

Critical Review

Systematic Review of Fetal Alcohol Spectrum Disorder Interventions Across the Life Span

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Background: Individuals with fetal alcohol spectrum disorders (FASDs) can experience profound impairments and long-term adverse outcomes. This systematic review adopts a life span perspective providing an extensive analysis of the available literature.

Methods: Studies were identified from PsycInfo, PubMed, Scopus, Web of Knowledge, CINAHL, ERIC, The Cochrane Central Register of Controlled Trials, and gray literature. Two reviewers independently screened the title and abstract of each reference, and the methodological rigor of the included studies was assessed using the Effective Public Health Project assessment tool.

Results: Thirty-two studies met the inclusion criteria, of which the vast majority targeted early to middle childhood. Two studies focused on early intervention in the postnatal period, and 6 studies aimed to improve attention and/or self-regulation in childhood. Three of these provided promising evidence on improving self-regulatory difficulties for children with FASDs. Nine studies focused on improving specific areas of dysfunction. Six studies addressed social skills; 3 of these used an adaptation of a well-validated social skills program. Three studies provided promising initial evidence that parents and caregivers could benefit from support with child behavior and a further 4 studies provided education and advocacy for parents/caregivers, teachers, or child welfare workers. The final 2 studies were aimed at supporting parents who were themselves affected by prenatal alcohol exposure.

Conclusions: There is growing evidence for interventions that improve outcomes for early to middle childhood. However, a lack of research exists outside of this developmental period. This lack of research is concerning given the potential positive impact of early intervention, for individuals and, financially, for governments. In addition, the lack of interventions for adolescents and adults further highlights the widening developmental gap and the potential influence of secondary disabilities for this at-risk population.

Key Words: Fetal Alcohol Spectrum Disorders, Prenatal Alcohol Exposure, Systematic Review, Intervention, Treatment.

FETAL ALCOHOL SPECTRUM disorder (FASD) is an umbrella term that refers to the spectrum of damage that can occur due to prenatal alcohol exposure (PAE; Chudley et al., 2005). The consequences can be profound for affected individuals, with impairments experienced in all areas of social, behavioral, and cognitive functioning.

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Prevalence rates vary, with the most recent review suggesting that 2.4 to 4.8% of first grade children in a representative Midwestern U.S. community were affected by FASDs (May et al., 2014). Ospina and Dennett (2013) highlighted the high rates of FASDs in foster care settings (305 to 520 per thousand) and the considerable variability in rates in Aboriginal populations. This finding was reflected in a recent Australian study of a remote Indigenous population (prevalence rate of 120 per 1,000 of fetal alcohol syndrome [FAS]/partial fetal alcohol syndrome [pFAS]; Fitzpatrick et al., 2015). While primary prevention is critically important in reducing the incidence of FASDs, there is a growing recognition that diagnosis and intervention may ameliorate some of the difficulties that result from PAE (Kodituwakku and Kodituwakku, 2011). In many high income countries such as Australia (Australian Government, 2013), Canada (Public Health Agency of Canada, 2005), and the United States (Olson et al., 2009a), policy development has emphasized the importance of secondary prevention through better diagnosis and intervention for individuals with FASDs.

Despite this clear imperative, relatively few treatment studies exist in the field. A systematic review (Peadon et al.,

2009) evaluated the impact of pharmacological ($n = 2$) and nonpharmacological ($n = 10$) interventions for children. This review included randomized controlled trials (RCTs), quasi-RCTs, non-RCTs, and cohort studies with pre- and postintervention measurements. Meta-analysis was not possible because of the highly variable nature of the interventions, leading the authors to conclude that there was currently a lack of good quality evidence for specific interventions for children with FASDs. Subsequently, there have been a number of narrative reviews of interventions for children and adolescents with FASDs (Kodituwakku, 2010; Olson et al., 2009b; Paley and O'Connor, 2011; Petrenko, 2015). Importantly, Kodituwakku (2010) and Olson and colleagues (2009b) proposed theoretical frameworks to guide the development of interventions. Olson and colleagues (2009b) integrated developmental and family systems theory, and Kodituwakku (2010) presented a neurodevelopmental framework in which it was proposed that early intervention in self-regulation and attention is likely to have more far-reaching effects than specific training in other domains. More recently, Petrenko (2015) has called for a unification of these conceptual frameworks and the inclusion of information from the lived experiences of parents and individuals with FASDs.

