A Systematic Review of Early Intensive Intervention for Autism Spectrum Disorders

AUTHORS: Zachary Warren, PhD,[a,b] Melissa L. McPheeters, PhD, MPH,[c,d] Nila Sathe, MA, MLIS,[c] Jennifer H. Foss-Feig, MA,[e] Allison Glasser, BA,[c] and Jeremy Veenstra-VanderWeele, MD[b,f,g]

[a]Departments of Psychiatry and Pediatrics, [b]Vanderbilt Kennedy Center/Treatment and Research Institute for Autism Spectrum Disorders, [c]Vanderbilt Evidence-Based Practice Center, Institute for Medicine and Public Health, and [d]Department of Obstetrics and Gynecology, Vanderbilt Medical Center, [e]Department of Psychology and Human Development, and [f]Departments of Psychiatry, Pediatrics, and Pharmacology, [g]Center for Molecular Neuroscience, Vanderbilt University, Nashville, Tennessee

KEY WORDS
autism spectrum disorders, early intervention, behavioral intervention

ABBREVIATIONS
ASD—autism spectrum disorder
AHRQ—Agency for Healthcare Research and Quality
ADOS—Autism Diagnostic Observation Schedule
UCLA—University of California Los Angeles
EIBI—early intensive behavioral intervention
SOE—strength of the available evidence
RCT—randomized controlled trial
ESDM—Early Start Denver Model

We acknowledge that all authors of this article meet authorship criteria and have made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; have participated in drafting the article or revising it critically for important intellectual content; and have given final approval of the version to be published.

www.pediatrics.org/cgi/doi/10.1542/peds.2011-0426

doi:10.1542/peds.2011-0426

Accepted for publication Mar 1, 2011

Address correspondence to Zachary Warren, PhD, Vanderbilt University, 230 Appleton Place/PMB 74, Nashville, TN 37203-5721. E-mail: zachary.warren@vanderbilt.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: *Dr Warren has received research support from the Marino Autism Research Institute, Autism Speaks, and the Simons Foundation; and Dr Veenstra-VanderWeele has received research support from Autism Speaks, the American Academy of Child and Adolescent Psychiatry, NARSAD, Seaside Therapeutics, Roche Pharmaceuticals, and Novartis. The other authors have indicated they have no financial relationships relevant to this article to disclose.*

COMPANION PAPERS: Companions to this article can be found on pages e1312 and e1322 and online at www.pediatrics.org/cgi/doi/10.1542/peds.2011-0427 and www.pediatrics.org/cgi/doi/10.1542/peds.2011-0428.

abstract

CONTEXT: Early intensive behavioral and developmental interventions for young children with autism spectrum disorders (ASDs) may enhance developmental outcomes.

OBJECTIVE: To systematically review evidence regarding such interventions for children aged 12 and younger with ASDs.

METHODS: We searched Medline, PsycINFO, and ERIC (Education Resources Information Center) from 2000 to May 2010. Two reviewers independently assessed studies against predetermined inclusion/exclusion criteria. Two reviewers independently extracted data regarding participant and intervention characteristics, assessment techniques, and outcomes and assigned overall quality and strength-of-evidence ratings using predetermined criteria.

RESULTS: Thirty-four unique studies met inclusion criteria. Seventeen studies were case series; 2 were randomized controlled trials. We rated 1 study as good quality, 10 as fair quality, and 23 as poor quality. The strength of the evidence overall ranged from insufficient to low. Studies of University of California Los Angeles/Lovaas–based interventions and variants reported clinically significant gains in language and cognitive skills in some children, as did 1 randomized controlled trial of an early intensive developmental intervention approach (the Early Start Denver Model). Specific parent-training approaches yielded gains in short-term language function and some challenging behaviors. Data suggest that subgroups of children displayed more prominent gains across studies, but participant characteristics associated with greater gains are not well understood.

CONCLUSIONS: Studies of Lovaas-based approaches and early intensive behavioral intervention variants and the Early Start Denver Model resulted in some improvements in cognitive performance, language skills, and adaptive behavior skills in some young children with ASDs, although the literature is limited by methodologic concerns. *Pediatrics* 2011;127:e1303–e1311

Autism spectrum disorders (ASDs) are characterized by impairments in social interaction, behavior, and communication. Although once considered untreatable, findings published by Lovaas[1] in 1987 suggested that with intensive intervention using applied behavioral analysis, some children may experience a degree of improvement. That report, in which "recovery" of just less than 50% of a subgroup of young children who were receiving intensive intervention was described, initiated a growing body of research. Results of individual studies have suggested that some children who enter into intensive autism-specialized intervention services at young ages may show larger gains in terms of cognitive and adaptive functioning and early educational attainment than children who do not receive such services.[2–6] This research led to a reconceptualization of ASDs as a group of disorders marked by plasticity and heterogeneity and for which there was hope for better outcomes for some children who receive appropriate intervention. Subsequent research has focused on social communication and behavioral impairments and used highly structured approaches, developmental approaches that deliver intervention within natural contexts, and integrative approaches.

