standardized mean difference: 0.30). Autism severity was not examined/reported	Evidence reviewed and included in the meta-analysis did not support ABA as more effective than other comprehensive/standard care interventions	[5]
Medium ES for change in ABC (0.66). Autism severity not examined/reported	The authors were cautious about drawing any firm conclusions as the comparison groups were different in terms of the amount of intervention, supervision and training, but their findings suggest that EIBI is more effective than 'eclectic' treatments	[10]

Author (year)	Original authors' evaluation of methodological quality of studies included in review/meta-analysis	Reported cognitive/intellectual and/or educational outcomes	Reported communication/language and/or social outcomes
Meta-analyse	es (cont.)		
Reichow and Wolery (2009)	Quality criteria used: Reichow <i>et al.</i> [65] Three studies strong, five adequate, five weak. There may have been publication bias	Standardized mean change of IQ ES: -0.19–1.58. Standardized mean difference of ESs between EIBI and comparison treatments favored EIBI (range: 0.27–1.12); 65% of EIBI participants in regular education classrooms at follow-up	EIBI group had higher scores in expressive (ES difference range: 0.17–0.56) and receptive (0.38–0.59) language
Ospina <i>et al.</i> (2008)	Quality criteria used: checklist including items from other published scales addressing design, execution and analysis used, but no total scores/ratings reported Overall quality of RCTs, controlled studies and cohort trials was modest to low, with the majority of studies rated with at least some major methodological flaw	Lovaas/UCLA models found superior to standard care or regular instruction for cognitive functioning, but findings were inconsistent across the 31 different studies included in the systematic review of this approach. Weighted mean difference score for IQ was insignificant (0.95) for overall intellectual functioning between EIBI based on UCLA/Lovaas model and special education in three studies included in a meta-analysis	Some evidence for positive outcomes in language and communication abilities were reported for Lovaas/UCLA model EIBI and contemporary ABA (specifically pivotal response training), but generally speech- related outcomes were less pronounced compared with motor or functional outcomes. Weighted mean difference score for communication was 16.63 in three studies included in a meta-analysis between the two groups, and 15.05 for expressive language, in favor of Lovaas/ UCLA model EIBI
Systematic re	eviews		
Reichow (2012)	Quality criteria used: critical overview of five meta-analyses in terms of inclusion criteria, interpretation, statistical analyses, and publication and selection biases Two meta-analyses reported possible publication bias and two did not (one not reported). All meta-analyses had at least one limitation (small sample sizes of included studies, quasi-experimental designs, narrow outcome measures, lack of fidelity data or inadequate participant characterization)	Across the five meta-analyses, weighted mean effect (<i>g</i>) sizes ranged from 0.38 to 1.19 for IQ	Not examined/reported
Warren <i>et al.</i> (2011)	Quality criteria used: prespecified quality assessment form developed by review team and available at [101] One good, 12 fair and 21 poor quality	There is evidence that children in UCLA/Lovaas-based EIBI improved in cognitive outcomes, but strength of evidence was insufficient to low. Some evidence that ESDM contributes to IQ improvements, but ESDM findings have not been replicated yet (strength of evidence insufficient)	Evidence that children in UCLA/Lovaas- based/EIBI improved in language outcomes, but strength of evidence low. Some evidence that ESDM also resulted in language improvements, but strength of evidence currently insufficient

ABA: Applied behavior analysis; ABC: Adaptive behavior composite; ABI: Applied behavioral intervention; ASD: Autism spectrum disorder; d: Cohen's d effect size; EBI: Early intensive behavioral intervention; ES: Effect size; ESDM; Early Start Denver Model; OQAQ: Overview Quality Assessment Questionnaire; PEDro: Physiotherapy Evidence Database RCT: Randomized controlled trial; SD: Standard deviation; SE: Standard error; SMA: Sequential meta-analysis; SS: Standard score; TAU: Treatment as usual; TEACCH: Treatment and Education of Autistic and Related Communication Handicapped Children; UCLA: University of California, Los Angeles; VABS: Vineland Adaptive Behavior Scales.

Reported adaptive behavior and/or autism symptom severity outcomes	Original authors' summary and conclusions regarding the comparative effectiveness of reviewed interventions	Ref.
Standardized mean change of ES for adaptive behavior ranged from -0.25	Children receiving EIBI made more gains than children	[16]
to 0.86 for studies that reported it. Four out of five studies that compared EIBI with other treatments and had data on adaptive behavior, favored EIBI (range of ES difference: 0.47–1.17); one study reported that the control group had equal or better scores than EIBI group (ES difference: -0.15). 18% of EIBI participants across samples that reported these data met criteria for diagnostic reclassification	receiving minimal behavioral intervention, 'eclectic' treatment or TAU, but a lack of adequate comparison groups and nonrandom assignment of many studies limit conclusions. Evidence suggests that EIBI can be effective for some children, although not for all	
Some evidence of positive outcomes in adaptive behaviors was reported for Lovaas/UCLA models in the systematic review. Some evidence for positive	Compared with other special education interventions, there is some evidence that Lovaas programs result	[6]
outcomes from the systematic review was obtained for overall pathology following Lovaas/UCLA model EIBI. Three controlled studies included in a meta-analysis yielded statistically significant superiority for Lovaas treatment compared with special education in overall adaptive behavior (weighted mean difference was 11.8 IQ points), but was small in daily living skills (5.6) and socialization (9.2)	in more intellectual, social and adaptive behavior gains; however, data are limited and inconsistent, and evidence is less consistent for communication skills; there is less evidence for the use of contemporary ABA approaches and developmental approaches	
		[4]
Across the five meta-analyses, weighted mean ESs (<i>g</i>) ranged from 0.30 to 1.09 for adaptive behavior. Autism severity not examined/reported	Four out of five meta-analyses concluded that EIBI was effective; the one that did not [5] is likely to have reached erroneous conclusions. EIBI can produce large gains in IQ and adaptive behavior for many young children with ASD; EIBI comprehensive treatment model has the most empirical support to date, but not all children benefit	[4]
Evidence that UCLA/Lovaas-based interventions and EIBI contributed to improvements in adaptive outcomes (strength of evidence low). Some evidence that ESDM contributed to adaptive behavior gains (strength of evidence currently insufficient). Autism severity was not examined/reported	Children in EIBI and ESDM programs improved more in cognitive, language and adaptive behavior skills compared with those in broadly defined 'eclectic' treatments, suggesting benefit of EIBI and ESDM for some children that should continue to be studied; currently, there are too few methodologically strong studies so it is difficult to draw firm conclusions	[7]

original stud			
Author (year)	Original authors' evaluation of methodological quality of studies included in review/meta-analysis	Reported cognitive/intellectual and/or educational outcomes	Reported communication/language and/or social outcomes
Systematic re	eviews (cont.)		
Howlin <i>et al.</i> (2009)	Specific quality assessment tool not employed; descriptive discussion of included studies concluded overall quality poor for a number of studies	Mean IQ increase: 18.3 points (SD: 11.5) in EIBI group and 5.4 points (SD: 9.3) in comparison groups. Nine studies reported higher IQ for EIBI than comparison at follow-up. ESs moderate to large for most studies. Only a small minority of children achieve educational independence (mainstream school without support)	From baseline to follow-up, expressive language scores increased by an average of 11.6 SS points for EIBI groups (SD: 10.8) and 1.7 for comparison groups (SD: 8.5). Language comprehension SS increased 15.7 for EIBI (SD: 6.0) and 4.5 (SD: 12.1) for comparison groups
Eikeseth (2009)	Quality criteria used: Scientific Merit Scoring according to diagnosis, study design, dependent variables and treatment fidelity criteria outlined in detail by the author One study was strong, four were good/adequate, 11 were weak and nine were poor/insufficient	There is evidence from good/strong quality studies for children receiving ABA interventions scoring higher in intellectual abilities than comparison group at follow-up	Some evidence from good-/strong-quality studies for ABA group scoring higher on language abilities than comparison group at follow-up
Seida <i>et al.</i> (2009)	Quality criteria used: OQAQ [75] Overall methodological quality of included reviews was poor (median OQAQ score: 2 out of 7); 83% of reviews had major or extensive methodological flaws; only five reviews had minor or minimal flaws, none of which focused on behavioral interventions	Two included systematic reviews and one meta-analysis reported increases in cognitive skills following behavioral interventions	One systematic review and one meta-analysis reported favorable outcomes for behavioral interventions in language skills
Rogers and Vismara (2008) ABA: Applied be	Quality criteria used: Nathan and Gorman [72] Four type I (best quality); six type II and 12 type III studies	Evidence suggests that best outcome status (defined as normal-range IQs and unsupported placement in typical classrooms) may be possible for a subgroup of children following Lovaas treatment	Less consistent evidence for greater effectiveness of Lovaas model in language skills; few significant differences in language skills between developmental treatment and comparison groups

