

# Early Behavioral Interventions for Children with Autism Spectrum Disorder in Routine Clinical Care: A Systematic Review and Meta-analysis

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## Author note

Conflict of interest: Maj-Britt Posserud holds a position at the scientific advisory board for Takeda regarding a slow-release formulation of melatonin for children with ASD. No other potential conflict of interest was reported for any of the other authors.

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## **Contributors**

LGÖ designed the meta-analysis and together with GJW wrote the protocol. GJW conducted literature searches in collaboration with an academic librarian. KWF, MBP, and UN contributed in the screening process, the extraction of data, and writing of the paper. LGÖ wrote the coding scheme, meta-analyzed the included studies, and wrote the first draft of methods and results. GJW and LGÖ rated the methodology, and Risk of Bias of the included studies. GJW wrote the first draft of the introduction and discussion. All authors have approved the final manuscript.

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## **Abstract**

The current paper systematically reviews and meta-analyses the effectiveness of early behavioral interventions (BI) for children with autism spectrum disorder (ASD) in routine clinical care. The effectiveness of BI, methodological study quality, and moderators of treatment outcome were examined and benchmarked with efficacy studies. The quality of the evidence was assessed with the Cochrane risk of bias tool. Twenty-nine studies were included, comprising 1422 participants. Medium to large within-group effect sizes ( $g = 0.76-1.27$ ) were found post-treatment for the outcome domains adaptive behavior, cognition, communication, and socialization, with large average effect size at post ( $g = 0.94$ ) and at follow-up ( $g = 1.08$ ). Comparison of effectiveness and efficacy studies showed that evidence-based early BI in routine clinical care yielded effects comparable to university research settings. The limitations include potential language and publication bias. The findings support evidence-based behavioral treatments delivered in routine clinical care as efficacious in reducing ASD symptoms. PROSPERO registration: ID CRD42020212833.

*Keywords:* Autism spectrum disorders, routine care; effectiveness, early behavior interventions, children, meta-analysis

*Public Health Statements:* Early behavioral interventions for autism spectrum disorders in children treated in routine clinical care was found efficacious in reducing symptoms within the outcome domains adaptive behavior, cognition, communication, and socialization, with medium to large within-group effect sizes at post-treatment and follow-up. The outcome of effectiveness studies was similar to that of efficacy studies. Our findings suggest that clinicians and patients can be confident about the effectiveness of early behavioral interventions with already established efficacy when delivered in routine clinical care. As treatment effects are not lost when evidence-based treatment programs are

transported from research clinics to routine clinical care, further implementation of evidence-based interventions is needed in routine clinical care for children with autism disorders.

## **Early Behavioral Interventions for Children with Autism Spectrum Disorder in Routine Clinical Care: A Systematic Review and Meta-analysis**

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by challenges in social interaction, communication, as well as restricted and repetitive interests or behaviors (American Psychiatric Association, 2013). ASD usually emerges in childhood, and prevalence estimates indicate that ASD affects more than 0.6 % of children (Elsabbagh et al., 2012). However, more recent studies have reported prevalence rates between 1.0-1.9% (Maenner et al., 2020; Posserud et al., 2021). Individuals with ASD are highly heterogeneous with diverse clinical manifestations, behavioral phenotypes, and cognitive functioning levels (Baio et al., 2018; Lord et al., 2018). A significant proportion of individuals with ASD have challenges in social function, communication, and adaptive functioning throughout life (Magiati et al., 2014). However, it is commonly acknowledged that early intervention can alleviate these challenges and mitigate core and associated ASD features (Smith & Iadarola, 2015).

Early intervention programs targeting ASD aim to enhance functioning in daily life in children with ASD. Several systematic reviews and meta-analyses of studies on early intervention programs for ASD have been published (e.g., Nevill et al., 2018; Rodgers et al., 2021; Sandbank et al., 2020). Because the field is diverse, these evaluation studies have varied in the key methodological features they considered, including treatment format, dose and intensity, and outcome measures. However, this variability challenges the interpretation and generalization of findings. A key challenge to summarizing existing evidence is that the reviewed intervention programs vary considerably in terms of theoretical frameworks, and of particular importance, in levels of scientific evidence. Some early intervention programs have been associated with

subsequent improvements in communication, language, cognition, and/or adaptive behavior, and may also affect long-term outcomes (Orinstein et al., 2014). There have been substantial advances in early detection and diagnosis of ASD in recent years, and the need for evidence-based early interventions has increased. Furthermore, the increasing empirical support for some early interventions highlights the necessity of a meta-analysis of evidence-based early interventions for children with ASD.

Systematic reviews and meta-analyses have identified applied behavior analysis (ABA), and developmental social-pragmatic (DSP) models as the best supported interventions for children with ASD (Rogers & Vismara, 2008; Smith & Iadarola, 2015). Individual, comprehensive ABA is commonly referred to as early intensive behavioral intervention (EIBI). EIBI is a structured teaching approach for children with ASD that is recommended to start before the age of five years (Lovaas, 1987; Smith, 2010). Key elements include highly specialized, individualized services for two or more years, the use of specific teaching procedures and behavioral strategies, supervision by ABA trained personnel, a 1:1 child to trainer ratio, and implementation in settings like home or school for 25+ hours/week (Lovaas, 1987; Smith, 2011). Complex tasks and skills are broken down into small steps and taught systematically. The structure of the intervention strategies is gradually reduced with the goal to improve the child's functioning in everyday life situations. In developmental social-pragmatic models (DSP), the main theoretical principle is that the core ASD feature is difficulties in reciprocal social interaction, leading to a multitude of downstream challenges with communication, functioning, and development (Mundy & Crowson, 1997). Studies using EIBI and DSP interventions have reported efficacy and clinical utility, with reductions in symptom severity, and improvement in adaptive behavior, cognitive functioning, and communication (Smith & Iadarola, 2015).

In the most recent Evidence Based Update for Autism Spectrum Disorder, Smith and Iadarola (2015) evaluated psychological and behavioral interventions for children with ASD, under the age of five years. Two interventions were identified as well-established and three as probably efficacious. Interventions with well-established efficacy were individual, comprehensive ABA, and teacher-implemented, focused ABA+DSP. The interventions evaluated as probably efficacious were individual, focused ABA for alternative communication systems, individual, focused ABA in combination with DSP, and focused DSP parent training. It is encouraging that an increasing number of methodologically sound early intervention studies are being carried out for children with ASD, and that several interventions have empirical support. However, more attention should be directed at investigations of clinical effectiveness, i.e., how the interventions with established efficacy such as early behavioral interventions perform when delivered in routine clinical care (Lake et al., 2020; Nahmias et al., 2019; Wood et al., 2015).

The majority of the studies evaluating early interventions for children with ASD have been efficacy studies conducted in controlled research settings (Nahmias et al., 2019). Important differences between research clinics and routine clinical care regarding patients, therapists, and treatment contexts may impact the generalizability of results from efficacy studies to routine clinical care (Weisz, Ng, et al., 2013; Weisz, Ugueto, et al., 2013). For example, in efficacy research the intervention is tested with a methodologically stringent procedure to ensure high internal validity. Furthermore, the clinicians are often well trained and supervised and deliver the intervention with high fidelity (Bauer et al., 2015; Weisz, Ng, et al., 2013). Effectiveness trials, on the other hand, evaluate whether an intervention produces good effects under “real world” conditions such as routine clinical care. In these studies, the samples are often more heterogeneous, the training and supervision of clinicians vary



more than in efficacy trials, and the delivery of the intervention provided is not typically implemented and monitored with the same level of fidelity as in university research settings (Hunsley, 2007; Hunsley & Lee, 2007). Such differences between university settings and routine clinical care suggest that findings obtained in university research settings may not be directly transferable to clinical practice. Routine clinical care is a crucial service site where the majority of children with ASD will receive their mental health services (Brookman-Frazee et al., 2010). It is important for clinicians to know what outcomes to expect from empirically supported treatments of ASD when they are delivered in routine clinical practice, and how results compare with outcomes obtained in specialized university research settings.

Previous meta-analyses comparing studies from routine clinical care to efficacy studies have shown different results for different disorders. Two recent meta-analyses of effectiveness studies for children and adolescents with internalizing disorders (Wergeland et al., 2021) and externalizing disorders (Riise et al., 2021), respectively, reported treatment outcomes in routine clinical care that were comparable to those in university settings. Contrary to this, for ASD, a recent meta-analysis of studies of community-based early intervention programs found smaller effect sizes for community-based studies than for university-based clinical trials (Nahmias et al., 2019), indicating a gap between research settings and routine clinical care for ASD interventions. However, an updated meta-analysis is warranted due to some limitations in the Nahmias et al., (2019) review. Nahmias et al. (2019) included a wide range of interventions, not limiting the meta-analysis to interventions with established evidence. Furthermore, the comparison between university-based trials and routine clinical care in Nahmias et al. (2019) is questionable as four of the five university-based trials (Cohen et al., 2006; Howard et al., 2005; Magiati et al., 2007; Remington et al., 2009) in the systematic review by Reichow et al. (2012) that were used as comparison were included as “community-based early intervention studies” in

the Nahmias meta-analysis. This means that the comparison is flawed since these studies are counted in both categories of studies. Finally, Nahmias et al. used within-group effect size whereas Reichow et al. used between-group effect size, making the comparison of results challenging. These factors make an update about the current state of effectiveness of evidence-based early behavioral interventions for children with ASD in routine clinical care warranted.

The present study aims to provide a meta-analysis of the effectiveness of early behavioral interventions considered well-established (level 1) or probably efficacious (level 2) according to Smith and Iadarola (2015) for children with ASD treated in routine clinical care. We have included studies investigating the effectiveness of empirically supported treatment programs, delivered by practicing clinicians in routine clinical care, to patients referred for treatment through usual clinical routes. In the present meta-analysis, efficacy studies were directly meta-analyzed in comparison with effectiveness studies, using the same effect size measure. Our aims were threefold. First, to examine the effectiveness of evidence-based early behavioral interventions for ASD in young children (i.e., samples with a mean age below 5 years). Second, to evaluate the methodological quality of the effectiveness studies, and investigate potential moderators of treatment outcome. Third, to examine how the treatments delivered in routine clinical care fare in comparison to efficacy studies, in order to evaluate if early behavioral interventions in effectiveness studies lead to equivalent effect sizes as in efficacy studies.