There continues to be no global consensus on what treatment strategies are most effective for patients with ASDs, although it is clear that chronic management is often necessary to maximize independence and quality of life. Children frequently receive combinations of interventions that may include behavioral, educational, and medical therapies as well as allied health and complementary approaches. For many children, behavioral interventions form the cornerstone of their treatment. As results of studies on behavioral interventions that present a range of outcomes for potentially different subgroups of children continue to be published, it is imperative to summarize the evidence so that parents and care providers can make informed decisions for specific children.

In this systematic review we examined the available published evidence regarding the effectiveness of early intensive behavioral and developmental interventions for children with ASDs. This review is a component of an Agency for Healthcare Research and Quality (AHRQ)–commissioned comparative-effectiveness review of therapies for children with ASDs that was conducted by the Vanderbilt Evidence-Based Practice Center. The full comparative-effectiveness review[7] is available at www.effectivehealthcare.ahrq.gov.

METHODS

Search Strategy

We searched Medline via the PubMed interface, PsycINFO (psychology/psychiatry literature), and ERIC (Education Resources Information Center) (educational literature) from 2000 to May 2010 using controlled vocabulary terms and key words related to ASDs and therapy-related terms. We also hand-searched the reference lists of all included articles to identify additional studies and reviewed clinical trials related to therapies for ASDs.

Study Selection

We developed study inclusion and exclusion criteria in consultation with an expert panel of clinicians, researchers, and educators involved in the care of children with ASDs. We included all study designs except single case reports and required that studies include at least 10 participants younger than 13 years of age with a diagnosis of ASD. Given concerns about diagnostic certainty in very young children, we also included studies with children younger than 2 years if they included children who were at risk for an ASD.

Studies had to be published after or in the year 2000, coincident with the revision of the *Diagnostic and Statistical Manual of Mental Diseases, Fourth Edition*[8] and widespread implementation of gold-standard assessment tools including the Autism Diagnostic Observation Schedule (ADOS)[9] and the Autism Diagnostic Interview-Revised[10] over the same time frame.

Characterization of Studies

We considered interventions to be early intensive behavioral and developmental if their approach was primarily behavioral and if they were comprehensive (ie, targeted multiple areas of functioning). Studies of intensive interventions that were focused on single target areas (ie, joint attention, imitation) or delivered primarily in educational settings were addressed elsewhere in the full review[7] (see www.effectivehealthcare.ahrq.gov).

We further classified studies into 1 of 3 categories: (1) University of California Los Angeles (UCLA)/Lovaas–based interventions and approaches that are often termed early intensive behavioral intervention (EIBI) in the literature; (2) comprehensive interventions for children younger than 2 years; and (3) parent-training protocols. We note that the studies in the first category used a range of specific methodologies, but they all emphasized core tenets of intensive (ie, many hours per week) approaches and often through 1-on-1 instruction.

Data Extraction

Using standardized forms, 2 investigators independently extracted data regarding study design; descriptions of the study populations, comparison groups, and intervention; and baseline and outcome data. We also extracted data about harms or adverse effects of

therapies. We captured data on the conduct of assessments to inform the evaluation of quality. Principal outcomes of interest included effects on core symptoms of ASDs and other symptoms commonly associated with ASDs, including cognitive functioning and behavioral challenges.

Study-Quality Assessment

Two investigators independently assessed each study by using a prespecified quality-assessment form developed and tested by the review team with input from experts in the field. We evaluated the following elements with a series of yes/no questions related to each of them:

TABLE 1 Domains Used to Assess Strength of Evidence

Risk of bias: Reflects issues in study design and conduct that could result in biased estimates of effect
Consistency: Reflects similarity of effect sizes seen across studies; consistency cannot be assessed when only 1 study is available
Directness: Reflects the relationship between the intervention and the ultimate health outcome of interest
Precision: Reflects the level of certainty around the effect observed

- study design (eg, randomized controlled trial [RCT], group design);
- diagnostic approach (eg, ADOS, Autism Diagnostic Interview-Revised, clinical diagnosis, combination);
- participant ascertainment and characterization (eg, baseline characteristics assessed);
- intervention description (eg, manualized intervention, treatment description, fidelity measurement);
- outcomes measurement (eg, standardized measures, blinded assessment, multiple informants); and
- statistical analysis (eg, appropriate statistical methodology).

Disagreements between assessors were resolved through discussion to reach consensus, and studies could receive an overall score of good, fair, or poor. The full quality tool and approach to assessment are available in the full report[7] (see www.effectivehealthcare.ahrq.gov), as are assessments for each individual study.

We also assessed the strength of the available evidence (SOE), which is our degree of confidence that the observed effect of an intervention is unlikely to change with further research. The SOE can be regarded as insufficient, low, moderate, or high. SOE assessments were based on consideration of 4 domains (Table 1). Our full methodology and algorithm for structuring the SOE are presented in the full AHRQ report[7] (see www.effectivehealthcare.ahrq.gov).

Role of the Funding Source

The topic of therapies for children with ASDs was nominated by the Centers for Medicare and Medicaid Services and Autism Speaks and selected by the AHRQ for a comparative-effectiveness review by the Vanderbilt Evidence-Based Practice Center. A task-order officer from the AHRQ provided technical assistance during the conduct of the evidence report and commented on report drafts.