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> outcome (see 'Factors related to outcome' section). Another conclusion reached by many of the reviews is that, although there is evidence that EIBI is generally effective, we still need to know more about what specific child characteristics, intervention techniques and implementation, family or other factors predict response to this intervention.

Recently published empirical studies (2008 to July 2012)

Nine recently published controlled empirical studies of early intensive comprehensive interventions that had not been included in the reviews above were identified. Two were RCTs [19,20], five compared EIBI (community-based, delivered in mainstream preschool settings or low-intensity programs) with other 'eclectic' interventions or 'treatment as usual' [21–25], one compared intensive with nonintensive intervention based on applied behavior analysis (ABA) [26], and one compared clinic-based with parent-managed EIBI [27]. Seven studies focused on EIBI, one compared the ESDM with typically available community intervention services [19], and finally, one evaluated Learning Experiences and Alternative Program for Preschoolers and their Parents (LEAP; an inclusive intervention

Reported adaptive behavior and/or autism symptom severity outcomes	Original authors' summary and conclusions regarding the comparative effectiveness of reviewed interventions	Ref.
EIBI group improved in VABS ABC by a mean SS of 5.1 (SD: 6.2) compared with comparison group whose VABS decreased on average by 2.4 (SD: 4.5). Improvement small in this domain of functioning. Autism severity was not examined/reported	ES estimates of EIBI vs comparison groups ranged from 0.23 (small) to 1.28 (large); most studies reported moderate and large ESs. However, there is wide variability in response to intervention; EIBI treatment is effective for some, but not all, children; gains likely to be greatest in the first 12 months of treatment	[13]
Some evidence from good-/strong-quality studies for ABA groups scoring higher on adaptive functioning than comparison groups at follow-up. Autism severity was not examined/reported	Based on guidelines by [73,74], author considered ABA 'well established', TEACCH and Colorado Health Science model neither 'well established' nor 'probably efficacious'	[8]
Three meta-analyses showed that behavioral interventions reduce problem behavior. One additional systematic review also reported increases in functional skills	Psychosocial interventions are better than no interventions. There is consistent evidence, but from low-quality reviews, for favorable outcomes following behavioral interventions. There is little evidence of relative effectiveness of these treatments; conclusions cannot be drawn due to the potential bias and low quality of reviews and included studies	[12]
Less consistent evidence of improvement of adaptive behavior for Lovaas treatment. Some evidence for better performance in adaptive behavior skills for developmental treatment relative to comparison groups	Conclusions regarding the effectiveness of different treatments are difficult due to a lack of comparative studies. Lovaas treatment meets 'well-established' criteria; pivotal response training 'probably efficacious'	[11]

model utilizing peer-mediated interventions, errorless learning, incidental teaching, pivotal response training and positive behavior support approaches) and the authors compared the full LEAP model with a manuals-only comparison group [20].

In the five studies comparing EIBI with treatment as usual or 'eclectic' interventions, the EIBI group significantly outperformed the comparison group in cognitive scores in two studies [22,24] and in adaptive behavior in four [21-24]. Only one study assessed autism symptom severity and no group differences at follow-up were found [24].

The RCT by Dawson and colleagues demonstrated the effectiveness of the ESDM (for an average of 15.2 therapist-delivered h/week in addition to 16.3 h/week of parent-reported use of ESDM strategies at home in daily activities over 2 years) compared with a group that received commonly available individual and group interventions in the community for an average of 18.4 h/week at 1- and 2-year followup [19]. Children in the ESDM group showed more improvements in IQ and language skills than the comparison group. Adaptive behavior scores remained stable after 2 years for the ESDM group, although these scores decreased

developme	ntally focused interve	ntions for you	ing children with autism spectrum disorder.		
Author (year)	Participants; n (diagnosis)	Follow-up	Intervention(s)	Age at intake; years (SD)	Intake IQ (SD)
Eikeseth <i>et al.</i> (2012)	59 (autism; diagnosis based on ICD-10 criteria)	1 year	Community mainstream school-based EIBI based on UCLA model using school staff as therapists receiving EIBI specialist supervision ($n = 35$, six girls); mean intensity of 23 h/week in first year; TAU 'eclectic' education group with special needs teacher incorporating elements from different approaches, including some ABA ($n = 24$, four girls)	Autism: 3.9 Comparison: 4.4	Not examined/reported, but VABS ABC: 67 (10.3)
Eldevik <i>et al.</i> (2012)	43 (independent diagnosis of autism or PDD-NOS based on ADI-R)	2 years	EIBI based on various EIBI manuals [76] and employing various operant conditioning techniques/discrete trial/naturalistic teaching in local mainstream preschool settings supervised by experienced EIBI supervisors ($n = 31$) or TAU ($n = 12$), a mix of ABA, sensory motor, TEACCH-informed teaching and others supervised by special education teacher	2–6 Mean intake age: 3.7 years	EIBI: 51.6 (16.9) TAU: 51.7 (18.1)
Grindle <i>et al.</i> (2012)	29 (autism; diagnosis by multidisciplinary team)	1 and 2 years after intervention onset	ABA classroom in mainstream school setting employing behavior analytic, discrete trial training and generalization procedures, elements of natural environment training and verbal behavior methods for 30 h/week (18 h one-to-one teaching; n = 11); TAU (n = 18) received education of similar intensity in mainstream or special education settings within the context of UK National Curriculum	ABA: 4.9 TAU: 5.3	ABA: 59.5 (13.2) TAU: 61.0 (27.3)
Fernell <i>et al.</i> (2011)	208 (autism; assessed by team of medical doctors and psychologists; 198 seen at follow-up)	2 years	EIBI provided at preschool and by parents at home (n = 93) or nonintensive targeted intervention based on ABA (n = 105) comprising different targeted training (e.g., toilet training, compliance training, speech and language training)	1.5–4.5	EIBI: 39% learning disability, 48% developmental delay, 13% normal Nonintensive: 35% learning disability, 32% developmental delay, 32% normal
Strain and Bovey (2011)	294 (ASD)	2 years	Inclusive preschool classes provided with LEAP intervention manuals, videos and training materials, inclusive classes that received manuals-only intervention	LEAP: 4.2 (0.38) Manuals only: 4.2 (0.35)	LEAP: 59.6 (6.9) Manuals only: 63.2 (6.6)
Interview-Revise intensive behavi	ed; ADOS: Autism Diagnostic (ioral intervention; ES: Effect siz	Dbservation Schedu e; ESDM: Early Start	Adaptive behavior composite; ABLLS: Assessment of Basic Langu Ile; ASD: Autism spectrum disorder; CARS: Childhood Autism Rat Denver Model; g: Hedge's g; ICD: WHO International Classificatic Ilen Scales of Early Learning; PDD-NOS: Pervasive developmenta	ing Scale; CD: Clinic- on of Diseases; LEAP: I	directed treatment; EIBI: Early Learning Experiences and

Table 3. Summary of recently published (between 2008 and July 2012) empirical studies on early comprehensive behavioral and/or stally focused interventions for young children with autism -----

Alternative Program for Preschoolers and their Parents; MSEL: Mullen Scales of Early Learning; PDD-NOS: Pervasive developmental disorder not otherwise specified; PLS: Preschool Language Scale; PM: Parent-managed treatment; RBS: Repetitive Behavior Scale; SD: Standard deviation; SS: Standard score; TAU: Treatment as usual; TEACCH: Treatment and Education of Autistic and Related Communication Handicapped Children; UCLA: University of California, Los Angeles; VABS: Vineland Adaptive Behavior Scales.