## **Methods**

The protocol for this meta-analysis was pre-registered at PROSPERO with ID [CRD42020212833](#). The meta-analysis was conducted according to the PRISMA guidelines (Liberati et al., 2009), and reported according to AMSTAR 2 (Shea et al., 2017), see Supplement S8 and

S9. Two independent raters were involved in the process of selecting studies, data extraction and categorization. The meta-analysis was designed according to the PICOS acronym in the following way:

- Population: children with ASD.
- Intervention: Behavioral intervention (BI) for ASD delivered in routine clinical care. For the search, the umbrella construct CBT was used, to include cognitive, behavioral, and combined treatments (CBT and BI).
- Comparison: within-group change, i.e., pre vs. post-data (and pre vs. follow-up data).
- Outcome: primary continuous measure.
- Study design: randomized controlled trials (RCTs) and open trials.

### **Literature Search**

Studies were identified by a systematic and comprehensive literature search of electronic databases and scanning of the included articles' reference lists. The search was applied to Ovid MEDLINE, Embase OVID, PsycINFO, ERIC, and Web of Science from the start of the data bases to September 1<sup>st</sup>, 2020. An updated search was done April 7<sup>th</sup>, 2021. The list of search terms utilized to identify potential studies were generated by all five authors in collaboration with a university librarian, who conducted the database searches. For search strategy for Ovid MEDLINE, Embase OVID, PsychINFO, ERIC, and Web of Science, see the Supplement S1.

Three author pairs read the titles and abstract of all the papers from this initial search. When there was an indication of a group of patients receiving early BI in a non-university setting, the full-text was retrieved. The reference lists in the retrieved articles were then checked. In total,

267 full-text articles were considered for inclusion. The final decision for article inclusion was made using a stricter set of inclusion and exclusion criteria. The full text articles were read by author pairs and disagreements were resolved by consensus discussion. It was determined that 29 studies (presented in 33 articles) could be included.

### ***Inclusion Criteria***

In order to be included in the review and meta-analysis a study had to:

1. Be published, or in press, in an English language journal.
2. Have participants diagnosed with some form of ASD according to DSM or ICD.
3. Be testing a form of early BI for ASD classified as well-established or probably efficacious in the evidence base update review of Smith and Iadarola (2015).
4. Have participants referred for treatment through usual clinical routes (i.e., not recruitment via advertisements).
5. Be an effectiveness study, i.e., carried out in a non-university setting such as routine clinical care, preschools, or homes.
6. Have therapists/supervisors who are practicing clinicians with regular caseload for whom provision of service is a substantial part of the job (Shadish et al., 2000).
7. Have a treated sample consisting of at least 10 participants.
8. Have a maximum mean participant age of 60 months (i.e., 5 years).
9. Provide a continuous measure of the principal disorder treated.

### ***Exclusion Criteria***

1. The study is a secondary analysis of a previously published study. Separate follow-up studies to the basic study are included to provide follow-up data.
2. The study is an evaluation of a service where the results for individual disorders cannot be extracted.
3. The study is testing a combination of early behavioral intervention and pharmacological treatment and 100% of the participants in that condition receive both treatments.

Figure 1 shows a flowchart of the inclusion of studies in the present meta-analysis. For references to included studies, these are marked with an asterisk in the reference list. For references to studies excluded in the meta-analysis, see Supplement S2.

### ***Potential Categorical Moderators***

To include any potential categorical or continuous moderator in the analysis we required that at least 70% of the studies provided information on that variable. With lower proportions it is questionable if the information extracted is representative of the entire body of studies.

### ***Type of Study and Statistical Analysis***

Type of study was either RCT (when an early BI-condition was compared with some kind of control/comparison condition) or open trial (when only an early BI-condition was used in the study). Statistical analysis was categorized as intent-to-treat if all randomized or starting participants were included in the statistical analysis or completers if dropouts were deleted.

### ***Target of Treatment and Setting***

Treatments were classified according to the description in the study (i.e., ABA, EIBI, Joint Attention Mediated Learning). However, it was not possible to classify the various components included in the interventions as the information in the studies most often did not provide this level of detail. Instead, we categorized the primary recipient of treatment as: child, or child and parent (if parents were trained in applying various treatment techniques), and treatment setting as: clinic, community center, home, preschool, or home + preschool. We also categorized the different target areas of the intervention (Supplement S6).

### ***Continent***

The country in which the study was carried out was categorized as North America, South America, Europe, Asia, Australia, or Africa.

### **Potential Continuous Moderators**

The following continuous measures on which at least 70% of the studies provided information were used as potential moderators: year of publication, number of participants in the study, percent boys, mean age (in months), pre-treatment severity (calculated as percentage of the maximum score of the rating scale applied), methodology score (see below), risk-of-bias score (see below), months of treatment, hours of treatment/week, and percentage attrition in the treatment condition.

We also extracted information on a few other categorical and continuous variables, but these did not reach the 70% criterion and were excluded. A coding scheme and manual including the variables of interest were developed. The data extraction and categorizations were done independently by author pairs and any disagreements were solved after discussion.

### **Methodological Quality**

### ***The Psychotherapy Outcome Study Methodology Rating Scale (POMRS)***

Methodological quality was assessed using the POMRS (Öst, 2008). The scale consists of 22 items covering various important aspects of the methodology in psychotherapy outcome research. Each item is rated as 0 = poor, 1 = fair, and 2 = good, and each step has a short qualitative description. Possible range is 0-44 points. Since not all items were applicable to all studies the total score was recalculated as a percentage of the maximum score possible for the individual study. The internal consistency of the scale was good with a McDonald's  $\omega$  of .80. The inter-rater reliability of the scale (between the first and the last author), based on 20% randomly selected and blindly rated studies was ICC = 0.92 (95% CI 0.49-0.99,  $p = 0.009$ ) which is excellent according to Cicchetti (1994).

### ***Risk-of-Bias***

The Cochrane Collaboration tool for assessing risk-of-bias (Sterne et al., 2019) was used, and the following domains were rated: the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. A high risk-of-bias in a domain was given 1 point, an unclear risk 0.5, and a low risk 0 point. Across the five domains the total score could vary between 0 and 5, with higher scores indicating higher risk-of-bias. Inter-rater reliability was assessed between the first and the last author based on 20% randomly selected and masked rated studies. This yielded an intra-class correlation, ICC = 0.96 (95% CI 0.32-0.99,  $p < 0.001$ ) which is excellent according to Cicchetti (1994).

### **Effect Size Measures**

In accordance with previous reviews and meta-analyses (Nahmias et al., 2019; Smith & Iadarola, 2015) we extracted data on the following constructs commonly assessed in ASD studies:

1. *Adaptive behavior* (e.g., Adaptive Behavior Assessment System-II; Harrison & Oakland, 2003; Vineland Adaptive Behavior Scales-Adaptive Behavior Composite; Sparrow, Balla, & Cicchetti, 1985; Sparrow, Cicchetti, & Balla, 2005).
2. *Cognitive* (e.g., Bayley Scales of Infant Development, Second Edition; Bayley, 1993; Mullen Scales of Early Learning; Mullen 1995; Wechsler Preschool and Primary Scale of Intelligence-Revised; Wechsler, 1990).
3. *Communication* (e.g., Reynell Developmental Language Scales; Reynell, 1990; Vineland Adaptive Behavior Scales-Communication domain; Sparrow, Balla, & Cicchetti, 1985; Sparrow, Cicchetti, & Balla, 2005).
4. *Socialization* (e.g., Adaptive Behavior Assessment System-II; Harrison & Oakland, 2003; Vineland Adaptive Behavior Scales-Socialization domain; Sparrow, Balla, & Cicchetti, 1985; Sparrow, Cicchetti, & Balla, 2005).

A list of the various instruments used in the effectiveness studies and that provided data to calculate effect sizes (ES) is presented in Supplement S3. When a study named its primary outcome measure among rating scales we used that. If no primary outcome was pinpointed we selected measures according to the following hierarchy: independent assessor or observer rating, teacher report scale, and parent report scale.

Ten (34.5%) of the 29 studies provided outcome data for all four constructs, 11 (37.9%) had data for three, five (17.2%) had for two, and three (10.3%) had data for only one of the constructs. On average, the studies had data on three of the four constructs. The basic meta-analytic



statistic uses the mean ES across the constructs each study provides data on. However, to obtain a tentative indication of possible differences in ES between the constructs we also compared the ES across the constructs, aware of the fact that these data are not independent.

### **Meta-Analysis**

To obtain as large as possible a body of effectiveness studies we included both RCTs and open trials in the meta-analysis since within-group ES can be calculated from both types of studies. Within-group ES was calculated as  $(M_{pre} - M_{post})/SD_{pre}$  according to recommendation by Lakens (2013) as the interventions may influence not only the means but also the standard deviations. The mean ES was computed by weighting each ES by the inverse of its variance. When a study presented intent-to-treat data (34.0%) these were used, if not, completer data (66.0%) were used.

Before pooling the effect sizes, we screened for statistical outliers, defined as outside  $M \pm 2SD$ . At the post-treatment assessment, five (5.2%) of the ESs were outliers, and at follow-up assessment there was one (7.7%). For these ESs *winsorizing* (Lipsey & Wilson, 2001) was used by reducing outliers to the exact value of  $M+2D$ . The software *Comprehensive Meta-Analysis v.3* (CMA; Borenstein et al., 2013) was used for all analyses and to correct for small sample sizes Hedges's  $g$  was calculated. A random effects model was used since it cannot be assumed that the ESs come from the same population.

Heterogeneity among ESs was assessed with the  $Q$ - and the  $I$ -square statistic. The possibility of publication bias was analyzed with the trim-and-fill method of Duval and Tweedie (2000) as well as Egger's regression intercept (Egger et al., 1997). Moderator analyses of continuous variables were carried out with meta-regression and for categorical variables with subgroup analysis using the mixed effect model.

## **Efficacy Studies for Comparison**

To obtain the efficacy studies to be used in comparison of the effect of early BI in effectiveness studies we consulted the most recent evidence base update review of psychosocial treatments for ASD published in the Journal of Clinical Child and Adolescent Psychology. We chose this journal because it provides regular updates classifying treatment methods for different youth disorders according to the APA system for evaluating the evidence base. This was the Smith and Iadarola (2015) review, but we also checked the previous review of ASD (Rogers & Vismara, 2008) to get as comprehensive a list of efficacy RCTs as possible. From these reviews we listed the RCTs of some kind of BI evaluated as well-established or probably efficacious according to the criteria adopted by the Society of Clinical Child and Adolescent Psychology (Southam-Gerow & Prinstein, 2014). We then removed the RCTs which were already included among the effectiveness studies. This resulted in 16 efficacy RCTs for our comparison and these references are listed in the Supplement S4.