Data Synthesis

Considerable heterogeneity in the interventions and outcome measures used in studies that met our inclusion criteria precluded a meta-analysis. We

TABLE 2 Summary of Results

Intervention	Study Design/Quality	Study Results and Overall Strength of Evidence
UCLA/Lovaas–based interventions and EIBI variants	1 RCT/fair quality[3]; 3 nRCTs/fair quality[12,19,34]; 5 prospective cohorts/3 of fair quality[4,33,37]; 2 retrospective cohorts/poor quality[14,38]; 6 prospective case series[5,11,13,16,21,26]; 6 retrospective case series[20,22,25,28,29,35,39]	Young children who received high-intensity interventions (>30 h/wk for 1–3 y by well-trained therapists) displayed improvements in areas of cognitive, language, and adaptive functioning; subgroups of children displayed a positive response to this intervention, although this subgroup has not yet been clearly described; there have been few randomized studies; few have used approaches as outlined in treatment manuals; there have been variations in interventions delivered and participant characteristics within studies; strength of evidence for UCLA/Lovaas–based intervention and EIBI variants in affecting language, cognitive, educational, and adaptive outcomes and ASD symptom severity is low
Comprehensive approaches for children <2 y old	1 RCT/good quality[2]; 1 nRCT/fair quality[15]; 2 prospective case series[32,39]	Improvements in cognitive, language, and adaptive behavior skills have been seen over 2 y of ESDM intervention; ESDM findings have not yet been replicated, and it is unclear how core ASD symptoms change in response to treatment; strength of evidence for comprehensive interventions for children <2 y of age is currently insufficient
Parent training	3 RCTs/fair quality[17,18,43]; 1 nRCT/fair quality[15]; 3 prospective case series[23,24,36]	There is some indication of short-term improvements in language, social, and adaptive skills for children whose parents receive training in these areas; there has been a lack of standardized measures and baseline differences among participants in some studies; data have not yet demonstrated long-term functional improvements across domains for any specific form of training; strength of evidence for changing core ASD deficit areas is insufficient

nRCT indicates non-randomized controlled trial.

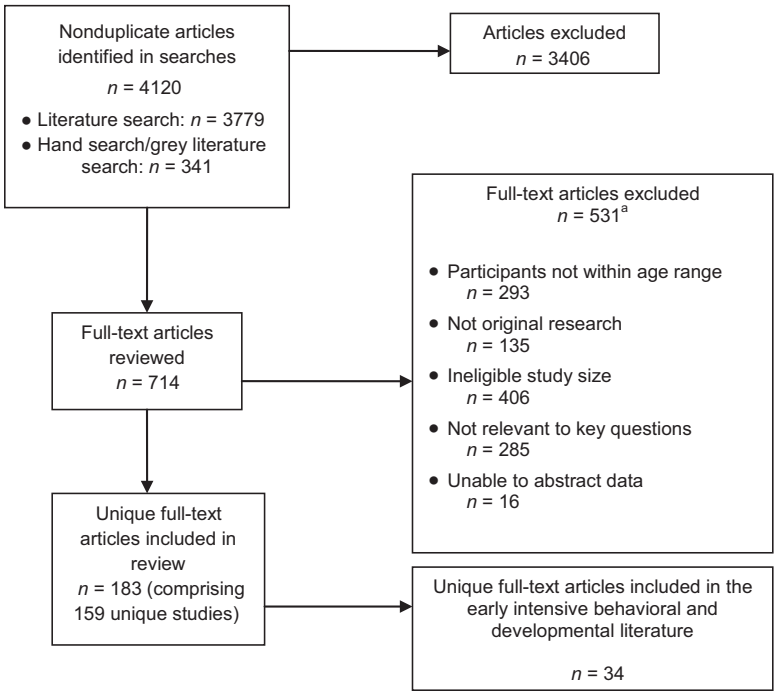

FIGURE 1
Location of studies of early intensive behavioral and developmental intervention. [a] The total number of articles in the exclusion categories exceeds the number of articles excluded because most of the articles fit into multiple exclusion categories.

summarized characteristics of study populations and interventions and used descriptive statistics to report study outcomes.

RESULTS

Search Results

Among 4120 articles located for the full review, 38[2–6,11–43] (comprising 34 unique studies) met study inclusion criteria and addressed early intensive behavioral and developmental interventions (Fig 1).