Cognitive and/or educational outcomes	Communication and/or social outcomes	Adaptive behavior and/or autism severity/other outcomes	Predictors of long-term outcomes	Ref.
Not examined/reported		EIBI group scored higher on all VABS compared with TAU group at 1-year follow-up. Between-group ES was 0.92 for ABC; 1.08 for communication; 0.71 for daily living skills; 0.75 for socialization; 0.70 for motor; CARS scores decreased from 37.2 to 30.6 (ES: 0.92)	No regression or moderator analyses; no relationship was found between age, VABS or CARS intake scores and change after 1 year	[21]
EIBI group made significantly more gains in IQ (increase of 15.1 points) than TAU group (0.5 points; $g = 1.03$). Six EIBI children (no TAU children) met criterion for reliable IQ change		EIBI group made more gains on VABS composite scores (5.9 points) than TAU group (0.7 points). EIBI group made larger gains in communication and socialization (8.6 and 5.8 points, respectively) compared with TAU group (0 and -2.3 points, respectively). Difference between group change scores for daily living skills was nonsignificant. Two EIBI and no TAU children met the criterion for reliable change in VABS ABC	Intake age correlated positively with ABC score gains. Diagnoses other than autism (i.e., PDD-NOS or Asperger's syndrome) associated with larger gains in VABS ABC, communication and daily living skills subdomain scores. Intake IQ correlated positively with socialization change	[22]
At 1-year follow-up, IQ of ABA class group increased (p = 0.051; ES: 0.52). No significant improvement in IQ in second year of intervention (ES: 0.32). Although not statistically significant, mean IQ scores of ABA and TAU groups differed by 8 points at follow-up (ES: 0.60)	At 1-year follow-up, ABLLS total score increased significantly for ABA group (ES: 0.90). Improvement continued in second year of intervention (ES: 0.81). No comparisons with TAU were carried out as ABLLS was not administered in the comparison group	At 1-year follow-up, VABS composite score increased for ABA group (ES: 0.58). Improvement continued in second year of intervention (ES: 0.61). ABA group improved more on the VABS composite score after two years than TAU group (ES: 2.15). ES was 1.76 for VABS communication; 2.44 for daily living skills and 1.08 for socialization	-	[23]
		VABS composite score improved for total group by 1.07 points. No differences between intensive EIBI and nonintensive ABA groups. Autism Behavior Checklist scores decreased (improved; $\eta^2 = 0.184$) at follow-up with no group differences	Normal intellectual level associated with improvement in VABS composite	[26]
LEAP group showed greater improvement on the MSEL [77] Early Learning Composite SS than the manuals- only group (increase of 8.9 points compared with decrease of 1.8 points); ES: 0.89	LEAP group showed greater improvement of 18.5 points on the PLS total language score than manuals-only group, which improved by 9.4 points; ES: 0.92	On the CARS, LEAP group showed greater reduction in autism severity (decrease of 6.1 points) compared with manuals-only group (decrease of 2.8 points). On the Social Skills Rating System, the LEAP group showed a positive percentile change of 28.6 points compared with 11.9 points for the manuals-only group. On the Problem Behavior Scale of this rating, the LEAP group showed a positive percentile change of 7.0 compared with 4.3 points for the manuals-only group. ES was 0.59 for autism severity; 1.22 for social skills; and 0.62 for problem behaviors		[20]

Author (year)	Participants; n (diagnosis)	Follow-up	Intervention(s)	Age at intake; years (SD)	Intake IQ (SD)
Dawson <i>et al.</i> (2010)	48 (autistic disorder or pervasive developmental disorder)	1 year after intervention onset, and 2 years after onset or 4 years of age (whichever later)	ESDM for an average of 15 therapist-delivered h/week (an additional 16.2 h/week were reported by parents using ESDM strategies at home (n = 24) or A/M group, which received commonly availably community interventions (A/M; n = 24; received yearly assessments, intervention recommendations, referrals to community services and community interventions; three participants later lost to follow-up)	1.5-2.5	MSEL: ESDM: 61.0 (9.2) A/M: 59.4 (8.6)
Peters- Scheffer <i>et al.</i> (2010)	34 (autistic disorder or PDD-NOS and intellectual disabilities based on DSM-IV)	8 months	Low-intensity behavioral treatment based on [76] for an average of 6.3 h/week (treatment group; $n = 12$; range: 5–10 h/week) in addition to an average of 24.8 h/week at special preschool educational settings (receiving an 'eclectic' mix of TEACCH, behavioral teaching, incidental teaching, 'eclectic' treatment and other generic special education therapies); comparison group received special preschool provision only as above (TAU group; $n = 22$)	Treatment group: 4.5 (0.46) TAU group: 4.4 (0.93)	Treatment group: 47.00 (10.33) TAU group: 45.73 (15.99)
Zachor and Ben Itzchak (2010)	71 (ASD; evaluated by neurodevelopmental pediatrician)	1 year	Community center-based ABA implemented in autism-specific preschools for 40 h/week (20 h one-to-one teaching) based on manuals (n = 45); 'eclectic' group of similar intensity and in similar settings using range of developmental, relationship-based and TEACCH approaches (n = 33)	ABA: 2.1 (0.33) Eclectic: 2.2 (0.38)	ABA: 72.2 (19.2) Eclectic: 73.3 (22.2)
Hayward et al. (2009)	44 (autism; based on ICD-10 criteria)	1 year	CD (n = 23) and PM (n = 21) in which parents recruited and managed tutors, both based on UCLA model	CD: 3.0 PM: 2.8	CD: 53 PM: 54

Language Scale; PM: Parent-managed treatment; RBS: Repetitive Behavior Scale; SD: Standard deviation; SS: Standard score; TAU: Treatment as usual; TEACCH: Treatment and Education of Autistic and Related Communication Handicapped Children; UCLA: University of California, Los Angeles; VABS: Vineland Adaptive Behavior Scales.