As for the effectiveness studies we extracted data for the primary continuous outcome measure, separately at post-treatment and follow-up assessment. To compare the two categories of studies on background variables we also extracted data on proportion of boys, mean age (in months), pre-treatment severity (calculated as percent of maximum score on the continuous measure), treatment duration (in months), treatment time (hours/week), and attrition rate. Other variables were not reported systematically, or not at all in a sufficient proportion of studies, which precluded inclusion as a background variable.

## **Power Analysis**

In the overall comparison of effectiveness and efficacy studies we have the following number of studies and treatment conditions, which is the unit of analysis: effectiveness studies 29/32 and efficacy studies 16/18. This gives a total of 45 studies and 50 conditions with an average of 44 participants per condition. According to the formulas for power analysis in meta-analyses by Valentine et al. (2010) we would have 91% power to detect an effect size of 0.20, when assuming a high heterogeneity of effect sizes.

## **Results**

### **Description of the Studies**

#### *Study Characteristics*

Background data for the included studies are presented in Table 1. The majority of the 29 studies were conducted in North America ( $n = 13$ ) or Europe ( $n = 10$ ), whereas four came from Asia and two from Australia. Five studies (17.2%) provided information on ethnicity, see Supplement S7. Only four (13.8%) of the studies were RCTs whereas 25 (86.2%) were uncontrolled open trials. The total number of participants receiving early BI in these studies was 1422. There was an overall majority of boys in the studies; with a mean of 84.5% and a range from 71.4% to 96.4%. Five studies (17%) did not provide information on participant gender. The mean age when starting treatment across all studies was 38.7 ( $SD 7.9$ ) months, varying from 25.1 (Zachor & Ben Itzhak, 2010) to 54 months (Perry et al., 2008).

#### *Treatment Data*

Treatment data for the included studies are presented in Table 2. In labelling the programs we used the same names as provided in the original studies (second column). We classified the treatments according to the definitions provided by Smith and Iadarola (2015) as either

“*comprehensive*, aiming to address all areas of need, or *focused*, having a more circumscribed set of goals” (p. 902). Almost all (93.1%) studies used EIBI or ABA or modifications thereof and were comprehensive interventions. The child was always the target of treatment with varying degree of parental participation. Various clinicians (e.g., preschool teachers, counselors) delivered the treatment working at the center in question. These were supervised by professionals (e.g., psychologists) who usually were Board Certified Behavioral Analysts. In 15 studies (51.7%) the parents of the child with ASD also received training in how to apply ABA treatment in the home and other settings. Treatments were carried out in community centers (n = 8), preschools (n = 7), in patients’ homes (n = 7), in home + preschool (n = 6), at outpatient clinics (n = 3). Treatments were carried out over 18.6 (*SD* 11.4) months on average (range 3-48) and the mean hours of treatment/week was 24.1 (*SD* 9.6). The mean attrition rate was 5.7% (*SD* 6.3) with a range of 0-20.3%. Only four studies (13.8%) presented follow-up data, either in the original or a separate article, giving a total number of 33 papers included. The mean time since the end of treatment was 58.0 (*SD* 56.8) months, with a range from 12 to 138 months.

## **Methodological Data**

### ***Methodology Ratings***

The research methodology score (% of maximum possible score for the instrument used in the individual study) had an overall mean of 45.5% (*SD* 6.9), which corresponds to a raw score of 19.4 points (see Table 1). RCTs (*M* 48.6%, *SD* 3.8) had a nonsignificant higher methodology score ( $p = 0.28$ ) than the open trials (*M* 44.9%, *SD* 7.2).

### ***Risk of Bias***

The risk of bias categorization is presented in the Supplement S5. The different factors had the following proportions of a high risk-of-bias: the randomization process 73%, deviations from intended interventions 100%, missing outcome data 24%, measurement of the outcome 59%, and selection of the reported results 0%. In order to score the risk-of-bias a low risk was given 0, an unclear risk (some concerns) 0.5, and a high risk 1 point, which means that the total score could vary from 0 to 5 points. The total mean score was 2.94 ( $SD$  0.90) and the RCTs ( $M$  1.60,  $SD$  0.42) had a significantly lower risk-of-bias ( $t(30) = 4.67, p < 0.0001$ ) than the open trials ( $M = 3.19, SD = 0.74$ ).

## **Meta-Analysis**

### ***Attrition***

Eighteen studies (62.1%) provided information on the number of participants who dropped out of treatments. Using treatment condition ( $k = 21$ ) as the unit of analysis the overall attrition rate was 8.8% (95% CI 6.4–12.1,  $z = 13.03, p < 0.0001$ ). The difference between RCTs (6.4%) and open trials (9.0%) was not significant ( $Q_{\text{between}} = 0.42, df. = 1, p = 0.52$ ).

### ***Primary Outcome Measure***

The mean effect sizes of the primary continuous measure for all studies at post-treatment and follow-up assessment, which was done on average 50 months after the end of therapy, are presented in Table 3. The mean ES at post-treatment was large ( $g = 0.94$ ) and significantly different from zero. As indicated by the  $Q$ - and  $I^2$ -values heterogeneity was significant and large. At follow-up, the mean ES ( $g = 1.08$ ) was also significantly different from zero and significantly heterogeneous.

The effect sizes for the four constructs we extracted data on are presented in Table 4. Since these data usually emanate from the same informant (e.g., an independent assessor or a parent) often using the same instrument (e.g., the Vineland Adaptive Behavior Scales) they are not independent. This lack of independence needs to be considered for the results presented in Table 4, which shows that the mean ES varies between 0.76 and 1.27, are all significantly different from zero, and significantly heterogeneous. There was a significant difference in ES between the constructs ( $Q_{\text{between}} = 9.78$ ,  $df. = 3$ ,  $p = 0.021$ ), which was followed by pairwise Q-tests. These showed that the ES for communication (1.27) was significantly higher than the 0.76 for cognitive ( $Q_{\text{between}} = 8.82$ ,  $df. = 1$ ,  $p = 0.003$ ), and the 0.81 for adaptive measures ( $Q_{\text{between}} = 4.64$ ,  $df. = 1$ ,  $p = 0.021$ ). None of the other differences were statistically significant.

### ***Publication Bias***

The possibility of publication bias in the post-treatment data was investigated using Duval and Tweedie's trim-and-fill method and Eggers regression intercept. The trim and fill method suggested that 13 studies should be trimmed, which would reduce the ES to 0.58 (95% CI 0.37-0.79). Egger's regression intercept yielded a  $t$ -value of 2.13 ( $p = 0.04$ ). Thus, publication bias may be an issue for these studies.

### ***Moderator Analyses***

Since the mean post-treatment ES was significantly heterogeneous we followed up with moderator analyses. The results for categorical variables using subgroup analysis are presented in Table 5. There was no significant difference between RCTs and open trials, indicating that participants in RCTs improved as much as (or non-significantly more than) patients in open trials. Regarding statistical analyses, studies with intent-to-treat analysis yielded non-significantly lower ES than studies using completer analysis. There was no significant difference in ES

depending on target of treatment. However, the setting yielded a significant  $Q_{\text{between}} = 12.55$ ,  $df = 4$ , ( $p = 0.014$ ), which was followed by pairwise Q-tests. The ES for home treatments (1.34) was significantly higher than the 0.69 for community centers ( $Q_{\text{between}} = 9.41$ ,  $df = 1$ ,  $p = 0.002$ ), the 0.72 for preschools ( $Q_{\text{between}} = 7.12$ ,  $df = 1$ ,  $p = 0.008$ ), and the 0.84 for home + preschool ( $Q_{\text{between}} = 4.42$ ,  $df = 1$ ,  $p = 0.026$ ). None of the other differences were significant. The continent at which the study was carried out was not associated with a significant difference. However, since so few studies originated from Asia ( $n = 4$ ) or Australia ( $n = 2$ ) we only compared the ESs for North America ( $n = 15$ ) and Europe ( $n = 12$ ), which yielded a non-significant difference  $Q_{\text{between}} = 1.81$ ,  $df = 1$ , ( $p = 0.18$ ).

Continuous variables on which at least 70% of the studies provided information were analyzed with the meta-regression module in the CMA program using the random effects analysis (see Table 6). Since 10 variables were included we used the Holm-Bonferroni correction (see Jaccard & Guilamo-Ramos, 2002). There was one positive moderator; hours of treatment/week, i.e., more intensive treatment was associated with higher ES. There was one negative moderator; year of publication, i.e. later publication year was associated with lower the ES. None of the other moderators was significant.

### **Efficacy-Effectiveness Comparison**

In the following section (see Tables 7-8) data for the effectiveness studies reviewed so far were compared with data for the efficacy studies obtained from the evidence base update reviews on ASD (Rogers & Vismara, 2008; Smith & Iadarola, 2015).

### ***Background and Treatment Variables***

Table 7 displays comparisons between effectiveness and efficacy studies on some background variables and treatment variables. Since there are six variables tested, the Holm-Bonferroni correction was used. The only significant differences were on treatment period in months and treatment hours/week. Effectiveness studies had significantly longer treatments with higher intensity. This is due to the fact that among the effectiveness studies 93% were comprehensive, whereas only 6% of the efficacy studies were categorized as comprehensive. This yielded a significant difference using Fisher's exact probability test (2-tailed)  $p = 0.0001$ . There were no significant differences between the two types of studies regarding mean age, proportion of boys, pre-treatment severity, and percent attrition. Thus, judging from the background and treatment variables which could be extracted the effectiveness studies do not comprise participants who are easier to treat than do the efficacy studies.

#### ***Effect Size on Primary Outcome Measure***

Table 8 presents the subgroup analyses comparing the within-group effect size for effectiveness and efficacy studies within each outcome. Neither at post-treatment assessment (upper part) nor at follow-up (middle part) were there any significant differences between the two types of studies. For both types the ESs were significantly different from zero and the effects were maintained, or somewhat higher, at follow-up, which was done on average 58 months after treatment for effectiveness and 8.1 months for efficacy studies.