UCLA/Lovaas–Based Interventions and EIBI Variants

Among the 23 unique studies from which UCLA/Lovaas–based interventions and EIBI variants were reported, 8 were rated as being of fair quality* and 15 were of poor quality (Table 2).†

The 1 RCT on the UCLA/Lovaas–based treatment that met inclusion criteria was considered to be of fair quality.[3] This study, the first attempted replication of Lovaas' manualized intervention to use random assignment, a standardized assessment battery, and explicit accounting of intervention hours, compared a clinic-based method to a parent program. The study randomly assigned 28 children with a mean IQ of 51 to either an intensive treatment group (UCLA/Lovaas model with an average of 25 hours/week of individual treatment per year with reduced intervention over the next 1–2 years) or a parent-training group (3–9 months of parent training). Gains in IQ were much more tempered than those in Lovaas' original noncontrolled study.[1] Children in the treatment group gained a mean of 15 IQ points in comparison with the relatively stable cognitive functioning of the control group, although average IQ in the treatment group remained in the impaired range. Most of the children who demonstrated large IQ gains were within the subgroup diagnosed with pervasive development disorder-not otherwise specified, whereas children with classically defined autistic disorder demonstrated modest improvements. Although the study replicated cognitive improvements for some children as seen in Lovaas' studies, it revealed a less dramatic effect for the population of children for whom this approach is often recommended (ie, children with classically defined autistic disorder) compared with what was reported previously. An additional study that attempted to approximate an RCT format[45] did not meet methodologic inclusion criteria in this capacity and, as such, was addressed in the moderators-of-treatment-effect portion of the full review.

Seven prospective cohort studies and nonrandomized trials were available on UCLA/Lovaas–based or EIBI methodologies, but none made the same comparisons in terms of either interventions or populations. Hayward et al[34,41] examined the progress of children who received either intensive clinic-directed UCLA/Lovaas–based intervention or an intensive parent-managed model over the course of 1 year. At follow-up, children in both groups had improved significantly in IQ, nonverbal IQ, language use/understanding, and most areas of adaptive functioning with the exception of daily living skills, but there were no differences between the groups.

Two studies compared intensive center-based treatment to community care. Howard et al[37] studied preschool-aged children who received intensive behavior analytic treatment, intensive "eclectic" intervention, and general intervention in public early-intervention programs. Groups were assigned via educational placement teams that specifically included parent input. Controlling for age at diagnosis and combined parental education, children in the intensive behavior analytic group dem-

*Refs 3, 4, 12, 16, 33, 34, 37, 41, 42, and 44.
†Refs 5, 6, 11, 13, 20, 21, 25, 26, 28–31, 35, 38, and 40.

onstrated significant improvements in all areas assessed at follow-up, including an average IQ of 89 (41-point improvement over baseline) and a 24-point difference from the combined mean of the other intervention groups. Significant differences between the eclectic and general-intervention groups were not present at follow-up. Findings suggest substantial improvement via an intensive approach for young children with autism; however, important differences in group assignment at baseline, difficulties with systematic measurement overtime, the lack of reported treatment fidelity or adherence characteristics, and the small number of children in the comparison group limit interpretation of these findings.

These results were echoed in another study[4] of 42 children in which those who received the Lovaas intervention had significantly higher IQs and adaptive behavior skills at follow-up compared with children in undefined community care. Receptive language improvements were not significant, and expressive language skills and socialization scores were not different for the 2 groups at year 3. Twelve of the 21 children in the Lovaas group had IQs higher than 85 compared with 7 of 21 in the eclectic treatment group at outcome. Likewise, more children in the Lovaas group were in typical schools subsequent to intervention (17 vs 1), although this specific outcome may have been attributable to factors, including differences in socioeconomic status and family constellation, that were evident between the groups.

One study[33] of 2 centers compared an eclectic approach to EIBI-based intervention alone. Children received 8 hours of intervention per day and were assessed over 1 year. Significant group differences were noted in language/communication and reciprocal social interaction measures; both groups showed decreases in symptom tallies, but there were more substantial decreases in the UCLA/Lovaas–based group. No significant differences in IQ change were reported. In a subsequent study on diagnostic stability[31] with unclear sample overlap, most children who received the intervention continued to display scores in the ASD range on the ADOS ($n = 53$).

Finally, 1 study tried to assess the role of intensity of the intervention on outcomes. Reed et al[12] studied the effectiveness of varying-intensity home-based and Lovaas–based programs that offered primarily 1-to-1 teaching. Assignment to high-intensity or low-intensity interventions (30 vs 13 hours/week on average) was based on geographic location. Children in the high-intensity group had higher ability and cognitive scores and lower autism severity scores at baseline. At the follow-up assessment 9 to 10 months after beginning the intervention, children who received the high-intensity intervention demonstrated statistically significant improvements in intellectual and educational functioning. Children who received the low-intensity intervention demonstrated statistically significant changes in educational functioning and nonsignificant improvement in cognitive functioning. The only significant difference between the groups was improved educational functioning associated with high-intensity intervention.

Three additional cohort studies[6,14,38] provided inconsistent data on the benefit of behavioral approaches, but all 3 of them had substantial risk of bias. Case series of early-intervention approaches[13,22,25,26,40] had mixed results, likely in part because of the substantial heterogeneity of interventions examined even within individual studies, little or no control of concomitant interventions, and poor fidelity to any given approach. Outcomes in these studies were more likely to be parent-reported and not based on validated tools.

Several chart reviews and other retrospective analyses have been used to understand treatment patterns and effects.[5,20,21,28–30] Interpretation of findings is most appropriately confined to noting that some children who receive intervention have displayed improvements during intervention in cognitive, adaptive, and autism-specific impairments, that characteristics of starting treatment and baseline abilities are correlated with improvement in some instances, and heterogeneity in terms of improvement is quite common. One chart review of 322 children served in a large catchment area,[29] however, provided some evidence for the feasibility of providing intensive behavioral interventions on a larger scale. Given the methodologic limits, including lack of clearly defined intervention characteristics, lack of a comparison group, retrospective collection, and lack of key measures for certain children at certain times, the intervention results were limited.