Cognitive and/or educational outcomes	Communication and/or social outcomes	Adaptive behavior and/or autism severity/other outcomes	Predictors of long-term outcomes	Ref.
At 1-year follow-up, mean IQ of ESDM group increased by 15.4 points; A/M group increased by 4.4 points (group difference was significant). At 2-year follow-up, ESDM group improved 17.6 points on the MSEL composite SS, A/M improved by 7.0 points	At 1-year follow-up, ESDM group gained 17.8 points on receptive language; A/M group gained 9.8 points (group difference p = 0.05). At 2-year follow-up, ESDM improved by 18.9 and 12.1 points for receptive and expressive language, respectively; A/M improved by 10.2 and 4.0 points. Both were statistically significant group differences in favor of ESDM	At 1-year follow-up, ESDM and A/M groups declined 3.8 and 6.3 points, respectively, on the VABS composite SS (group difference was nonsignificant). At 2-year follow-up, VABS composite SSs were stable for ESDM, but declined by 11.2 points for A/M (group difference was significant at p = 0.01). ADOS severity scores and RBS total scores did not differ between groups at either follow-up		[19]
Treatment group made greater gains than TAU group in measures of developmental ability (by 8.91 vs 2.41 months, respectively) and mental developmental index (8.83-point improvement vs 2-point decrease, respectively)		VABS composite improved for both groups, with treatment group (average gains of 10.92 months) gaining more than comparison group (average gains of 2.87 months). Both groups decreased in autism symptom severity with no significant group differences		[24]
There was significant progress in cognitive abilities at follow-up $(\eta^2 = 0.780)$, but no significant group differences	On the MSEL, receptive and expressive language SSs increased ($\eta^2 = 0.307$ and 0.314, respectively) with no group differences	VABS communication SSs increased for both groups ($\eta^2 = 0.276$). VABS motor skills SSs decreased for both groups ($\eta^2 = 0.320$). There were no group differences	Children with lower intake ADOS scores made more gains than those with higher intake ADOS scores in MSEL visual ($\eta^2 = 0.144$), receptive language ($\eta^2 = 0.075$) and expressive language ($\eta^2 = 0.264$) domains. Low ADOS group improved more in VABS communication ($\eta^2 = 0.282$), daily living ($\eta^2 = 0.102$) and socialization ($\eta^2 = 0.242$) domains	[25]
Mean IQ improved significantly by 16.1 points for total sample; there were no group IQ differences	Reynell [78] comprehension and expressive age equivalents improved by 7.2 and 6.5 points, respectively, for total sample with no group differences	VABS composite improved by 6.4 points for total sample. Scores for communication, socialization and motor subdomains increased by 7.6, 5.0 and 6.0 points, respectively. There was no significant change in daily living subdomain scores. There were no group differences	Visual–spatial IQ at intake predicted change scores in IQ (r = 0.38) and VABS composite (0.64)	[27]

	of predictors of outcome following early comprehensive behavioral/developmental interventions as repo nd systematic reviews published between 2005 and July 2012.	rted
Author (year)	Predictors of outcome/progress as reported in original reviews/meta-analyses	Ref.
Reichow (2012)	Higher pretreatment adaptive behavior skills associated with larger language abilities, adaptive behavior and IQ change and larger group differences in these domains Inclusion of parent training associated with larger adaptive behavior group differences. UCLA procedures-based training for supervisors was associated with greater IQ score increases Longer treatment duration associated with higher expressive and receptive language scores and larger adaptive behavior group differences	[4]
Peters-Scheffer <i>et al.</i> (2011)	Authors speculate that differences in outcomes could be due to quality of EIBI, intensity of supervision and characteristics of participants, but no data were reported	[15]
Eldevik <i>et al.</i> (2010)	Intensity of intervention predicted gains in both IQ and adaptive behavior Intake adaptive behavior and IQ only predicted gains in adaptive behavior	[3]
Makrygianni and Reed (2010)	Higher intake adaptive behavior abilities were associated with greater effectiveness of early intervention programs in improving language abilities and greater effectiveness than 'eclectic' programs in improving adaptive behavior abilities Intellectual and language abilities did not correlate with any of the effects Intensity was associated with higher gains in intellectual and adaptive behavior abilities and greater effectiveness compared with control programs for those abilities Effectiveness seemed to be independent of duration	[17]
Virués-Ortega (2010)	Language skills tended to benefit more from intervention duration and adaptive behavior more from intensity of intervention Effects of ABA were similar for clinic-based and parent-managed programs, with slightly better outcomes for clinic-based programs for IQ, nonverbal IQ and adaptive behavior Intensity and duration did not seem to be associated with progress	[9]
Howlin <i>et al.</i> (2009)	Initial IQ predicted later positive outcome in four studies, with no relationship in one study Initial language abilities associated with outcome in four out of seven studies One study reported that lower autism symptomatology was associated with better progress, another study that individuals with higher intake symptomatology were likely to show gains	[13]
Seida <i>et al.</i> (2009)	Parent training was reported to lead to better child communication	[12]
Reichow and Wolery (2009)	Results were mixed for the comparison of clinic- and parent-coordinated EIBI, with different studies reporting variable results Greatest gains in IQ may be moderated by training of supervisors using UCLA model, long intervention duration and high total hours of therapy	[16]
Rogers and Vismara (2008)	Higher initial IQ, lower intake age and lower social avoidance may be associated with better gains One study reported that dysmorphic features predicted treatment change	[11]
ABA: Applied behavioral a	nalysis; EIBI: Early intensive behavioral intervention; UCLA: University of California, Los Angeles.	

in the comparison group. Strain and Bovey compared two different delivery formats of the LEAP model (a full replication vs manual only) [20]. The full program resulted in gains comparable with those reported in other early intervention studies (IQ +9 standard points) and language functioning (+18 months), but there were significantly fewer gains in the manualonly group. Effect sizes of group differences were large and significant in these domains (effect size: 0.60-0.92) and were also large for social skills development (effect size: 1.22). The authors discussed the importance of treatment fidelity as a factor contributing to the group differences reported, as well as the challenges and duration of coaching necessary to achieve high levels of fidelity.

In terms of intensity or type of EIBI delivery, Fernell and colleagues found no differences in adaptive behavior or autism severity between intensive and nonintensive ABA-based groups [26], although there was little information on the intensity of the interventions. No differences were reported between clinic-directed and parent-managed EIBI in Hayward *et al.* [27], supporting earlier findings by Sallows and Graupner [28].

In summary, findings from the most recently published empirical studies indicate the potential value of interventions with a broader developmental and social base, such as ESDM and LEAP, although these programs still need to be evaluated relative to other early comprehensive behavioral programs of comparable intensity and quality. The findings also continue to indicate that children in EIBI interventions outperform their peers in 'eclectic' programs, although these continue to be poorly described and/or of lower quality and the results are not consistent across all studies or domains of functioning.

Factors related to outcome

Across all reviews and empirical studies evaluated, it is evident that large individual differences exist in response to treatment, and outcomes vary across children and different domains of functioning. A small number of the reviews have summarized findings on factors related to outcome (Table 4) [3,4,9,11-13,15-17], although it should be noted that most studies from which these summary results are drawn have explored factors associated with or predicting later outcomes using correlational or regression analyses. Very few have carried out any formal mediator or moderator analyses.

Child characteristics

Preintervention cognitive, language and, to some extent, adaptive behavior levels are among the most consistent prognostic variables of treatment outcome (Table 4) [26,29-34]. Nevertheless, not all studies have found a relationship between these characteristics and response to intervention [17]. There is also evidence that the impact of child characteristics may vary according to the intervention followed. Makrygianni and Reed found that, for children receiving EIBI, higher adaptive behavior scores at intake predicted better language skills postintervention [17]; by contrast, for children receiving 'eclectic' programs in specialist nursery placements, a higher initial adaptive behavior level was associated with a greater improvement in adaptive behavior.

Although some reviews or recent studies suggest that a younger age at treatment onset is positively correlated with response to intervention [11,22,33], others have reported mixed or nonsignificant findings [3,9,35]. Few researchers have examined the possible impact of pretreatment autism severity or diagnostic subtype on outcome, although it seems that children with less severe autism symptoms or with diagnoses of pervasive developmental disorder not otherwise specified (PDD-NOS) or Asperger syndrome may respond more positively to treatment [22,25,33,34,36]. Nevertheless, other studies (e.g., [37]) have found that children with higher levels of autism symptoms at intake were likely to make greater progress. Zachor and Ben Itzchak [25] reported an intervention × severity interaction effect, with children with less severe autism symptoms improving more in Vineland communication and socialization when receiving 'eclectic' (largely developmental and TEACCH approaches) compared with ABA-based intervention ($\eta^2 = 0.56$ and 0.45). Klintwall and Eikeseth found that just under 50% of the variance in treatment gains after 1 year of EIBI could be explained by response to reinforcement, with children who responded more to social reinforcers making significantly greater progress than those who showed greater response to sensory or perceptual (automatic) reinforcers [38]. This study highlights the need systematically to explore other factors that may moderate outcome in addition to those traditionally investigated.