#### ***Comparison of RCTs Only***

Since the outcomes presented in Table 8 may have been unduly influenced by open trials we repeated the analyses using only RCT effectiveness studies. The lower part of Table 8 shows that the effectiveness studies had a nominally higher ES than the efficacy studies, however the difference was not significant.



## **Discussion**

The primary aim of this meta-analysis was to examine the effectiveness of early BI considered well-established or probably efficacious (Smith & Iadarola, 2015) for ASD in children when delivered in routine clinical care. The overall within-group effect size was large and significant, and medium to large and significant across the domains of adaptive behavior, cognition, communication, and socialization. Furthermore, the results showed that the outcomes were maintained at follow-up, and that a mean of 91% of the participants with ASD completed the intervention. The comparisons showed no significant differences in effect sizes between effectiveness and efficacy studies. Our results suggest that early BI for ASD are effective in routine clinical care, have a low attrition rate, and that the outcomes are comparable with how effective these interventions are in university research settings.

Our findings are in contrast with what was reported in a recent meta-analysis on the effectiveness of community-based early intervention for children with ASD (Nahmias et al., 2019; ESs [0.21-0.32]). The contrasting results may be due to several important differences between Nahmias et al. (2019) and the present meta-analysis. First, some inclusion and exclusion criteria were different yielding only 42% overlap in studies published during the same time period used in Nahmias et al. Importantly, whereas the present meta-analysis included only effectiveness and efficacy studies of early behavioral treatment methods evaluated as well-established or probably efficacious (Smith & Iadarola, 2015), Nahmias et al. (2019) also included studies of methods with a lower evidence-base level. The latter difference is important, as Nahmias et al. found variability across program outcomes with an indication of stronger results for programs based on evidence-based interventions. Also, Nahmias et al. (2019) employed different effect size measures when comparing effectiveness studies and efficacy studies, whereas the same

effect size measure for both categories of studies were used in the present meta-analysis. These important differences between the Nahmias et al. (2019) and the current meta-analysis in the body of studies included and statistical methods used, impedes the direct comparison of results.

Regarding the magnitude of effect sizes across the domains of adaptive behavior, cognition, communication, and socialization, our findings are difficult to compare as we are not aware of any other meta-analysis on the effectiveness of early interventions for ASD in children besides Nahmias et al. (2019).

We found that over 72% of the studies assessed outcomes across three or four domains. The variability probably reflects differences in the intervention targets across the studies. Furthermore, the tools utilized to measure outcome domains also varied across the studies. Currently, no uniform and common standard of outcome measures exists to assess the effects of interventions for children with ASD (Smith & Iadarola, 2015). As such, there is no consensus regarding type of outcome measure regarded as most clinically meaningful and psychometrically sound, challenging the comparison of outcomes across interventions.

Due to significant heterogeneity in the effect sizes, we examined some characteristics of the patient sample and treatment variables as potential moderators influencing treatment outcome. The number of hours/week was a significant positive moderator of effect size (i.e., more hours yielded higher effect size), and there was a nonsignificant trend that months of treatment moderated ES. The majority of the interventions were comprehensive with a mean hours of treatment per week of 24 across a mean of 19 months. The different EIBI interventions are highly intensive with up to 40 hours per week (Eldevik et al., 2009), with subsequent adaptations incorporating the EIBI techniques with varying treatment intensity (Smith & Iadarola, 2015). ASD is highly heterogeneous, and there is limited information on what degree of treatment

intensity is more effective for children and families. Previous meta-analyses and a recent study have demonstrated similar findings of a dose-response relationship between treatment intensity and outcome (Eldevik et al., 2020; Reichow, 2012; Virues-Ortega, 2010).

Later publication year was associated with lower effect sizes. The studies were conducted over a period of 33 years, during which the methodology of research designs, identification, and diagnosis of children with ASD, interventions, and inclusive educational support have evolved (Rodgers et al., 2021). It is likely that older studies may have observed larger effects, and that there are important differences in the contexts in which the interventions have been delivered during these years that may impact the effects. However, others have not found year of publication being related to outcome (e.g. Nahmias et al., 2019).

Several interesting patterns emerged in the moderator analyses of categorical variables, though mainly not to the point of statistical significance. There was no difference in effect sizes between RCTs and open trials. Only a small proportion (<13%) included a control group in the study design, and a similar small proportion (14%) included a follow-up assessment. In routine clinical care, it may be more challenging to include a control group and follow-up assessments for ethical, logistical, or financial reasons (Lake et al., 2020). For example, it may be a particular challenge to delay or withhold treatment for ASD as most of the interventions have shown efficacy for children aged five years or younger (Smith & Iadarola, 2015; Warren et al., 2012). Also, early intervention is suggested to have a larger impact as young children with ASD have not yet fallen as far behind compared to typically developing peers, and may be more amenable to change (Myers & Johnson, 2007). There is little data for comparison of follow-up across studies. Few studies report outcome beyond treatment termination, and with few exceptions there is a lack of information on long term effects (Rodgers et al., 2021). A follow-up of the children over extended periods of time in routine clinical

care could also be a challenge due to organizational and financial reasons (Lake et al., 2020). Thus, there could be several reasons for the low proportion of studies employing a control group and including follow-up assessments for children with ASD in routine clinical care. It is therefore encouraging that the effect sizes were similar across the study designs, even if the finding needs to be interpreted with caution given the small number of RCTs.

There were no differences in effect size across treatment targets (i.e., child and parent vs. child only). However, regarding setting our results showed that interventions delivered in the home resulted in a significantly higher effect size compared to the other settings. Best practice guidelines consistently identify active parent participation as an important intervention for children with ASD (Stadnick et al., 2015). Commonalities across interventions are the focus on systematically reinforcing target behaviors and promoting social communication and interacting, helping acquisition of skills, and interacting with others. Parents generally represent the most proximal and powerful environmental influence during early childhood. Family involvement is suggested to facilitate generalization and maintenance of acquired skills and to promote consistency across settings, by overcoming difficulties a child with ASD may have in conveying information across various settings (Smith & Iadarola, 2015; Stadnick et al., 2015). Thus, by involving the parents and guiding them to customize the intervention flexibly to their child's individual learning style, implement and deliver the intervention in everyday situations, one may surpass what clinicians can provide (Smith & Iadarola, 2015). The possibility of a higher degree of family involvement when interventions are delivered in homes compared to the other settings could therefore explain the higher effect size. The finding of no differences across treatment targets, however, could be explained by the variation in parental participation across the different interventions. Furthermore, it could be explained by the smaller unique contribution of an

added parental component in addition to child only, which would have required a much larger body of studies to detect. This suggestion corresponds with studies reporting overall small effects of parent-mediated interventions (Nevill et al., 2018). Overall, an important implication is that positive outcomes for the domains of adaptive behavior, cognition, communication, and socialization can be obtained across treatment targets for children with ASD in routine clinical care.

Regarding methodological aspects, all studies were evaluated by using the psychotherapy outcome study methodology rating scale developed by Öst (2008). The results showed an overall mean of 19.2 points, which is encouraging with such a high proportion of open trials. This result is comparable to a recent meta-analysis on CBT for externalizing disorders in children and adolescents (Riise et al., 2021). Methodological flaws were noted in several of the studies, with RCTs having a significantly lower risk of bias. Overall, the effect size was not moderated by risk-of-bias score or methodology score. These results provide confidence in the overall findings of the meta-analysis.

We statistically compared our outcomes to efficacy studies to evaluate whether the magnitude of improvement achieved in routine clinical care is at the same level as randomized controlled trials from specialized research settings. The most encouraging and important finding from the present meta-analysis was that the effectiveness–efficacy comparison demonstrated no significant differences in effect size at post-treatment and follow-up. Importantly, there were no differences between the effectiveness and efficacy studies on effect sizes when only RCTs were analyzed, providing confidence in the findings. The only difference in the background and treatment variables was a higher number of treatment months, and higher number of treatment hours per week in the effectiveness studies, which is explained by the fact that 93% of the effectiveness studies were comprehensive, whereas only 6% of the efficacy studies had such a focus. Studies of treatments which are comprehensive will be more

intense and have a longer duration than studies focusing on one domain in ASD. The difference between comprehensive and focused treatments is also reflected in the measures used to evaluate treatment outcome across the four domains (i.e., adaptive, cognitive, communication, and social functioning). On average, the effectiveness studies provided data on three of the four domains, whereas the efficacy studies provided data on a mean of 1.6 domains, which aligns with a focused treatment study primarily needs to assess the domain covering the treatment's focus. Overall, the results provide positive evidence for the transportability of empirically supported treatments for children with ASD from university research settings to routine clinical care.

Our meta-analysis contained several strong methodological elements; a power analysis indicating a high power to detect a small effect size; screening of abstract and extractions of information from the included studies in pairs of researchers where disparities were solved in consensus with all authors; ratings of methodological quality and risk-of-bias was done by one of the authors and independently by another, yielding excellent inter-rater reliability (ICC 0.92; 0.96). However, there are some limitations to consider. We only included peer-reviewed published or in press studies in English language journals. Studies published in other languages could have provided additional information about the effectiveness of early BI for ASD in children. Furthermore, the inclusion of only published studies could be viewed as a limitation. However, our pool of studies spanned four decades. Including unpublished studies could have introduced bias as it could have been easier to identify unpublished studies from more recent compared to earlier decades. For the included studies, only a small number (17%) provided information on ethnicity, which is too low to draw any conclusions. Furthermore, the difference in the percentage of comprehensive compared to focused interventions in the effectiveness versus efficacy studies complicated the comparison. It should also be noted that the review of efficacy studies

used for comparisons was published in 2015, and the early interventions for children with ASD have developed since then. Finally, it may be claimed that the effectiveness of an intervention is demonstrated when it exceeds the effects of the treatment youth and families usually received in the clinic, i.e. usual clinical care. However, our aim was to examine the degree of improvement that can be expected following early behavioral interventions with established evidence for ASD when delivered in routine clinical care. Thus, we included both open trials and RCTs to better capture all research conducted in routine clinical care contexts and be as comprehensive as possible.

The current meta-analysis suggests that early BI for ASD are effective in routine clinical care. However, it also highlights areas of improvements and opportunities, including a more detailed classification of the programmes used based on the core components, and a common standard of outcome measures for assessing the effectiveness of interventions. With the heterogeneity of ASD, more careful characteristics of children and their families would be beneficial to include in future studies so that clinicians may have a better understanding of whether a particular intervention is appropriate for the child and family.