Comprehensive Intervention Approaches for Children Younger Than 2 Years

We identified 4 articles[2,15,32,39] with unique study populations that addressed treatment approaches for children younger than 2 years: 2 of the studies were prospective case series[32,39]; 1 was a nonrandomized controlled trial of fair quality[15]; and 1 was an RCT of good quality (Table 2).[2]

The Dawson et al[2] trial evaluated the effectiveness of the Early Start Denver Model (ESDM), an intervention approach in which applied behavior analysis techniques are blended within a functional developmental framework, for young children (mean age: 23 months) with ASDs. After 2 years of intensive intervention, children who received the ESDM displayed signifi-

cantly larger IQ gains compared with those in a community sample of children who received less-intensive intervention. Children in the experimental group also demonstrated significantly larger gains in adaptive behavior than did controls. Although the authors also reported diagnostic shifts within the spectrum in the sample (ie, autism to pervasive development disorder-not otherwise specified), these shifts were not matched with clinically significant improvements in terms of ADOS severity scores or measurements of repetitive behaviors.

The ESDM has also been studied in an early effectiveness trial[39] wherein the research team compared distance learning and live instruction for community-based therapists implementing intervention and training parents. Results suggest that both modalities were effective in teaching therapists to implement and train parents. There were significant child gains over time and across modalities; however, the results also suggested that implementation with fidelity required specific and explicit supervision. Thus, although promising in terms of treatment efficacy and extension to a younger population of children with ASDs, training demands for broad implementation seem substantial. In addition, the average age for enrollment was close to 2 years of age. As such, questions remain about how this model would apply to children younger than 2 years.

In another evaluation of an early-intervention approach, parents of 51 preschool-aged children suspected of having an ASD participated in the Hanen More Than Words program either immediately or after a delay.[15] Investigators' operationalization of "suspected ASD" included identification of language delay and concerns about social behavior by a pediatrician and/or a speech and language therapist, which resulted in inclusion of children without ASDs within the intervention and control groups. Investigators grouped pervasive development disorder-not otherwise specified and other developmental concerns under a category of "non–core autism." After the intervention period, reported language use was substantially higher for children in the intervention group, and both children with core autism and non–core autism demonstrated improvements. No group differences were found for ADOS scores or behavior issues. It is notable that more children in the intervention group had ASDs, and children in the intervention group had also received more "substantial intervention" outside of the treatment context. Thus, although potential benefit from parent training in social communication for young children with ASDs was demonstrated, the unique impact of this program for specific children remains unclear.

A prospective case series by Wetherby and Woods[32] served as a preliminary study for the Early Social Interaction Project, which emphasizes a parent-implemented individualized curriculum in a natural environment. The authors found significant within-group differences from before to after the test on social-communication measures in the early-social-interaction group. The number of children considered verbal also increased in the treatment group. These findings suggest that the Early Social Interaction Project has a positive effect on ASD symptoms, but findings have been limited by a lack of baseline comparisons and lack of documentation of parental implementation.

Parent Training

Of the 7 studies[17,18,23,24,27,36,43] on parent training, 4[17,18,28,43] included comparison groups; 3 of these studies[17,18,43] were of fair quality (Table 2). Three case series addressed parent-training approaches.[23,24,36]

Three RCTs in this category[17,18,43] compared parent training to eclectic approaches or pivotal response training. Drew et al[18] compared the effects of a home-based, parent-delivered intervention aimed at improving social communication and managing challenging behavior for 12 children with ASDs with a community-based control intervention group of 12 children. One year after treatment initiation, parents in the parent-training group reported that their children used more words than those in the community group. There were no group differences on nonverbal IQ, autism symptom severity, or words/gestures observed during follow-up assessment. Children in the treatment group unexpectedly lost IQ points during the study, whereas those in the control group demonstrated relatively stable cognitive abilities, although children in the treatment group had a higher IQ at study initiation.

Aldred et al[17] compared a social communication parent-based intervention with treatment as usual. Parents participated in initial workshops, monthly intervention sessions for which videotaped interactions were reviewed, and 6 months of maintenance visits. Twelve months after baseline, blinded evaluations revealed improvements on ADOS scores, and there was substantial improvement within the social domain, increased expressive vocabulary, and improved communication-related behaviors coded during interactions. Language gains were most prominent in younger, lower-functioning children. A lack of standardized measures of developmental performance, including baseline cognitive skills, and challenges in understanding and defining "treatment as usual" limit interpretation of the findings.

In a later report of this model, 152 children were randomly assigned to treat-

ment as usual or treatment as usual plus parent training.[43] Time in treatment-as-usual interventions was similar across groups, as were the types of interventions used. Similar numbers of children in both groups experienced diagnostic shifts from core autism to other diagnoses on the ASD spectrum. Teacher ratings of language and communication after intervention were not significantly different between groups, although ratings of parent-child interactions by independent assessors were positive for children in the social-communication group. Parent ratings of language and social communication were also more positive in the parent-training group.