Family & other factors

Data on the impact of family, socioeconomic and cultural characteristics are limited and inconclusive [11]. Ben Itzchak and Zachor [33] found that having an older, higher educated mother, together with child's pretreatment autism severity and age, best predicted cognitive gains in preschool children after 1 year of intervention. They suggested that advanced maternal age and education may enable better implementation of interventions and/or more efficient child rearing. Others have found no relationship between these variables, or socioeconomic status, and treatment outcome [20,39,40]. Family stress was found to be negatively related to children's outcomes by Osborne et al. [41], but Rickards et al. [42] found that improvements were positively associated with higher family stress.

Intervention characteristics

In their meta-analysis, Makrygianni and Reed [17] concluded that EIBI intensity was associated with greater cognitive and adaptive behavior gains (see also [3,9]), while Reichow and Wolery [16] conducted moderator analyses indicating that gains in IQ were moderated by total hours of therapy. Others have found no relationship between intensity and treatment outcomes [22,26]. Howlin *et al.* noted that the gains achieved during EIBI tended to reduce after the first year [13], whilst Virués-Ortega suggested that treatment duration may be important for specific outcomes (e.g., language skills) [9]. At present, however, there is insufficient evidence to draw conclusions about the role of treatment duration.

Author (year)	Number of participants (diagnosis)	Follow-up	Intervention(s)	Age at intake; years (SD)	Intake IQ (SD)
Kovshoff <i>et al.</i> (2011)	41 (independent diagnosis of autism – meeting ADI-R criteria)	2 years after 24-month intensive intervention (i.e., 4 years post-treatment)	EIBI (Southampton Childhood Autism Program; n = 23; 14 university supervised and nine parent commissioned); and TAU (n = 18)	EIBI: 3 TAU: 3.2	EIBI: 61.43 (16.43) TAU: 63.83 (13.98)
Magiati <i>et al.</i> (2011)	36 (independent diagnosis of autism or ASD – meeting ADI-R criteria)	6–7 years after start of early intervention	Community-based largely parent-directed EIBI based on UCLA model but less frequent supervision; 'eclectic' treatment group received range of interventions (TEACCH, PECS, SLT, occupational therapy and specialist education); average intensity: 30 h/week; average duration: 58 months	3.4 (0.6)	64.4 (30.0)
Sallows and Graupner (2005)	23 (autism based on independent diagnosis using DSM-IV and ADI-R)	4 years	CD EIBI; using methods initially described by Lovaas <i>et al.</i> [79]; no aversives were used and additional procedures were also employed (i.e., [80]); PM EIBI with less supervision	CD: 2.77 (0.32) PM: 2.85 (0.42)	CD: 50.85 (10.6) PM: 52.10 (8.98)
Smith <i>et al.</i> (2000)	28 (independent diagnosis of autism or PDD-NOS)	4–5 years	EIBI IT (n = 15; 24.5 h/week of one-to-one treatment for 1 year, gradually reducing hours in next 1–2 years; independent site of UCLA YAP model relying initially on discrete trial format, then naturalistic instruction); and PT (n = 13; 3–9 months of 5 h/week parent training in EIBI at home)	IT: 3.01 (0.50) PT: 2.98 (0.45)	Autism: IT: 51.00 (13.94); PT: 50.71 (14.24) PDD-NOS: IT: 50.13 (9.11); PT: 50.67 (14.79)

Cognitive and/or educational outcomes	Communication and social outcomes	Adaptive behavior and/or autism severity/other outcomes	Predictors of long-term outcomes	Ref.
Group differences diluted during follow-up when baseline differences controlled for, but varied considerably between university-supervised and parent-commissioned subgroups, favoring the latter. IQ stable for parent- commissioned EIBI and comparison groups; decreased for university-supervised group. More EIBI children (61%) in mainstream education compared with TAU (22%)	More EIBI children (96%) able to score on Reynell Receptive Language Scale [78] than comparison (72%); no difference in expressive language. Raw, age-equivalent and SSs not reported	Adaptive behavior SSs decreased or remained stable for all groups; no group differences at follow-up. No group differences in behavioral problems	Higher initial skills (i.e., IQ and less severe ADI-R scores), higher treatment intensity and type of delivery model may have affected long-term outcomes and better maintenance of intervention in parent-commissioned subgroup	[44]
Age-equivalent scores increased by an average of 41 months; IQ scores decreased (-11 points). Most children were attending specialist facilities; six children in mainstream education (only one unsupported)	Expressive and receptive language increased by an average of 31 and 32 raw score points, respectively; 50% used phrase or sentence speech at follow-up (increase from 8% at initial assessment)	Age equivalent composite scores increased (by 23 months); standard composite scores decreased (by 21 SS points)	Initial child IQ, adaptive behavior and receptive language skills predicted long-term outcomes. No evidence that family socioeconomic status, intake age, intensity or type of intervention was related to outcomes	[46]
No differences between CD and PM groups. Average IQ for all 23 children increased from 51 to 76; 75% of children with intake IQ >55 achieved follow-up IQ of >85, while only 17% of those with intake IQ <50 did so	No group differences at follow-up; receptive language improved from 38.8 to 55.8 and 65.6 for the clinic- and parent- commissioned groups, respectively; expressive language changed little (from 48.2 to 56.2 at follow-up)	No group differences; significant gains in VABS communication (16 SS points) and socialization (15–18 SS points for the two subgroups) at 4-year follow-up, but not for daily living skills. Significant decreases in ADI-R social and communication raw score symptoms, but not in ritualistic behaviors	Parent-directed group had similar outcomes as clinic-directed group despite less supervision. Outcomes significantly better for rapid learners compared with moderate learners, thus previous rapid acquisition of skills is likely to predict better outcomes; ability to imitate was highly correlated with outcome in all domains. Pretreatment IQ and social communication scores also predicted post-treatment IQ. Number of intervention hours seemed less related to outcome than pretreatment variables	[28]
IT group (+16 IQ points) outperformed PT group (-0.5 IQ points) on IQ and visuospatial nonverbal IQ measures (+43 vs +28 points, respectively). More IT participants in regular education (with or without support) than PT group	IT group outperformed PT group in Reynell language developmental age scores (+29 vs +20 months in receptive and expressive language, respectively)	Vineland ABC scores remained stable for the IT group (-2 points) and decreased in the PT group (-7 points), but there were no significant group differences. Little difference between groups for parent- or teacher-reported behavioral problems. Parents in both groups favorably rated treatment quality, impact on family and staff-family relationships	No relationship between intake and follow-up IQ. Mastery of expressive labels may be associated with higher follow-up scores	[36]

Author (year)	Number of participants (diagnosis)	Follow-up	Intervention(s)	Age at intake; years (SD)	Intake IQ (SD)
McEachin <i>et al.</i> (1993)	38 (independent diagnosis of autism)	10 years (EIBI 5 years after end of treatment; 3 years after end of treatment for comparison group)	EIBI based on UCLA/YAP model; less intensive behavioral intervention control group	EIBI: 2.67 Control: 2.92	EIBI: 53 Control: 46

Table 5. Summary of empirical studies published up to July 2012 reporting on long-term outcomes of early comprehensive behaviorally/developmentally based interventions (>4 years after start of intervention) (cont.).

ABC: Adaptive behavior composite; ADI-R: Autism Diagnostic Interview-Revised; ASD: Autism spectrum disorder; CD: Clinic-directed management; ElBI: Early intensive behavioral intervention; IT: Intensive treatment; PM: Parent-managed treatment; PDD-NOS: Pervasive developmental disorder not otherwise specified; PECS: Picture Exchange Communication System; PT: Parent training; SD: Standard deviation; SLT: Speech language therapy; SS: Standard score; TAU: Treatment as usual; TEACCH: Treatment and Education of Autistic and Related Communication Handicapped Children; UCLA: University of California, Los Angeles; VABS: Vineland Adaptive Behavior Scales; YAP: Young Autism Project.