In conclusion, our findings demonstrate the effectiveness of behavioral interventions considered well-established or probably efficacious according to the Smith and Iadarola (2015) update review for ASD in children, and suggest that clinicians can be confident about the effectiveness of these interventions in routine clinical care. Effect sizes are comparable to those in university research clinic settings. As treatment effects are not lost when these evidence-based treatment programs are transported from research clinics to routine clinical care, there is a need to further implement effective and evidence-based interventions in routine clinical care for children with ASD.





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**Table 1**

Background data of the included studies.

Study	Country	Continent	Type of study	Analysis	Methodology		N	% boys	Mean age in months	Age range in months
					score (%)	Severity				
Anderson, 1987	USA	North America	Open trial	ITT	35.0		14		43.0	18-64
Ben-Itzchak, 2007	Israel	Asia	Open trial	ITT	40.0		25	92.0	26.6	20-32
Ben-Itzchak, 2014	Israel	Asia	Open trial	Compl.	42.5	0.760 [a]	46	84.8	25.5	17-33
Bibby, 2002	UK	Europe	Open trial	Compl.	40.0	0.613 [b]	66	83.3	45.0	
Cohen, 2006	USA	North America	Open trial	Compl.	55.0	0.463 [c]	21	85.7	30.2	20-41
Eikeseth, 2012	Sweden	Europe	Open trial	Compl.	36.4	0.620 [d]	35	82.9	47.0	25-76
Eldevik, 2012	Norway	Europe	Open trial	ITT	52.3	0.519 [c]	31	80.6	42.2	24-72
Eldevik, 2020a	Norway	Europe	Open trial	ITT	50.0	0.515 [d]	21	90.5	46.8	32-69
Eldevik, 2020b	Norway	Europe	Open trial	ITT	50.0	0.677 [d]	36	80.6	44.1	21-77
Goin-Kochel, 2007	USA	North America	Open trial	Compl.	35.0	0.499 [c]	29	93.1	45.7	30-61
Hayward, 2009a	UK	Europe	Open trial	Compl.	54.5	0.521 [c]	23	82.6	37.4	24-42
Hayward, 2009b	UK	Europe	Open trial	Compl.	54.5	0.474 [c]	21	71.4	34.2	24-42
Howard, 2005; 2014	USA	North America	Open trial	Compl.	40.9	0.585 [c]	29	86.2	30.9	
Janson, 2020	Sweden	Europe	RCT	Compl.	47.7	0.760 [c]	19	78.9	40.1	30-48
Luiselli, 2000	USA	North America	Open trial	Compl.	42.5		16	93.8	39.7	26-57

Magiati, 2007, 2011	UK	Europe	Open trial	Compl.	54.5	0.542 [c]	28	96.4	38.0	23-54
Makrygianni, 2018	Greece	Europe	Open trial	Compl.	38.6	0.424 [e]	10		54.0	30-78
Perry, 2008	Canada	North America	Open trial	Compl.	40.0	0.602 [d]	332	83.1	54.0	20-86
Rad, 2019	Romania	Europe	Open trial	Compl.	47.7	0.529 [a]	48	81.3	42.7	24-60
Remington, 2007; 2011	UK	Europe	Open trial	Compl.	54.8	0.568 [f]	23		35.7	30-42
Rivard, 2014; 2019	Canada	North America	Open trial	ITT	47.7	0.587 [d]	93	75.3	46.0	33-57
Sallows, 2005a	USA	North America	RCT	Compl.	45.5	0.542 [c]	13	84.6	35.0	35-37
Sallows, 2005b	USA	North America	RCT	ITT	45.5	0.532 [c]	10	80.0	37.1	35-37
Schertz, 2013	USA	North America	RCT	Compl.	54.5	0.650 [a]	11		24.6	25-28
Sheinkopf, 1998	USA	North America	Open trial	Compl.	36.4	0.546 [g]	11		33.8	23-47
Smith, 2015	USA	North America	Open trial	ITT	52.5	0.850 [a]	71	84.5	39.2	24-58
Smith, 2019	Canada	North America	Open trial	Compl.	31.8	0.382 [c]	147	76.5	41.0	
Tonge, 2014	Australia	Australia	RCT	ITT	50.0	0.687 [d]	35	74.3	46.0	24-65
Waters, 2020	USA	North America	Open trial	ITT	50.0	0.461 [c]	48	93.8	37.8	
Wood, 2018	Australia	Australia	Open trial	Compl.	42.5	0.603 [d]	45	78.0	40.7	24-64
Zachor, 2007	Israel	Asia	Open trial	ITT	40.9		20	95.0	27.7	22-34
Zachor, 2010	Israel	Asia	Open trial	Compl.	45.5		45	91.0	25.1	17-35

*Note.* RCT = randomized controlled trial, ITT = intent-to-treat, Compl. = completers, Severity = percentage of the maximum score on the primary outcome measure, [a] = Autism Diagnostic Observation Schedule, [b] = Pathology score, [c] = Vineland Adaptive Behavior Scales, [d] = Childhood Autism Rating Scale, [e] = Autism Behavior Checklist, [f] = Autism Screening Questionnaire, [g] = Percent of DSM-III-R symptoms rated positive. Blank fields = data not provided.

**Table 2.**

Treatment data of the included studies.

Study	Treatment method	Treatment target	Setting	Treatment hrs/week	Months of treatment	Percent attrition	F-up months
Anderson, 1987	EIBI*	I+P	H	20.0	12.0	0.0	
Ben-Itzhak, 2007	ABA*	I+P	CC	35.0	12.0	0.0	
Ben-Itzhak, 2014	EIBI*	I+P	CC	20.0	24.0		138
Bibby, 2002	EIBI*	I+P	H	30.3	32.8	0.0	
Cohen, 2006	EIBI*	I+P	H+P	37.5	36.0	12.5	
Eikeseth, 2012	EIBI*	I	P	23.0	12.0	7.9	
Eldevik, 2012	EIBI*	I	P	13.6	25.1	0.0	
Eldevik, 2020a	EIBI-lower*	I	P	11.1	12.5	0.0	
Eldevik, 2020b	EIBI-higher*	I	P	18.2	12.1	0.0	
Goin-Kochel, 2007	ABA*	I	P	30.0	23.7		
Hayward, 2009a	EIBI-clinic*	I+P	C	37.4	12.0	13.0	
Hayward, 2009b	EIBI-parent*	I+P	H	34.2	12.0	9.5	
Howard, 2005	IBT*	I	H+P	32.5	14.2	9.8	
Janson, 2020	IBT*	I+P	P	14.4	3.0	9.5	
Luiselli, 2000	EIBI*	I	H	13.7	9.4		
Magiati, 2007	EIBI*	I	H	32.8	24.0	15.2	58
Makrygianni, 2018	ABA*	I	P	23.8	9.0		
Perry, 2008	IBI*	I	CC+H	30.0	18.0		
Rad, 2019	ABA*	I	C	10.0	12.0		
Remington, 2007	EIBI*	I+P	H+P	18.1	23.0		24
Rivard, 2014	EIBI*	I+P	CC	18.0	12.0	0.0	12
Sallows, 2005a	EIBI-clinic*	I+P	C	37.6	48.0	7.7	
Sallows, 2005b	EIBI-parent*	I+P	H	35.7	48.0	0.0	
Schertz, 2013	JAML	I+P	H	9.4	7.0		
Sheinkopf, 1998	EIBI*	I+P	H+P	27.0	15.7		
Smith, 2015	EIBI*	I	CC	18.4	24.0	9.9	
Smith, 2019	EIBI*	I	H+P	20.0	12.0		
Tonge, 2014	PEBM	I+P	CC	7.3	5.0	0.0	
Waters, 2020	EIBI*	I+P	H+P	37.5	36.0	4.2	



Wood, 2018	EIBI*	I	CC	20.3	24.3	20.3
Zachor, 2007	ABA*	I	CC	35.0	12.0	0.0
Zachor, 2010	ABA*	I+P	CC	20.0	12.0	

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*Note.* ABA = Applied Behavior Analysis, EIBI = Early Intensive Behavioral Intervention, IBI = Intensive Behavioral Intervention, IBT = Intensive Behavior Treatment, JAML = Joint Attention Mediated Learning, PEBM = Parent Education and Behavior Management. \* = comprehensive treatment. I = individual child, P = parent, C = Clinic, CC = Community center, H = Home, P = Preschool. Blank fields = data not provided.

**Table 3**

Within-group effect size (Hedges' *g*) for all studies (RCTs and open trials).

Time point	<i>k</i>	<i>g</i> -value	95% CI	z-value	Q-value	<i>I</i> <sup>2</sup> (%)
Post	33	0.94	0.76-1.13	9.93 <sup>b</sup>	199.9 <sup>b</sup>	84.0
Follow-up	4	1.08	0.17-1.98	2.34 <sup>a</sup>	42.1 <sup>b</sup>	92.9

*Note.* *k* = number of treatment conditions. <sup>a</sup> *p* < 0.05, <sup>b</sup> *p* < 0.0001.

**Table 4**

Within-group effect size (Hedges' *g*) at post-treatment for all studies divided on construct.

Construct	<i>k</i>	<i>g</i> -value	95% CI	z-value	Q-value	<i>I</i> <sup>2</sup> (%)
Adaptive	21	0.81	0.50-1.12	5.10 <sup>a</sup>	281.3 <sup>a</sup>	92.9
Cognitive	24	0.76	0.57-0.96	7.61 <sup>a</sup>	129.1 <sup>a</sup>	82.2
Communication	27	1.27	1.00-1.54	9.20 <sup>a</sup>	232.0 <sup>a</sup>	88.8
Socialization	24	1.01	0.76-1.26	7.91 <sup>a</sup>	216.0 <sup>a</sup>	89.4

Note. *k* = number of treatment conditions. <sup>a</sup> *p* < 0.0001.

**Table 5**

Subgroup analysis of the effect size for all studies at post-treatment.