Finally, Stahmer and Gist[27] examined the effects of a parent education support group with a parent education program that focused on pivotal response training, a treatment program designed to enhance core skill areas in autism by using naturalistic interactions. Involvement in the intervention was successful in changing parenting techniques and perceived language gain. However, the small sample size, lack of randomization, wide variation in children served, and the lack of objectively assessed changes in child behavior limit the reported results.

DISCUSSION

The evidence related to early intensive behavioral and developmental interventions comes primarily from 2 overlapping, but quite different, approaches: (1) UCLA/Lovaas–based intervention and EIBI variants; and (2) a developmentally focused comprehensive approach that uses the principles of applied behavior analysis (ie, the ESDM) geared toward very young children.[2,3] Individual studies of both approaches revealed greater improvements in cognitive performance, language skills, and adaptive behavior when compared with broadly defined eclectic treatments in subgroups of children.

In general, however, there have been too few studies of either approach to assert that observed estimates of effect for either approach are unlikely to change with future research. With a relatively larger (albeit still inadequate) body of literature, UCLA/Lovaas–based intervention and EIBI variant studies have revealed positive shifts in language, adaptive, cognitive, and educational outcomes, but our confidence (strength of evidence) in that effect is low because of the need for additional, confirmatory research, a lack of high-quality RCTs, and no studies that have directly compared effects of promising manualized treatment approaches. The evidence base for interventions for very young children, including the ESDM, is insufficient; there has been only 1 RCT, although results of this study were positive and the study warrants replication. On balance, however, the combined research on UCLA/Lovaas–based interventions and the ESDM suggests a benefit of early intensive approaches for some children that should continue to be studied.

Less-intensive interventions that provide parent training also may be useful for younger children with ASDs, particularly for improving social communication, language use, and, potentially, symptom severity and family functioning, but the current evidence base for such treatment remains insufficient.[17,18,27] Although parent-training programs can modify parenting behaviors during interactions, data are limited about their contribution to specific improvements in the short-term and long-term beyond simple language gains for some children. The few available studies used interventions that varied from study to study. Furthermore, outcomes assessed in these studies were frequently short-term, indirect (intermediate) measures.

One powerfully replicated finding across the available literature is that many children who receive early intensive intervention, across methodologies, will not demonstrate dramatic gains in social, cognitive, adaptive, and educational functioning. In addition, many children who do show robust gains in certain domains (ie, cognitive functioning or educational attainment) also continue to display other prominent areas of impairment. At the same time, although dramatic improvements in standardized scores have been observed in only a subset of children to date, it is important to note that even small improvements in standardized outcomes may translate into large, meaningful improvements in quality of life for children and their families. As such, early intensive behavioral and developmental approaches have significant potential but require further research. Specifically, research to better characterize subgroups of children who respond differently to individual approaches is much needed to make informed choices about which intervention is most likely to be beneficial for specific children.

We note that this review did not incorporate a selection of studies with fewer than 10 participants, many of which used the single-subject design methods that are common in the behavioral literature. Summary information on these studies is available in other reviews.[46] Furthermore, a particular challenge of conducting a systematic review of therapies for ASDs is the heterogeneity of the children within this spectrum disorder and the matching heterogeneity of populations across studies. Further complicating our assessment was the variety of intervention techniques and outcome measurements applied in this population.

The field of autism research is relatively young and growing, and as the body of literature develops further it is

likely that research methods and studies will coalesce in a way that will provide substantially more confidence in the evidence. At present, a paucity of research leaves us with individual studies that suggest promising outcomes but a critical need for replication, extension, and controlled studies of the factors that moderate treatment outcome. Thus, the low and insufficient strength of evidence reported in this review should not be interpreted as evidence that the interventions are not effective but, rather, as encouragement for additional research before effectiveness can be established.

CONCLUSIONS

There is not yet adequate evidence to pinpoint specific behavioral intervention approaches that are the most effective for individual children with ASDs. Authors of individual studies have reported positive outcomes from early and intensive behavioral and developmental intervention in cognitive performance, language skills, and adaptive behavior when delivered over substantial intervals of time (ie, 1–2 years) compared with broadly defined eclectic treatments. Variability in terms of response to such approaches seems great with subgroups of children who demonstrate more moderated response. To date, our ability to describe and predict these subgroups is limited.

ACKNOWLEDGMENTS

This project was supported by the AHRQ (contract number HHSA 290 2007 10065 I). Dr Warren has received research support from the National Institute of Mental Health, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the Maternal and Child Health Bureau, the National Science Foundation, and the AHRQ; and Dr Veenstra-VanderWeele has received research support from the National Institute of Mental Health, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, and the AHRQ.

We are grateful for the contributions of Wendy Stone, PhD, who provided guidance and mentorship including insight into the development of key questions and interpretation of the data. Allison Nahmias, MEd, was a tireless and positive part of the team, extracting data and providing input into the review process. We also appreciate the contributions of the parents who participated as we formulated our approach.