> With regards to the delivery model, some reviews indicate that clinic-, center- or universitydelivered programs may be more successful than parent-directed interventions [9,43], suggesting that their efficacy may be larger than their effectiveness in community settings, but this finding is inconsistent [16,26–28,44]. A small number of studies have also highlighted the importance of training, ongoing supervision and higher treatment quality/fidelity as factors relating to outcome [8,20].

Long-term outcomes

Although the short-term effects (1–3 years post-treatment) of early comprehensive behavioral programs are often positive, very few studies have reported on the outcome over longer periods. Five studies were identified for this article (see Table 5). The earlier studies by McEachin *et al.* [45] and Smith *et al.* [36] found that children in either intensive or clinic-directed EIBI outperformed their peers in less intensive or parentmanaged groups up to 5 years post-treatment. By contrast, Sallows and Graupner reported no differences between clinic-directed or parentmanaged EIBI groups after 4 years [28]. None of these studies included non-EIBI comparison groups.

More recently, Magiati *et al.* reported increases in age equivalent scores for cognitive and adaptive skills 5–6 years after the start of EIBI or 'eclectic' nursery-based interventions; however, standard scores did not improve [46]. There were no group differences in test scores and most children from both groups were being educated in specialist settings. Kovshoff *et al.* noted that the initial postintervention group differences had substantially decreased, and cognitive and adaptive behavior standard scores had generally either remained stable or decreased 2 years after the 24-month intervention program [44]. The parent-directed EIBI subgroup appeared to do better at maintaining the initial short-term gains, but this subgroup also had fewer autism symptoms, higher adaptive behavior and a trend towards higher IQ scores at intake.

In summary, the limited literature to date suggests that, following EIBI, children continue to make progress (as evidenced by reported increases in raw or age equivalent scores), but gains are often less than those achieved during the active treatment periods. However, data on longer-term progress are derived from very few studies with relatively small sample sizes. There are at present no data in support of claims [47–49] that access to EIBI programs results in a significantly reduced need for special services later in life.

Discussion

Many hundreds of papers have been published on the successful use of applied behavioral techniques, both in increasing skills and diminishing problem behaviors in individuals with ASD and other developmental disabilities, and it is evident that such methods are an important component of early comprehensive interventions for children with ASD. Recent reviews (Tables 1 & 2) also confirm that intensive comprehensive programs using ABA methods and techniques tend to be generally more effective than 'eclectic' programs or treatment as usual. The present paper aimed to provide a critical and comprehensive review of treatment outcomes of children with ASD following comprehensive interventions and, thus, focused on the effectiveness of such interventions. Odom and colleagues argued that analysis of intervention outcomes is

Cognitive and/or educational outcomes	Communication and social outcomes	Adaptive behavior and/or autism severity/other outcomes	Predictors of long-term outcomes	Ref.
EIBI group had higher mean IQ (84.5) than control (54.9). EIBI participants more likely to be placed in regular mainstream classes	Not reported	EIBI group scored higher on the VABS (mean ABC: 71.6) and had fewer maladaptive behaviors (mean: 10.6) than the control group (mean ABC: 45.7 and 17.1, respectively)	Not investigated	[45]

an important aspect of evaluating intervention programs, but a multidimensional evaluation of intervention programs is required for implementation and stakeholders' decision-making [50]. They systematically evaluated 30 USbased comprehensive intervention programs to determine those with the strongest evidence of 'model development', defined as high standards in operationalization and manualization, fidelity measurement, replication, empirical evidence, quality of research methodology and additional evidence from studies focused on intervention components, each rated on a 0-5-point scale. They reported that the University of California, Los Angeles (UCLA) EIBI model, LEAP and ESDM had fairly well-established evidence of model development, defined as receiving scores of 4 or 5 across at least four of the above dimensions. Two other ABA classroom-based programs (the May Institute and the Princeton Child Development Institute) also obtained high ratings in the domains assessed. The remaining 25 comprehensive programs reviewed received either mixed or low evaluation ratings. However, in the 'real world' there continue to be considerable challenges in disseminating and implementing such strong 'model development' programs. Capacity, access, professionals' training and expertise, funding resources and many other barriers have been reported [18,41,51-54], and for most young children with ASD an 'eclectic' approach to education is the norm. Unfortunately, there is currently little evidence to support the effectiveness of such 'eclectic' approaches or the components these should include. It is possible that a number of such 'eclectic' intervention programs could involve systematic and individualized integration and implementation of a number of evidence-based approaches and strategies, some of which may be highly manualized. However, how and why such strategies are chosen and how they are integrated with other approaches are, in most cases, not well described. Thus, a lack of description, limited fidelity and limited outcome reporting typically characterize 'eclectic' intervention efforts. Consequently, 'eclectic' treatment as usual and other comprehensive interventions with very weak evidence of model development [50] need to be described more systematically in order to explore which components, as well as which combinations of treatment components, may have a positive impact [55]. Some recent research studies evaluating early comprehensive interventions as implemented in community settings have been particularly informative in strengthening the research evidence for comprehensive interventions as implemented in real-life settings [20,22,29,30,56].

There is now a pressing need to explore the long-term effects of early intensive comprehensive behavioral and/or developmental interventions as well as to investigate whether these interventions can be equally effective for even younger children (i.e., <2 years of age [40]). Systematic exploration of mediators and moderators of outcome should also be a research priority [57]. A further target for future research is the inclusion of a much broader range of outcome measures. In addition to standard measures, such as IQ, adaptive behavior, language and diagnostic scores, assessments of child psychopathology and challenging behaviors, peer relationships, social skills, parental competence and satisfaction, family quality of life and stress levels, and negative impact of intervention should routinely be assessed (see [43] for a good example and [58,59] for reviews).

In a meta-analysis, Ma reported on the five most effective (mean effect size: >0.9) behavioral intervention strategies for children with ASD (priming, self-control, training, positive reinforcement for desirable behaviors plus punishment for undesirable behaviors and presenting preferential activities/reinforcers) [60]. Such efforts to understand the impact of specific strategies could improve current interventions by providing evidence for the most effective 'ingredients'. In addition, even with the highest quality interventions, treatment fidelity should be routinely monitored and reported (see [20,28,61] for good examples). Finally, studies employing multiple time point assessments are required to determine the optimal length of intervention in terms of cost-benefit. The development and evaluation of shorter interventions offering significant benefits to greater numbers of children would be welcomed by governments and families in times of economic restrictions.

Conclusion & future perspective

Recent systematic reviews, meta-analyses and empirical studies published since 2005 collectively provide evidence that, despite continuing methodological limitations, early comprehensive, behaviorally and/or developmentally based interventions, which include EIBI, ESDM and LEAP, are effective for many young children with ASD and are likely to be more successful than standard care or 'eclectic' approaches. However, there are still no comparative evaluations of these different programs. For example, is the developmentally based ESDM more, less or equally effective for particular children and families or in certain domains of functioning compared with UCLA EIBI programs? Similarly, we do not know whether other less intensive but nevertheless widely used comprehensive programs, such as TEACCH, may be effective, as they have limited documented empirical evidence. To evaluate their potential in meeting the needs of young children with autism and their families, 'eclectic' approaches to early intervention must be much more clearly defined, systematic and theory-driven, integrating "philosophy, theory and related principles as well as techniques" that can be empirically tested [62]. Increasing access to and improving implementation of evidencebased interventions for more young children with ASD as well as increasing consistency and quality of service delivery should become priorities for researchers, professionals and service providers.