Variable	Effect size		
	<i>k</i>	<i>g</i> -value	95% CI
<i>Type of study</i> ( $Q_b = 0.44, p = 0.51$ )			
RCT	5	1.12	0.55-1.70
Open trial	28	0.92	0.72-1.12
<i>Statistical analysis</i> ( $Q_b = 0.74, p = 0.39$ )			
Intent-to-treat	12	0.83	0.57-1.10
Completers	21	0.99	0.75-1.23
<i>Treatment target</i> ( $Q_b = 0.10, p = 0.76$ )			
Child	15	0.90	0.62-1.19
Child + parent	18	0.96	0.72-1.20
<i>Setting</i> ( $Q_b = 12.55, p = 0.014$ )			
Home	7	1.34	1.03-1.66
Clinic	3	1.33	0.63-2.02
Home + preschool	7	0.84	0.49-1.19
Preschool	7	0.72	0.39-1.05
Community centre	8	0.69	0.41-0.96
<i>Continent</i> ( $Q_b = 1.98, p = 0.58$ )			
Asia	4	0.93	0.36-1.50
Australia	2	0.80	0.32-1.29
Europe	12	0.82	0.58-1.05
North America	15	1.09	0.76-1.43

*Note.* *k* = number of treatment conditions,  $Q_b$  = *Q* between subgroups. The statistic in parenthesis tests if the subgroups within the individual category differ significantly from each other.

**Table 6**

Meta-regression analysis of the effect size for all studies at post-treatment.

Variable	<i>k</i>	Point estimate	z-value	<i>p</i> -value
Hours of tx/week	33	0.032	3.70	0.0002
Year of publication	33	-0.043	-3.60	0.0003
Months of treatment	33	0.017	1.83	0.07
Percent boys	28	0.020	1.32	0.19
Severity	28	-0.984	-1.03	0.30
Age	33	-0.012	-0.98	0.33
Percent attrition	22	0.018	0.95	0.34
Risk-of-bias score	33	-0.048	-0.43	0.66
Methodology score	33	-0.005	-0.38	0.70
Number of participants	33	0.0002	0.16	0.87

*Note.* *k* = number of treatment conditions. tx=treatment.

**Table 7**

Some background and treatment data (M and SD) for effectiveness and efficacy studies.

Study type	<i>k</i>	Boys (%)	Age (months)	Severity (%)	Treatment (months)	Treatment hours/week	Attrition (%)
Effectiveness	32	84.5 (6.8)	38.7 (7.9)	57.4 (10.7)	18.6 (11.4)	24.1 (9.6)	6.1 (6.2)
Efficacy	18	85.7 (6.4)	43.0 (8.8)	56.4 (16.6)	7.2 (7.6)	8.6 (9.1)	5.7 (8.7)
	<i>p:</i>	0.60	0.09	0.80	0.0004	0.0001	0.85

*Note.* *k* = number of treatment conditions, Severity = percentage of the maximum score on the primary outcome measure. Attrition (%) = proportion dropping out of those participating in at least one session.

**Table 8**Effect sizes (Hedges' *g*) for effectiveness and efficacy studies.

Time point	Study type	<i>k</i>	<i>g</i> -value	95% CI	z-value	<i>Q</i> <sub>between</sub>	<i>p</i> -value
<i>All studies</i>							
Post	Effectiveness	33	0.94	0.76-1.13	9.93 <sup>b</sup>	3.16	0.076
	Efficacy	18	0.69	0.48-0.90	6.39 <sup>b</sup>		
Follow-up	Effectiveness	4	1.08	0.17-1.98	2.34 <sup>a</sup>	0.64	0.42
	Efficacy	6	1.54	0.84-2.25	4.29 <sup>b</sup>		
<i>RCTs only</i>							
Post	Effectiveness	5	1.12	0.55-1.70	3.84 <sup>b</sup>	1.97	0.16
	Efficacy	18	0.69	0.48-0.90	6.39 <sup>b</sup>		

Note. *k* = number of comparisons. <sup>a</sup> *p* < 0.05, <sup>b</sup> *p* < 0.0001. *Q* between = comparison Effectiveness vs. Efficacy at the respective time points.

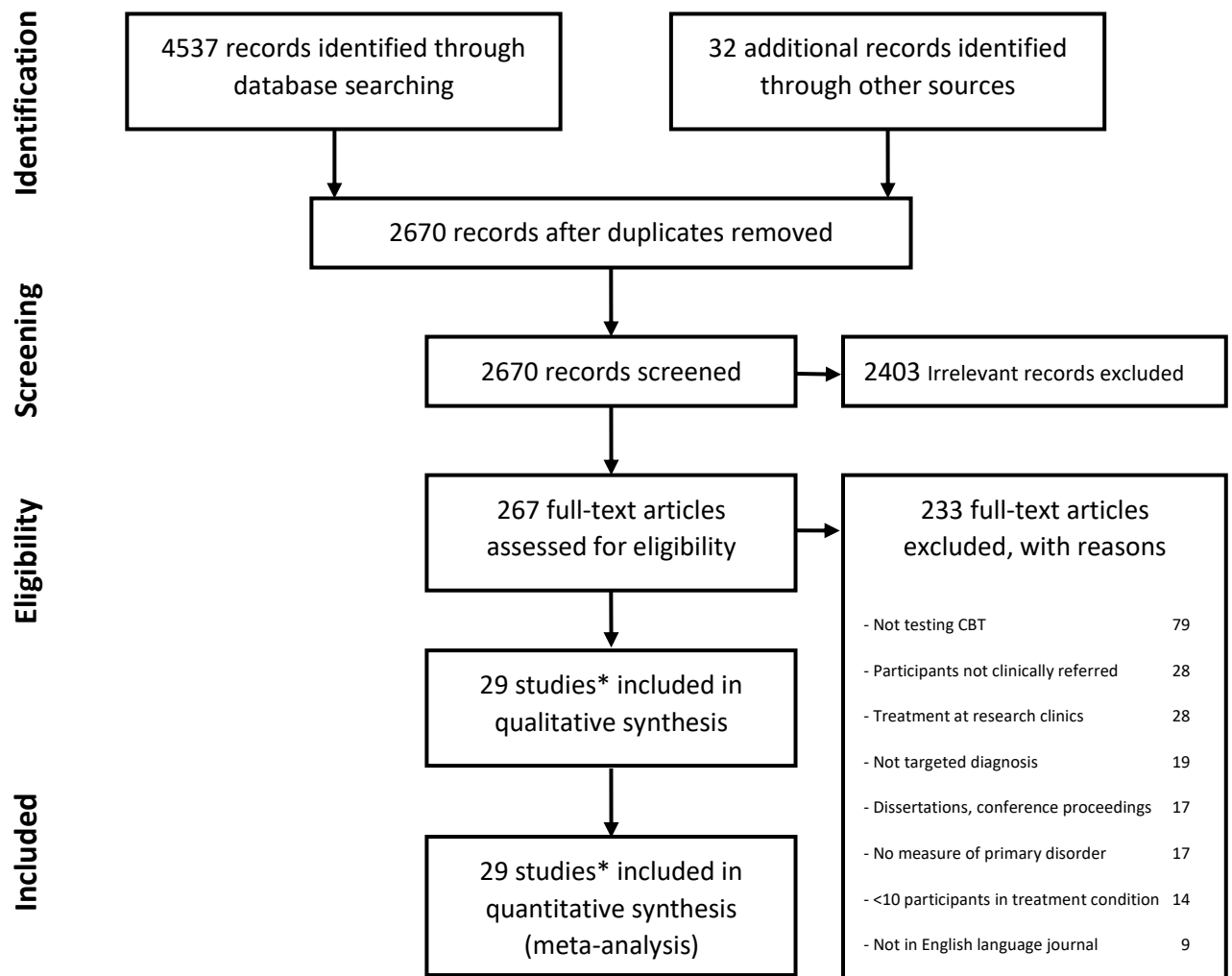


Figure 1. Flowchart of the inclusion of studies.

Note. \*29 unique studies across 34 articles.



## **Supplement to**

S1. Literature search strategies.

S2. References to excluded studies.

S3. Table of rating scales used for primary continuous measure.

S4. References to efficacy studies used for comparison.

S5. Table of risk-of-bias evaluation.

S6. Table of ethnicity.

S7. Table of focus of treatment.

S8. PRISMA Checklist.

S9. AMSTAR2.

*S1. Literature search strategies*

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to April 06, 2021> 07-04-21

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- 1 exp Behavior Therapy/ 78488
- 2 (CBT or behavior?r\* therapy or behavior?r\* intervent\* or behavior?r\* modification or behavior?r\* management or EIBI or behavior?r\* analys\* or ABA).ti,ab,kw. 60569
- 3 (Discrete-trial adj1 (instruction or training or teaching or intervention)).ti,ab,kw. 107
- 4 token economy/ or Conditioning, psychological/ or exp Reinforcement, Psychology/ or exp "Task performance and analysis"/ 102411
- 5 (contingency management or token economy or fading conditioning or omission conditioning or reinforcement or functional communication or picture exchange communication system or PECS or task analysis or response interruption or redirection).ti,ab,kw. 42988
- 6 1 or 2 or 3 or 4 or 5 244155
- 7 exp Child Development Disorders, Pervasive/ 37499
- 8 (autism or (autistic adj2 disorder\*) or asperger\* or pervasive development\* disorder\* or childhood disintegrative disorder\* or ASD or PDD or PDD-NOS).ti,ab,kw. 60779
- 9 7 or 8 66020
- 10 adolescent/ or exp child/ 3092326
- 11 (pediatric\* or paediatric\* or infant\* or infancy or toddler\* or preschool\* or pre-school\* or child\* or adolescen\* or youth).ti,ab,kw. 2135035
- 12 10 or 11 3948915
- 13 6 and 9 and 123113
- 14 Outpatient Clinics, Hospital/ 15725
- 15 Community Mental Health Services/ 18718
- 16 Schools/ 40428
- 17 (effectiveness or community clinic\* or outpatient clinic\* or routine care or regular care or daycare or day-care or school\* or kindergar?en).ti,ab,kw. 810070
- 18 14 or 15 or 16 or 17 844685
- 19 6 and 9 and 12 and 18 660

Database: Embase (Ovid) <1974 to 2021 April 06>  
07-04-2021

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- 1 exp behavior therapy/ or exp cognitive behavioral therapy/ 60460

2 (CBT or behavior\* therapy or behavior\* intervent\* or behavior\* modification or  
behavior\* management or EIBI or behavior\* analys\* or ABA).ti,ab,kw. 80865

3 (Discrete-trial adj1 (instruction or training or teaching or intervention)).ti,ab,kw.  
132

4 reinforcement/ or exp conditioning/ or task performance/ 230105

5 (contingency management or token economy or fading conditioning or omission conditioning  
or reinforcement or functional communication or picture exchange communication system or  
PECS or task analysis or response interruption or redirection).ti,ab,kw. 51093