The current systematic review expands upon these previous reviews in 3 ways. First, we include intervention studies that were identified by Peadon and colleagues (2009) as in progress or recently completed at the time of their review. Second, we assess the methodological quality of interventions using a standardized assessment rating tool. Third, we take a life span developmental perspective, rather than restricting our focus to children. As the impact of PAE is lifelong, there is a growing consensus that the needs of individuals should be considered from such an approach in order to investigate the potential to ameliorate difficulties and to improve well-being for all individuals with FASDs.

MATERIALS AND METHODS

This systematic review has been reported in line with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses PRISMA (Liberati et al., 2009; Moher et al., 2009). Details of the protocol for this systematic review were registered with PROSPERO (CRD42014015188).

Inclusion Criteria

Studies were considered for the review if (i) the target population consisted of individuals of any age with PAE that included FAS, pFAS, alcohol-related neurodevelopmental disorder (ARND), or PAE; (ii) the intervention could be classified as primarily focusing on improving well-being and functioning through the provision of behavioral treatment, advocacy, or support (thereby excluding pharmacological interventions); (iii) quantitative measures of functioning were reported in order that comparisons could be made about potential gains. No restrictions were placed on the type of outcomes or study design.

Search Strategy and Study Selection

Studies were identified during December 2014 from the following electronic databases: PsycInfo, PubMed, Scopus, Web of Knowledge, CINAHL, ERIC, and The Cochrane Central Register of Controlled Trials. Search terms were ["fetal alcohol spectrum disorder" OR "fetal alcohol syndrome" OR "alcohol-related neurodevelopmental disorder"] AND ["intervention" OR "treatment" OR "therapy"]. No date, document type, or language restrictions were placed on the searches. Forty FASD organizations were identified and webpages searched to locate non-peer-reviewed intervention trials that could be included (see Supporting Information for a complete list).

Two reviewers independently screened the title and abstract of each reference identified by the searches and determined the potential relevance of each article. For potentially relevant articles or, in cases of disagreement, the full article was obtained, independently inspected, and inclusion criteria applied.

Study Quality Assessment

The methodological rigor of the included studies was assessed using the Effective Public Health Project (EPHPP) assessment tool. The tool was developed to assess primary studies in public health (Thomas et al., 2004) and is based on guidelines set out by Jadad and colleagues (1996) and Mulrow and Oxman (1994). The EPHPP tool consists of 6 quality components: selection bias, study design, confounders, blinding, data collection methods, and withdrawals and dropouts. Each study was rated on these components as "strong," "moderate," or "weak" (see Table 1 for an overview of the EPHPP tool). Jüni and colleagues (1999) recommend that relevant methodological aspects of studies should be individually assessed, and a total score should not be used. Therefore, an overall rating of the quality of the studies was not carried out. The quality assessment was undertaken independently by 2 reviewers, and any disagreements were resolved by discussion.

Data Extraction and Synthesis

Considerable heterogeneity in both the nature of the interventions and the measures used in the studies precluded the use of meta-analysis (Higgins and Green, 2011); therefore, a narrative synthesis method was used. Data were extracted systematically using a preformulated tool consisting of study design, sample size and population, intervention approach, and main results. The studies were subsequently grouped according to key outcome domains and reported within a life span perspective by looking first at those studies focusing on early infancy, then early to middle childhood and, finally, adolescence and adulthood.

RESULTS

Study Characteristics

The electronic database search located 2,962 citations (after duplicates were removed) which then underwent title and abstract screening. An additional 5 sources were included after an examination of reference lists, and another 2 reports were found from the Internet searches of relevant FASD organizations' publication libraries. A full text review by 2 reviewers was undertaken for 51 studies; 29 met study inclusion criteria (see Fig. 1 for detailed information). An updated database search conducted prior to submission

Table 1. Quality Assessment Components and Ratings for Effective Public Health Project Instrument