REFERENCES

1. Lovaas OI. Behavioral treatment and normal educational and intellectual functioning in young autistic children. *J Consult Clin Psychol*. 1987;55(1):3–9
2. Dawson G, Rogers S, Munson J, et al. Randomized, controlled trial of an intervention for toddlers with autism: the Early Start Denver Model. *Pediatrics*. 2010;125(1). Available at: www.pediatrics.org/cgi/content/full/125/1/e17
3. Smith T, Groen AD, Wynn JW. Randomized trial of intensive early intervention for children with pervasive developmental disorder. *Am J Ment Retard*. 2000;105(4):269–285
4. Cohen H, Amerine-Dickens M, Smith T. Early intensive behavioral treatment: replication of the UCLA model in a community setting. *J Dev Behav Pediatr*. 2006;27(2 suppl):S145–S155
5. Harris SL, Handleman JS. Age and IQ at intake as predictors of placement for young children with autism: a four- to six-year follow-up. *J Autism Dev Disord*. 2000;30(2):137–142
6. Remington B, Hastings RP, Kovshoff H, et al. Early intensive behavioral intervention: outcomes for children with autism and their parents after two years. *Am J Ment Retard*. 2007;112(6):418–438
7. Warren Z, Veenstra-VanderWeele J, Stone W, Bruzek JL, Nahmias AS, Foss-Feig JH, et al. *Therapies for Children With Autism Spectrum Disorders*. Comparative Effectiveness Review 26. (Prepared by the Vanderbilt Evidence-based Practice Center under Contract 290-02-HHSA-290-2007-10065-I.) AHRQ Publication 11-EHC035-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2007Available at: www.effectivehealthcare.ahrq.gov/reports/final.cfm. Accessed March 2011
8. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 2000
9. Lord C, Risi S, Lambrecht L, et al. The Autism Diagnostic Observation Schedule-generic: a standard measure of social and communication deficits associated with the spectrum of autism. *J Autism Dev Disord*. 2000;30(3):205–223
10. 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*. 1994;24(5):659–685
11. Ben Itzchak E, Lahat E, Burgin R, Zachor AD. Cognitive, behavior and intervention outcome in young children with autism. *Res Dev Disabil*. 2008;29(5):447–458
12. Reed P, Osborne LA, Corness M. Brief report: relative effectiveness of different home-based behavioral approaches to early teaching intervention. *J Autism Dev Disord*. 2007;37(9):1815–1821
13. Ben-Itzchak E, Zachor DA. The effects of intellectual functioning and autism severity on outcome of early behavioral intervention for children with autism. *Res Dev Disabil*. 2007;28(3):287–303
14. Eldevik S, Eikeseth S, Jahr E, Smith T. Effects of low-intensity behavioral treatment for children with autism and mental retardation. *J Autism Dev Disord*. 2006;36(2):211–224
15. McConachie H, Randle V, Hammal D, Le Couteur A. A controlled trial of a training course for parents of children with suspected autism spectrum disorder. *J Pediatr*. 2005;147(3):335–340
16. Beglinger L, Smith T. Concurrent validity of social subtype and IQ after early intensive behavioral intervention in children with autism: a preliminary investigation. *J Autism Dev Disord*. 2005;35(3):295–303
17. Aldred C, Green J, Adams C. A new social communication intervention for children with autism: pilot randomised controlled treatment study suggesting effectiveness. *J Child Psychol Psychiatry*. 2004;45(8):1420–1430
18. Drew A, Baird G, Baron-Cohen S, et al. A pilot

randomised control trial of a parent training intervention for pre-school children with autism: preliminary findings and methodological challenges. *Eur Child Adolesc Psychiatry*. 2002;11(6):266–272