6 1 or 2 or 3 or 4 or 5 366684

7 exp autism/ 75407

8 (autism or (autistic adj2 disorder\*) or asperger\* or pervasive development\* disorder\* or  
childhood disintegrative disorder\* or ASD or PDD or PDD-NOS).ti,ab,kw. 85025

9 7 or 8 102686

10 child/ or preschool child/ or school child/ or adolescent/ 2882587

11 (pediatric\* or paediatric\* or infant\* or infancy or toddler\* or preschool\* or pre-school\* or  
child\* or adolescen\* or youth).ti,ab,kw. 2632354

12 10 or 11 3891767

13 6 and 9 and 125286

14 outpatient department/ 68138

15 community care/ 55952

16 exp community mental health service/ 364

17 exp school/ 364703

18 (effectiveness or community clinic\* or outpatient clinic\* or routine care or regular care or  
daycare or day-care or school\* or kindergar\*en).ti,ab,kw. 1075040

19 14 or 15 or 16 or 17 or 18 1399995

20 13 and 19 1076

21 limit 20 to conference abstracts 123

22 20 not 21 953

Database: APA PsycInfo (Ovid) <1806 to March Week 5 2021>  
07-04-21

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1 exp behavior therapy/ or exp cognitive behavior therapy/ 42514

2 (CBT or behavior\* therapy or behavior\* intervent\* or behavior\* modification or  
behavior\* management or EIBI or behavior\* analys\* or ABA).tw. 67160

3 (Discrete-trial adj1 (instruction or training or teaching or intervention)).tw.  
343

4	exp contingency management/	3112
5	exp classical conditioning/ or exp reinforcement/ or communication skills training/ or "extinction (learning)"/ or exp task analysis/	85139
6	(contingency management or token economy or fading conditioning or omission conditioning or reinforcement or functional communication or picture exchange communication system or PECS or task analysis or response interruption or redirection).tw.	50799
7	1 or 2 or 3 or 4 or 5 or 6	187365
8	autism spectrum disorders/	46071
9	(autism or (autistic adj2 disorder*) or asperger* or pervasive development* disorder* or childhood disintegrative disorder* or ASD or PDD or PDD-NOS).tw.	56059
10	8 or 9	58659
11	7 and 10	5737
12	limit 11 to (100 childhood <birth to age 12 yrs> or 200 adolescence <age 13 to 17 yrs>)	3516
13	(pediatric* or paediatric* or infant* or infancy or toddler* or preschool* or pre-school* or child* or adolescen* or youth).tw.	980226
14	11 and 13	4202
15	12 or 14	4716
16	exp outpatient treatment/	7137
17	exp schools/	71546
18	(effectiveness or community clinic* or outpatient clinic* or routine care or regular care or daycare or day-care or school* or kindergar?en).tw.	586336
19	16 or 17 or 18	605990
20	15 and 19	1400
21	limit 20 to dissertation	240
22	20 not 21	1160

Database: ERIC (Ebsco) Expanders - Apply equivalent subjects. Search modes - Boolean/Phrase Interface - EBSCOhost Research Databases. Search Screen - Advanced Search. 07-04-21.

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S1 DE "Behavior Modification" OR DE "Contingency Management" OR DE "Desensitization" OR DE "Positive Behavior Supports" OR DE "Classical Conditioning" OR DE "Operant Conditioning" OR DE "Verbal Operant Conditioning" OR DE "Reinforcement" OR DE "Negative Reinforcement" OR DE "Positive Reinforcement" OR DE "Punishment" OR DE "Rewards" OR DE "Social Reinforcement" OR DE "Timeout" OR DE "Token Economy"  
24,962

S2 DE "Task Analysis" 12,079

S3 TI ( CBT or "behavior\* therapy" or "behavior\* intervent\*" or "behavior\* modification" or "behavior\* management" or EIBI or "behavior\* analys\*" or ABA ) OR AB ( CBT or "behavior\* therapy" or "behavior\* intervent\*" or "behavior\* modification" or "behavior\* management" or EIBI or "behavior\* analys\*" or ABA ) 9,120

S4 TI ( (Discrete-trial or "discrete trial") N0 (instruction or training or teaching or intervention) ) OR AB ( (Discrete-trial or "discrete trial") N0 (instruction or training or teaching or intervention) ) 156

S5 TI ( "contingency management" or "token economy" or "fading conditioning" or "omission conditioning" or reinforcement or "functional communication" or "picture exchange communication system" or PECS or "task analysis" or "response interruption" or redirection ) OR AB ( "contingency management" or "token economy" or "fading conditioning" or "omission conditioning" or reinforcement or "functional communication" or "picture exchange communication system" or PECS or "task analysis" or "response interruption" or redirection ) 10,533

S6 S1 OR S2 OR S3 OR S4 OR S5 45,813

S7 DE "Pervasive Developmental Disorders" OR DE "Asperger Syndrome" OR DE "Autism" 16,247

S8 TI ( autism or (autistic N1 disorder\*) or asperger\* or "pervasive development\* disorder\*" or "childhood disintegrative disorder\*" or ASD or PDD or PDD-NOS ) OR AB ( autism or (autistic N1 disorder\*) or asperger\* or "pervasive development\* disorder\*" or "childhood disintegrative disorder\*" or ASD or PDD or PDD-NOS ) 15,264

S9 S7 OR S8 16,906

S10 DE "Adolescents" OR DE "Children" 88,938

S11 TI ( pediatric\* or paediatric\* or infant\* or infancy or toddler\* or preschool\* or pre-school\* or child\* or adolescen\* or youth ) OR AB ( pediatric\* or paediatric\* or infant\* or infancy or toddler\* or preschool\* or pre-school\* or child\* or adolescen\* or youth ) 376,716

S12 S10 OR S11 389,140

S13 S6 AND S9 AND S12 2,147

S14 DE "Schools" OR DE "Bilingual Schools" OR DE "Boarding Schools" OR DE "Colleges" OR DE "Community Schools" OR DE "Consolidated Schools" OR DE "Correspondence Schools" OR DE "Day Schools" OR DE "Disadvantaged Schools" OR DE "Elementary Schools" OR DE "Experimental Schools" OR DE "Folk Schools" OR DE "Free Schools" OR DE "International Schools" OR DE "Laboratory Schools" OR DE "Magnet Schools" OR DE "Middle Schools" OR DE "Military Schools" OR DE "Montessori Schools" OR DE "Multiunit Schools" OR DE "Neighborhood Schools" OR DE "Nursery Schools" OR DE "Open Plan Schools" OR DE "Private Schools" OR DE "Professional Development Schools" OR DE "Public Schools" OR DE "Racially Balanced Schools" OR DE "Regional Schools" OR DE "Rural Schools" OR DE "Schools of Education" OR DE "Secondary Schools" OR DE "Single Sex Schools" OR DE "Slum Schools" OR DE "Small Schools" OR DE "Special Schools" OR DE "State Schools" OR DE "Suburban Schools" OR DE "Summer Schools" OR DE "Traditional Schools" OR DE "Urban Schools" OR DE "Vocational Schools" OR DE "Year Round Schools" 142,134

S15 DE "Child Care" 4,623

S16 TI ( effectiveness or community clinic\* or "outpatient clinic\*" or "routine care" or "regular care" or daycare or day-care or school\* or kindergar#en ) OR AB ( effectiveness or

	community clinic* or "outpatient clinic*" or "routine care" or "regular care" or daycare or day-care or school* or kindergar#en )	597,381
S17	S14 OR S15 OR S16	629,068
S18	S6 AND S9 AND S12 AND S17	708

Web of science (Clarivate) Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=All years, search date 7.th April 2021.

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- # 1 102,757 - TOPIC: (CBT or "behavior\* therapy" or "behavior\* intervent\*" or "behavior\* modification" or "behavior\* management" or EIBI or "behavior\* analys\*" or ABA)
  - # 2 237 - TOPIC: (("Discrete-trial" or "discrete trial") NEAR/0 ("instruction" or "training" or "teaching" or "intervention"))
  - # 3 130,278 - TOPIC: ("contingency management" or "token economy" or "fading conditioning" or "omission conditioning" or "reinforcement" or "functional communication" or "picture exchange communication system" or PECS or "task analysis" or "response interruption" or "redirection")
  - # 4 230,931 - #3 OR #2 OR #1
  - # 5 88,661 - TS=("autism" or ("autistic" NEAR/1 disorder\*) or asperger\* or "pervasive development\* disorder\*" or "childhood disintegrative disorder\*" or ASD or PDD or PDD-NOS)
  - # 6 2,650,572 - TOPIC: (pediatric\* or paediatric\* or infant\* or infancy or toddler\* or preschool\* or pre-school\* or child\* or adolescen\* or "youth")
  - # 7 1,455,145 - TOPIC: ("effectiveness" or "community clinic\*" or "outpatient clinic\*" or "routine care" or "regular care" or "daycare" or "day-care" or school\* or "kindergar\$en")
  - # 8 1,056 - #7 AND #6 AND #5 AND #4

## *S2. References to excluded studies.*

Studies could be excluded for more than one reason and could thus potentially be listed in several of the categories below. However, reason for exclusion was categorized as the first exclusion criteria that became evident to the authors when reading the study.

### *Treatment at research clinics:*

Bagaiolo, L. F., Mari, J. D., Bordini, D., Ribeiro, T. C., Martone, M. C. C., Caetano, S. C. et al. (2017). Procedures and compliance of a video modeling applied behavior analysis intervention for Brazilian parents of children with autism spectrum disorders. *Autism* 21, 603-610.

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Contaldo, A., Colombi, C., Pierotti, C., Masoni, P., & Muratori, F. (2020). Outcomes and Moderators of Early Start Denver Model Intervention in Young Children with Autism Spectrum Disorder Delivered in a Mixed Individual and Group Setting. In *Autism: The International Journal of Research and Practice* (Vol. 24, pp. 718-729): Autism: The International Journal of Research and Practice.

Estes, A., Munson, J., Rogers, S. J., Greenon, J., Winter, J., & Dawson, G. (2015). Long-Term Outcomes of Early Intervention in 6-Year-Old Children With Autism Spectrum Disorder. *Journal of the American Academy of Child & Adolescent Psychiatry* 54, 580-587.