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References

- Howlin P, Charman T. Autism spectrum disorders: lifetime course and interventions. In: *The Sage Handbook of Developmental Disorders*. Howlin P, Charman T, Ghaziuddin M (Eds). Sage, London, UK, 307–328 (2011).
- 2 Lovaas OI. Behavioral treatment and normal educational and intellectual functioning in autistic children. J. Consult. Clin. Psychol. 55, 3–9 (1987).
- 3 Eldevik S, Hastings R, Hughes J, Jahr E, Eikeseth S, Cross S. Using participant data to extend the evidence base for intensive behavioral intervention for children with autism. Am. J. Intellect. Dev. Disabil. 115, 381–405 (2010).
- 4 Reichow B. Overview of meta-analyses on early intensive behavioral intervention for young children with autism spectrum

disorders. J. Autism Dev. Disord. 42, 512–520 (2012).

- 5 Spreckley M, Boyd R. Efficacy of applied behavioral intervention in preschool children with autism for improving cognitive, language, and adaptive behavior: a systematic review and meta-analysis. *J. Pediatr.* 154, 338–344 (2009).
- 6 Ospina M, Seida J, Clark B *et al.* Behavioural and developmental interventions for autism spectrum disorder: a clinical systematic review. *PLoS ONE* 3, e3755 (2008).
- 7 Warren Z, McPheeters M, Sathe N, Foss-Feig J, Glasser A, Veenstra-VanderWeele J. A systematic review of early intensive intervention for autism spectrum disorders. *Pediatrics* 127, e1303 (2011).
- 8 Eikeseth S. Outcome of comprehensive psycho-educational interventions for young

children with autism. *Res. Dev. Disabil.* 30, 158–178 (2009).

- 9 Virués-Ortega J. Applied behavior analytic intervention for autism in early childhood: meta-analysis, meta-regression and doseresponse meta-analysis of multiple outcomes. *Clin. Psychol. Rev.* 30, 387–399 (2010).
- 10 Eldevik S, Hastings R, Hughes J, Jahr E, Eikeseth S, Cross S. Meta-analysis of early intensive behavioral intervention for children with autism. *J. Clin. Child Adolesc. Psychol.* 38, 439–450 (2009).
- Rogers S, Vismara L. Evidence-based comprehensive treatments for early autism. J. Clin. Child Adolesc. Psychol. 37, 8–38 (2008).
- 12 Seida JK, Ospina MB, Karkhaneh M, Hartling L, Smith V, Clark B. Systematic reviews of psychosocial interventions for autism: an umbrella review. *Dev. Med. Child Neurol.* 51, 95–104 (2009).

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- 13 Howlin P, Magiati I, Charman T. Systematic review of early intensive behavioral interventions for children with autism. Am. J. Intellect. Dev. Disabil. 114, 23–41 (2009).
- 14 Kuppens S, Onghena P. Sequential metaanalysis to determine the sufficiency of cumulative knowledge: the case of early intensive behavioral intervention for children with autism spectrum disorders. *Res. Autism Spectr. Disord.* 6, 168–176 (2012).
- 15 Peters-Scheffer N, Didden R, Korzilius H, Sturmey P. A meta-analytic study on the effectiveness of comprehensive ABA-based early intervention programs for children with autism spectrum disorders. *Res. Autism Spectr. Disord.* 5, 60–69 (2011).
- 16 Reichow B, Wolery M. Comprehensive synthesis of early intensive behavioral interventions for young children with autism based on the UCLA young autism project model. J. Autism Dev. Disord. 39, 23–41 (2009).
- 17 Makrygianni M, Reed P. A meta-analytic review of the effectiveness of behavioural early intervention programs for children with autistic spectrum disorders. *Res. Autism Spectr. Disord.* 4, 577–593 (2010).
- 18 National Autism Center National Standards Report. The National Standards Project – Addressing the Need for Evidence-Based Practice Guidelines for Autism Spectrum Disorders. Randolph, MA, USA (2009).
- Dawson G, Rogers S, Munson J et al. Randomized, controlled trial of an intervention for toddlers with autism: the Early Start Denver Model. *Pediatrics* 125, e17 (2010).
- 20 Strain PS, Bovey EH 2nd. Randomized, controlled trial of the LEAP model of early intervention for young children with autism spectrum disorders. *Top. Early Child. Spec. Educ.* 31, 133–154 (2011).
- 21 Eikeseth S, Klintwall L, Jahr E, Karlsson P. Outcome for children with autism receiving early and intensive behavioral intervention in mainstream preschool and kindergarten settings. *Res. Autism Spectr. Disord.* 6, 829–835 (2012).
- 22 Eldevik S, Hastings RP, Jahr E, Hughes JC. Outcomes of behavioral intervention for children with autism in mainstream preschool settings. *J. Autism Dev. Disord.* 42, 210–220 (2012).
- 23 Grindle CF, Hastings RP, Saville M *et al.* Outcomes of a behavioral education model for children with autism in a mainstream school setting. *Behav. Modif.* 36, 298–319 (2012).

- 24 Peters-Scheffer N, Didden R, Mulders M, Korzilius H. Low intensity behavioral treatment supplementing preschool services for young children with autism spectrum disorders and severe to mild intellectual disability. *Res. Dev. Disabil.* 31, 1678–1684 (2010).
- 25 Zachor DA, Ben Itzchak E. Treatment approach, autism severity and intervention outcomes in young children. *Res. Autism Spectr. Disord.* 4, 425–432 (2010).
- 26 Fernell E, Hedvall Å, Westerlund J et al. Early intervention in 208 Swedish preschoolers with autism spectrum disorder. A prospective naturalistic study. *Res. Dev. Disabil.* 32, 2092–2101 (2011).
- 27 Hayward D, Eikeseth S, Gale C, Morgan S. Assessing progress during treatment for young children with autism receiving intensive behavioural interventions. *Autism* 13, 613–633 (2009).
- 28 Sallows GO, Graupner TD. Intensive behavioral treatment for children with autism: four-year outcome and predictors. *Am. J. Ment. Retard.* 110, 417–438 (2005).
- 29 Perry A, Cummings A, Dunn Geier J et al. Effectiveness of intensive behavioral intervention in a large, community-based program. Res. Autism Spectr. Disord. 2, 621–642 (2008).
- 30 Smith IM, Koegel RL, Koegel LK, Openden DA, Fossum KL, Bryson SE. Effectiveness of a novel community-based early intervention model for children with autistic spectrum disorder. Am. J. Intellect. Dev. Disabil. 115, 504–523 (2010).
- 31 Ben Itzchak E, Lahat E, Burgin R, Zachor AD. Cognitive, behavior and intervention outcome in young children with autism. *Res. Dev. Disabil.* 29, 447–458 (2008).
- 32 Ben Itzchak E, Zachor DA. Change in autism classification with early intervention: predictors and outcomes. *Res. Autism Spectr. Disord.* 3, 967–976 (2009).
- 33 Ben Itzchak E, Zachor DA. Who benefits from early intervention in autism spectrum disorders? *Res. Autism Spectr. Disord.* 5, 345–350 (2011).
- 34 Darrou C, Pry R, Pernon E, Michelon C, Aussilloux C, Baghdadli A. Outcome of young children with autism: does the amount of intervention influence developmental trajectories? *Autism* 14, 663–677 (2010).
- 35 Technology Evaluation Center. Special report: early intensive behavioral intervention based on applied behavior analysis among children with autism spectrum disorders. Assess. Program 23, 1–62 (2009).