19. Eikeseth S, Smith T, Jahr E, Eldevik S. Intensive behavioral treatment at school for 4- to 7-year-old children with autism: a 1-year comparison controlled study. *Behav Modif*. 2002;26(1):49–68
20. Boyd RD, Corley MJ. Outcome survey of early intensive behavioral intervention for young children with autism in a community setting. *Autism*. 2001;5(4):430–441
21. Gabriels RL, Hill DE, Pierce RA, Rogers SJ, Wehner B. Predictors of treatment outcome in young children with autism: a retrospective study. *Autism*. 2001;5(4):407–429
22. Mudford OC, Martin NT, Eikeseth S, Bibby P. Parent-managed behavioral treatment for preschool children with autism: some characteristics of UK programs. *Res Dev Disabil*. 2001;22(3):173–182
23. Anan RM, Warner LJ, McGillivary JE, Chong IM, Hines SJ. Group Intensive Family Training (GIFT) for preschoolers with autism spectrum disorders. *Behav Interv*. 2008; 23(3):165–180
24. Baker-Ericzén MJ, Stahmer AC, Burns A. Child demographics associated with outcomes in a community-based pivotal response training program. *J Posit Behav Interv*. 2007;9(1):52–60
25. Dillenburger K, Keenan M, Gallagher S, McElhinney M. Parent education and home-based behaviour analytic intervention: an examination of parents' perceptions of outcome. *J Intellect Dev Disabil*. 2004;29(2): 119–130
26. Arick JR, Young HE, Falco RA, et al. Designing an outcome study to monitor the progress of students with autism spectrum disorders. *Focus Autism Other Dev Disabl*. 2003; 18(2):75–87
27. Stahmer AC, Gist K. The effects of an accelerated parent education program on technique mastery and child outcome. *J Posit Behav Interv*. 2001;3(2):75–82
28. Luiselli JK, Cannon BOM, Ellis JT, Sisson RW. Home-based behavioral interventions for young children with autism/pervasive developmental disorder: a preliminary evaluation of outcome in relation to child age and intensity of service delivery. *Autism*. 2000; 4(4):426–438
29. Perry A, Cummings A, Geier JD, et al. Effectiveness of intensive behavioral intervention in a large, community-based program. *Res Autism Spectr Disord*. 2008;2(4): 621–642
30. Gabriels RL, Ivers BJ, Hill DE, Agnew JA, McNeill J. Stability of adaptive behaviors in middle-school children with autism spectrum disorders. *Res Autism Spectr Disord*. 2007;1(4):291–303
31. Zachor DA, Ben-Itzchak E, Rabinovich AL, Lahat E. Change in autism core symptoms with early intervention: predictors and outcomes. *Res Autism Spectr Disord*. 2009;3(4): 967–976
32. Wetherby AM, Woods JJ. Early social interaction project for children with autism spectrum disorders beginning in the second year of life: a preliminary study. *Topics Early Child Spec Educ*. 2006;26(2):67–82
33. Zachor DA, Ben-Itzchak E, Rabinovich AL, Lahat E. Change in autism core symptoms with intervention. *Res Autism Spectr Disord*. 2007;1(4):304–317
34. Hayward D, Eikeseth S, Gale C, Morgan S. Assessing progress during treatment for young children with autism receiving intensive behavioural interventions. *Autism*. 2009;13(6):613–633
35. Granpeesheh D, Tarbox J, Dixon DR, Carr E, Herbert M. Retrospective analysis of clinical records in 38 cases of recovery from autism. *Ann Clin Psychiatry*. 2009;21(4): 195–204
36. Keen D, Rodger S, Doussin K, Braithwaite M. A pilot study of the effects of a social-pragmatic intervention on the communication and symbolic play of children with autism. *Autism*. 2007;11(1):63–71
37. Howard JS, Sparkman CR, Cohen HG, Green G, Stanislaw H. A comparison of intensive behavior analytic and eclectic treatments for young children with autism. *Res Dev Disabil*. 2005;26(4):359–383
38. Farrell P, Trigonaki N, Webster D. An exploratory evaluation of two early intervention programmes for young children with autism. *Educ Child Psychol*. 2005;22(4):29–40
39. Vismara LA, Young GS, Stahmer AC, Griffith EM, Rogers SJ. Dissemination of evidence-based practice: can we train therapists from a distance? *J Autism Dev Disord*. 2009; 39(12):1636–1651
40. Bibby P, Eikeseth S, Martin NT, Mudford OC, Reeves D. Progress and outcomes for children with autism receiving parent-managed intensive interventions. *Res Dev Disabil*. 2002;23(1):81–104
41. Eikeseth S, Hayward D, Gale C, Gitlesen JP, Eldevik S. Intensity of supervision and outcome for preschool aged children receiving early and intensive behavioral interventions: a preliminary study. *Res Autism Spectr Disord*. 2009;3(1):67–73
42. Eikeseth S, Smith T, Jahr E, Eldevik S. Outcome for children with autism who began intensive behavioral treatment between ages 4 and 7: a comparison controlled study. *Behav Modif*. 2007;31(3):264–278
43. Green J, Charman T, McConachie H, et al. Parent-mediated communication-focused treatment in children with autism (PACT): a randomised controlled trial. *Lancet*. 2010; 375(9732):2152–2160
44. Russo NM, Skoe E, Trommer B, et al. Deficient brainstem encoding of pitch in children with autism spectrum disorders. *Clin Neurophysiol*. 2008;119(8):1720–1731
45. Sallows GO, Graupner TD. Intensive behavioral treatment for children with autism: four-year outcome and predictors. *Am J Ment Retard*. 2005;110(6):417–438
46. National Autism Center. *National Standards Report*. Randolph, MA: National Autism Center; 2009. Available at: www.nationalautismcenter.org/pdf/NAC Standards Report.pdf. Accessed March 10, 2011

A Systematic Review of Early Intensive Intervention for Autism Spectrum Disorders

Zachary Warren, Melissa L. McPheeters, Nila Sathe, Jennifer H. Foss-Feig, Allison Glasser and Jeremy Veenstra-VanderWeele

Pediatrics 2011;127;e1303
DOI: 10.1542/peds.2011-0426 originally published online April 4, 2011;

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

A Systematic Review of Early Intensive Intervention for Autism Spectrum Disorders

Zachary Warren, Melissa L. McPheeters, Nila Sathe, Jennifer H. Foss-Feig, Allison Glasser and Jeremy Veenstra-VanderWeele

Pediatrics 2011;127;e1303
DOI: 10.1542/peds.2011-0426 originally published online April 4, 2011;