Factor, R. S., Swain, D. M., Antezana, L., Muskett, A., Gatto, A. J., Radtke, S. R. et al. (2019). Teaching emotion regulation to children with autism spectrum disorder: Outcomes of the Stress and Anger Management Program (STAMP). *Bull Menninger Clin* 83, 235-258.

Fava, L., Strauss, K., Valeri, G., D'elia, L., Arima, S., & Vicari, S. (2011). The effectiveness of a cross-setting complementary staff- and parent-mediated early intensive behavioral intervention for young children with ASD. *Research in Autism Spectrum Disorders* 5, 1479-1492.

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Lovaas, O. (1987). Behavioral treatment and normal educational and intellectual functioning in young autistic children. *Journal of Consulting and Clinical Psychology* 55, 3-9.

Meachin, J. J., Smith, T., & Lovaas, O. (1993). Long-term outcome for children with autism who received early intensive behavioral treatment. *American Journal on Mental Retardation* 97, 359-372.

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*Age > 5 years:*

Brookman-Fraze, L. I., Drahota, A., & Stadnick, N. (2012). Training community mental health therapists to deliver a package of evidence-based practice strategies for school-age children with

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*Practicing clinicians:*

Mazza, M., Pino, M., Vagnetti, R. Filocamo, A., Attanasio, M., Calvarese, A. and Valenti, M. Intensive intervention for adolescents with autism spectrum disorder: Comparison of three rehabilitation treatments (2020). *International Journal of Psychiatry in Clinical Practice*.

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*Participants not clinically referred:*

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Freitag, C. M., Feineis-Matthews, S., Valerian, J., Teufel, K., & Wilker, C. (2012). The Frankfurt early intervention program FFIP for preschool aged children with autism spectrum disorder: a pilot study. *Journal of Neural Transmission* 119, 1011-1021.

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*Comb. of treatment and drug:*

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*S3. Rating scales used for primary continuous measure.*

*1. Cognitive*

Bayley Scales of Infant Development, Second Edition (BSID-II) (Bayley, 1993)

Early Learning Accomplishments Profile (ELAP) (Glover et al., 1988)

Learning Accomplishments Profile (LAP) (Sanford and Zelman, 1981)

Leiter International Performance Scale–Revised (Leiter-R; Roid & Miller, 1997)

Merrill-Palmer Scale of Mental Tests (MPS) (Roid, G.H., & Sampers, J.L., 2004).

Mullen Scales of Early Learning (MSEL; Mullen 1995)

Psychoeducational Profile–Revised (PEP-R) (Schopler et al., 1990)

Stanford-Binet Intelligence Scale Fourth Edition (Thorndike, Hagen, & Sattler, 1986)

Wechsler Preschool and Primary Scale of Intelligence-Revised (Wechsler, 1990)

Wechsler Intelligence Scale for Children. 3rd ed. (Wechsler, 1992)

*2. Communication*

Assessment of Basic Language and Learning Skills (ABLLS) (Partington & Sundberg, 1998)

Autism Diagnostic Observation Schedule (ADOS) (Lord, Rutter, DiLavore, & Risi, 1999).

Developmental-behavioral scales (Alpern, Boll, & Shearer, 2000)

Early Learning Accomplishments Profile (ELAP) (Glover et al., 1988)

Learning Accomplishments Profile (LAP) (Sanford and Zelman, 1981)

Reynell Developmental Language Scales (Reynell, 1990)

Uniform Performance Assessment System (UPAS) (White, Edgar, Haring, Afflick, & Hayden, 1978)

Vineland Adaptive Behavior Scales (VABS) (Sparrow, Balla, & Cicchetti, 1985; Sparrow, Cicchetti, & Balla, 2005)

### *3. Socialization*

Adaptive Behavior Assessment System-II (ABAS-II; Harrison & Oakland, 2003).

Assessment of Basic Language and Learning Skills (ABLBS) (Partington & Sundberg, 1998)

Autism Diagnostic Observation Schedule (ADOS) (Lord, Rutter, DiLavore, & Risi, 1999).

Early Learning Accomplishments Profile (ELAP) (Glover et al., 1988)

Learning Accomplishments Profile (LAP) (Sanford & Zelman, 1981)

Social Skills Improvement System (SSIS) (Elliott & Gresham, 2007)

Uniform Performance Assessment System (UPAS) (White, Edgar, Haring, Afflick, & Hayden, 1978)

Vineland Adaptive Behavior Scales (VABS) (Sparrow, Balla, & Cicchetti, 1985; Sparrow, Cicchetti, & Balla, 2005)

### *4. Adaptive*

Adaptive Behavior Assessment System-II (ABAS-II; Harrison & Oakland, 2003).

Assessment of Basic Language and Learning Skills (ABLBS) (Partington & Sundberg, 1998)

Vineland Adaptive Behavior Scales (VABS) (Sparrow, Balla, & Cicchetti, 1985; Sparrow, Cicchetti, & Balla, 2005)



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*S4. References to efficacy studies used for comparison.*

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S5. Table of risk-of-bias evaluation.

Study	1. Randomization	2. Deviation interventions	3. Missing data	4. Measurement of outcome	5. Selection of the results
Anderson , 1987	NA	H	S	S	L
Ben-Itzhak, 2007	NA	H	L	H	L
Ben-Itzhak, 2014	NA	H	H	H	L
Bibby, 2002	NA	H	S	H	L
Cohen, 2006	NA	H	S	L	L
Eikeseth, 2012	H	H	L	H	L
Eldevik, 2012	H	H	L	S	L
Eldevik, 2020	H	H	H	H	S
Goin-Kochel, 2007	NA	H	H	H	S
Hayward, 2009	H	H	L	L	L
Howard, 2005; 2014	H	H	S	H	L
Janson, 2020	L	H	L	S	L
Luiselli, 2000	NA	H	L	S	L
Magiati, 2007, 2011	H	H	L	H	L
Makrygianni, 2018	H	H	H	L	L
Perry, 2008	NA	H	H	H	L
Rad, 2019	NA	H	L	H	L
Remington, 2007	NA	H	L	S	L
Rivard, 2014; 2019	NA	H	L	H	L
Sallows, 2005	L	H	L	H	L
Schertz, 2013	L	H	L	L	L
Sheinkopf, 1998	H	H	L	S	L
Smith, 2015	NA	H	L	H	L
Smith, 2019	NA	H	H	H	L
Tonge, 2014	L	H	L	S	L
Waters, 2020	H	H	S	L	L
Wood, 2018	NA	H	H	H	L
Zachor, 2007	H	H	L	H	L
Zachor, 2010	H	H	S	H	L

Note: NA = Not applicable, H = high risk, L = low risk, S = some concerns.



S6. Table of ethnicity.

<b>Study</b>	<b>N</b>	<b>White/ Cacaustian/ European American</b>	<b>African American, Black British</b>	<b>Other</b>
Anderson, 1987				NI
Ben-Itzchak, 2007				NI
Ben-Itzchak, 2014				NI
Bibby, 2002				NI
Cohen, 2006				NI
Eikeseth, 2012				NI
Eldevik, 2012				NI
Eldevik, 2020a				NI
Eldevik, 2020b				NI
Goin-Kochel, 2007	29	86.2	10.3	3.4
Hayward, 2009a				NI
Hayward, 2009b				NI
Howard, 2005; 2014	29	72.4		27.6
Janson, 2020				NI
Luiselli, 2000				NI
Magiati, 2007, 2011	28	75.0	4.6*	21.4
Makrygianni, 2018				NI
Perry, 2008				NI
Rad, 2019				NI
Remington, 2007; 2011				NI
Rivard, 2014; 2019				NI
Sallows, 2005a				NI
Sallows, 2005b				NI
Schertz, 2013				NI
Sheinkopf, 1998				NI
Smith, 2015	71	88.7	7.0	4.2
Smith, 2019	185	95.0		5.0
Tonge, 2014				NI
Waters, 2020				NI

Wood, 2018	NI
Zachor, 2007	NI
Zachor, 2010	NI

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*Note.* NI= No information provided. \* = Black British



S7. Table of focus of treatment.

Study	Method	Components					
		Communication	Social skills	Daily living skills	Behavioral	Motor/Play	Prea
Anderson, 1987	EIBI*	+	+	+	+	+	+
Ben-Itzhak, 2007	ABA*	+	+	+	+	+	+
Ben-Itzhak, 2014	EIBI*	+	+	+	+	+	+
Bibby, 2002	EIBI*	+	+	+	+	+	+
Cohen, 2006	EIBI*	+	+	+	+	+	+
Eikeseth, 2012	EIBI*	+	+	+	+	+	+
Eldevik, 2012	EIBI*	+	+	+	+	+	+
Eldevik, 2020a	EIBI-lower*	+	+	+	+	+	+
Eldevik, 2020b	EIBI-higher*	+	+	+	+	+	+
Goin-Kochel, 2007	ABA*	+	+	+	+	+	+
Hayward, 2009a	EIBI-clinic*	+	+	+	+	+	+
Hayward, 2009b	EIBI-parent*	+	+	+	+	+	+
Howard, 2005; 2014	IBT*	+	+	+	+	-	+
Janson, 2020	IBT*	+	+	+	-	-	+
Luiselli, 2000	EIBI*	+	+	+	+	+	+
Magiati, 2007, 2011	EIBI*	+	+	+	-	+	+
Makrygianni, 2018	ABA*	+	+	+	-	-	+
Perry, 2008	IBI*	+	+	+	-	+	+
Rad, 2019	ABA*	+	+	-	-	+	-
Remington, 2007; 2011	EIBI*	+	+	+	+	+	+
Rivard, 2014; 2019	EIBI*	+	+	+	-	+	+
Sallows, 2005a	EIBI-clinic*	+	+	+	+	+	+
Sallows, 2005b	EIBI-parent*	+	+	+	+	+	+
Schertz, 2013	JAML	+	+	+	-	+	-
Sheinkopf, 1998	EIBI*	+	+	+	-	-	+
Smith, 2015	EIBI*	+	+	-	+	+	-
Smith, 2019	EIBI*	+	+	+	+	+	-

Tonge, 2014	PEBM	+	+	+	+	+	+
Waters, 2020	EIBI*	+	+	+	+	+	+
Wood, 2018	EIBI*	+	+	+	-	-	+
Zachor, 2007	ABA*	+	+	-	-	-	+
Zachor, 2010	ABA*	+	+	+	+	+	+

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*Note:* + = Indicated as a focus for the intervention; - = No information is provided