- 36 Smith T, Groen A, Wynn J. Randomized trial of intensive early intervention for children with pervasive developmental disorder. *Am. J. Ment. Retard.* 105, 269–285 (2000).
- Remington B, Hastings RP, Kovshoff H.
 Early intensive behavioral intervention: outcomes for children with autism and their parents after two years. *Am. J. Ment. Retard.* 112, 418–438 (2007).
- 38 Klintwall L, Eikeseth S. Number and controllability of reinforcers as predictors of individual outcome for children with autism receiving early and intensive behavioral intervention: a preliminary study. *Res. Autism Spectr. Disord.* 6, 493–499 (2012).
- 39 Magiati I, Charman T, Howlin P. A two-year prospective follow-up study of communitybased early intensive behavioural intervention and specialist nursery provision for children with autism spectrum disorders. J. Child Psychol. Psychiatry 48, 803–812 (2007).
- 40 Turner LM, Stone WL. Variability in outcome for children with an ASD diagnosis at age 2. *J. Child Psychol. Psychiatry* 48, 793–802 (2007).
- 41 Osborne LA, McHugh L, Saunders J, Reed P. Parenting stress reduces the effectiveness of early teaching interventions for autistic spectrum disorders. *J. Autism Dev. Disord.* 38, 1092–1103 (2008).
- 42 Rickards AL, Walstab JE, Wright-Rossi RA, Simpson J, Reddihough DS. One-year followup of the outcome of a randomized controlled trial of a home-based intervention program for children with autism and developmental delay and their families. *Child Care Health Dev.* 35, 593–602 (2009).
- 43 Roberts J, Williams K, Carter M et al. A randomised controlled trial of two early intervention programs for young children with autism: centre-based with parent program and home-based. *Res. Autism Spectr. Disord.* 5, 1553–1566 (2011).
- 44 Kovshoff H, Hastings RP, Remington B. Two-year outcomes for children with autism after the cessation of early intensive behavioral intervention. *Behav. Modif.* 35, 427–450 (2011).
- 45 McEachin JJ, Smith T, Lovaas OI. Long-term outcome for children with autism who received early intensive behavioral treatment. *Am. J. Ment. Retard.* 97, 359–372 (1993).
- 46 Magiati I, Moss J, Charman T, Howlin P. Patterns of change in children with autism spectrum disorders who received community based comprehensive interventions in their pre-school years: a seven year follow-up study. *Res. Autism Spectr. Disord.* 5, 1016–1027 (2011).

- 47 Chasson GS, Harris GE, Neely WJ. Cost comparison of early intensive behavioral intervention and special education for children with autism. *J. Child. Fam. Stud.* 16, 401–413 (2007).
- 48 Jacobson JW, Mulick JA, Green G. Costbenefit estimates for early intensive behavioral intervention for young children with autism – general model and single state case. *Behav. Intervent.* 13, 201–226 (1998).
- 49 Motiwala SS, Gupta S, Lilly MB, Ungar WJ, Coyte PC. The cost-effectiveness of expanding intensive behavioural intervention to all autistic children in Ontario. *Healthc. Policy* 1, 135–151 (2006).
- 50 Odom SL, Boyd BA, Hall LJ, Hume K. Evaluation of comprehensive treatment models for individuals with autism spectrum disorders. J. Autism Dev. Disord. 40, 425–436 (2010).
- 51 Boyd BA, Odom SL, Humphreys BP, Sam AM. Infants and toddlers with autism spectrum disorder: early identification and early intervention. *J. Early Interv.* 32, 75–98 (2010).
- 52 Stahmer AC. The basic structure of community early intervention programs for children with autism: provider descriptions. *J. Autism Dev. Disord.* 37, 1344–1355 (2007).
- 53 Hebbler K, Spiker D, Bailey D *et al.* Early intervention for infants and toddlers with disabilities and their families: participants, services and outcomes. *Final Report of the National Early Intervention Longitudinal Study (NEILS).* SRI International, CA, USA (2007).
- 54 National Research Council. *Educating Children with Autism*. The National Academies Press, Washington, DC, USA (2001).
- 55 Lechago SA, Carr JE. Recommendations for reporting independent variables in outcome studies of early and intensive behavioral intervention for autism. *Behav. Modif.* 32, 489–503 (2008).
- 56 Reed P, Osborne LA, Corness M. Effectiveness of special nursery provision for children with autism spectrum disorders. *Autism* 14, 67–82 (2010).
- 57 Yoder P, Compton D. Identifying predictors of treatment response. *Ment. Retard Dev. Disabil. Res. Rev.* 10, 162–168 (2004).

- 58 Gould E, Dixon DR, Najdowski AC, Smith MN, Tarbox J. A review of assessments for determining the content of early intensive behavioral intervention programs for autism spectrum disorders. *Res. Autism Spectr. Disord.* 5, 990–1002 (2011).
- 59 Matson JL. Determining treatment outcome in early intervention programs for autism spectrum disorders: a critical analysis of measurement issues in learning based interventions. *Res. Dev. Disabil.* 28, 207–218 (2007).
- 60 Ma H-H. The effectiveness of intervention on the behavior of individuals with autism: a meta-analysis using percentage of data points exceeding the median of baseline phase (PEM). *Behav. Modif.* 33, 339–359 (2009).
- 61 Hume K, Boyd B, McBee M et al. Assessing implementation of comprehensive treatment models for young children with ASD: reliability and validity of two measures. *Res. Autism Spectr. Disord.* 5, 1430–1440 (2011).
- 62 Patterson CH. Foundations for a systematic eclectic psychotherapy. *Psychother. Theory Res. Pract. Train.* 26, 427–435 (1989).
- 63 Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J. Consult. Clin. Psychol. 59, 12–19 (1991).
- 64 Green G, Brennan LC, Fein D. Intensive behavioral treatment for a toddler at high risk for autism. *Behav. Modif.* 26, 69–102 (2002).
- 65 Reichow B, Volkmar FR, Cicchetti DV. Development of the evaluative method for evaluating and determining evidence based practices in autism. *J. Autism Dev. Disord.* 39, 1311–1319 (2008).
- 66 Lord C, Rutter M, Le Couteur A. Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. J. Autism Dev. Disord. 24, 659–685 (1994).
- 67 Lord C, Rutter M, DiLavore PC, Risi S. Autism Diagnostic Observation Schedule. Western Psychological Services, CA, USA (1999).
- 68 Making A Difference: Behavioral Intervention for Autism. Maurice C, Green G, Foxx RM (Eds). Pro-Ed, TX, USA (2001).

- 69 Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomized and non-randomized studies of health care interventions. J. Epidemiol. Community Health 52, 377–384 (1998).
- 70 Sparrow SS, Balla DA, Cicchetti DV. Vineland Adaptive Behavior Scales. American Guidance Service, Circle Pines, MN, USA (1984).
- 71 Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro Scale for rating quality of randomized controlled trials. *Phys. Ther.* 83, 713–721 (2003).
- 72 Nathan P, Gorman JM. A Guide to Treatments That Work. Oxford University Press, NY, USA (2002).
- 73 Chambless DL, Hollon SD. Defining empirically supported therapies. J. Consult. Clin. Psychol. 66, 7–18 (1998).
- 74 Chambless DL, Sanderson WC, Shoham V et al. An update on empirically validated therapies. *Clin. Psychol.* 49, 5–18 (1996).
- 75 Oxman AD, Guyatt GH. Validation of an index of the quality of review articles. *J. Clin. Epidemiol.* 44, 1271–1278 (1991).
- 76 Lovaas OI. Teaching Individuals with Developmental Delays: Basic Intervention Techniques. Pro-Ed, TX, USA (2003).
- 77 Mullen EM. Mullen Scales of Early Learning. American Guidance Service, MN, USA (1995).
- 78 Edwards S, Fletcher P, Garman M, Hughes A, Letts C, Sinka I. *The Reynell Developmental* Language Scales III: The University of Reading Edition. NFER-Nelson, Berkshire, UK (1997).
- 79 Lovaas OI, Ackerman AB, Alexander D, Firestone P, Perkins J, Young D. *Teaching Developmentally Disabled Children: Theme Book.* Pro-Ed, TX, USA (1981).
- 80 Behavioral Intervention for Young Children with Autism: A Manual for Parents and Professionals. Maurice C, Green G, Luce SC (Eds). Pro-Ed, TX, USA (1996).

Website

 101 Agency for Healthcare Research and Quality. Effective healthcare program. http://effectivehealthcare.ahrq.gov/ehc/ products/106/656/CER26_Autism_ Report_04-14-2011.pdf