Components	Strong	Moderate	Weak
Selection bias	Very likely to be representative of the target population and >80% participation rate	Somewhat likely to be representative of the target population and 60 to 79% participation rate	Not likely to be representative (i.e., self-referred), <60% participation rate or not stated
Design	Randomized controlled trial and controlled clinical trial	Cohort analytic, case-control, cohort, or an interrupted time series	All other designs or designs not stated
Confounders	Controlled for at least 80% of confounders	Controlled for 60 to 79% of confounders	Confounders not controlled for, or not stated
Blinding	Blinding of outcome assessor and study participants to intervention status and/or research question	Blinding of either outcome assessor or study participants or blinding is not described	Outcome assessor and study participants are aware of intervention status and/or research question
Data collection methods	Tools are valid and reliable	Tools are valid but have not been shown to be reliable	No evidence of validity or reliability
Withdrawals and dropouts	Follow-up rate of >80% of participants	Follow-up rate of 60 to 79% of participants	Follow-up rate of <60% of participants or withdrawals and dropouts not described

identified an additional 3 studies, resulting in a final total of 32 studies (Table 2).

The vast majority of studies investigated the effectiveness of interventions that targeted aspects of neurocognitive functioning. Of these, 2 studies aimed to improve developmental outcomes in infants. Six studies targeted underlying self-regulatory deficits, or attentional control. Nine studies focused on specific areas of dysfunction, such as math skills ($n = 3$), language and literacy skills ($n = 2$), fire/street safety skills ($n = 2$), memory rehearsal ($n = 1$), and motor skills ($n = 1$). Six studies addressed social skills and 3 studies aimed to improve children's behavior and reduce parental stress by providing structured parenting programs. A further 4 studies provided education and advocacy knowledge for parents and caregivers ($n = 2$), teachers ($n = 1$), and child welfare workers ($n = 1$), and the final 2 studies were both aimed at supporting parents who were themselves affected by PAE.

Quality Rating

The details of the quality ratings for the included studies are shown in Table 3. It is notable that none of the studies received a rating of "strong" for the component of "selection bias" or "blinding." Nineteen of the studies were rated "strong" in study design; this reflects the number of RCTs and controlled clinical trials (CCTs) in the identified studies. Twenty-seven of the studies, across all study design types, used measures that were reliable and valid. Seventeen studies reached the criteria to be scored as "strong" for withdrawal/dropouts.

Efficacy of Interventions Targeting Individuals with FASD Across the Life Span

Developmental Outcomes in Infants. Two studies (Kartin et al., 2002; Yazdani et al., 2009) primarily focused on helping mothers to provide an optimal environment to promote their infant's development. Yazdani and colleagues (2009) found that following their home visiting service, children with PAE scored in the average range on developmental

tests, which may be interpreted to suggest that deficits were ameliorated through an intensive early intervention service. However, in a study with a considerably stronger design, Kartin and colleagues (2002) found no effect of the home visiting service on the same measures of developmental outcome, with children scoring significantly below age-expected norms.

Self-Regulation and Attentional Control. A range of approaches and intervention studies aimed to improve cognitive functioning in early to middle childhood. Three studies investigated the effectiveness of ALERT (Williams and Shellenberger, 1996), a program specifically adapted for children with FASDs, and designed to improve executive functioning (EF). These studies were methodologically robust albeit with small sample sizes and limited follow-up data. Nonetheless, gains were made in all 3 studies (Nash et al., 2015; Soh et al., 2015; Wells et al., 2012) on measures of EF, such as parent report using the Behaviour Rating Inventory of Executive Functioning (BRIEF; Gioia et al., 2000) and selected neuropsychological tests. Most recently, Soh and colleagues (2015) found changes in gray matter volume in critical regions for self-regulation in children in the immediate treatment group compared to children in the delayed treatment group who showed modest growth in one related area.

There is also some evidence that gains can be made on attention and that these gains can generalize to other areas. Kerns and colleagues (2010) found improvements in the immediate posttreatment assessment on measures of sustained and selective attention, and improvements also extended to math and reading fluency. In an unpublished thesis, Vernescu (2008) found that children showed significant improvements in auditory and visual sustained attention and on tasks assessing nonverbal reasoning. However, gains in cognitive functioning were not obtained in a pilot study by Adnams and colleagues (reported in Riley et al., 2003) using cognitive control therapy to enable children to learn metacognitive skills. This intervention was, however, limited by the small sample size, and the authors suggested that the duration was less than required.

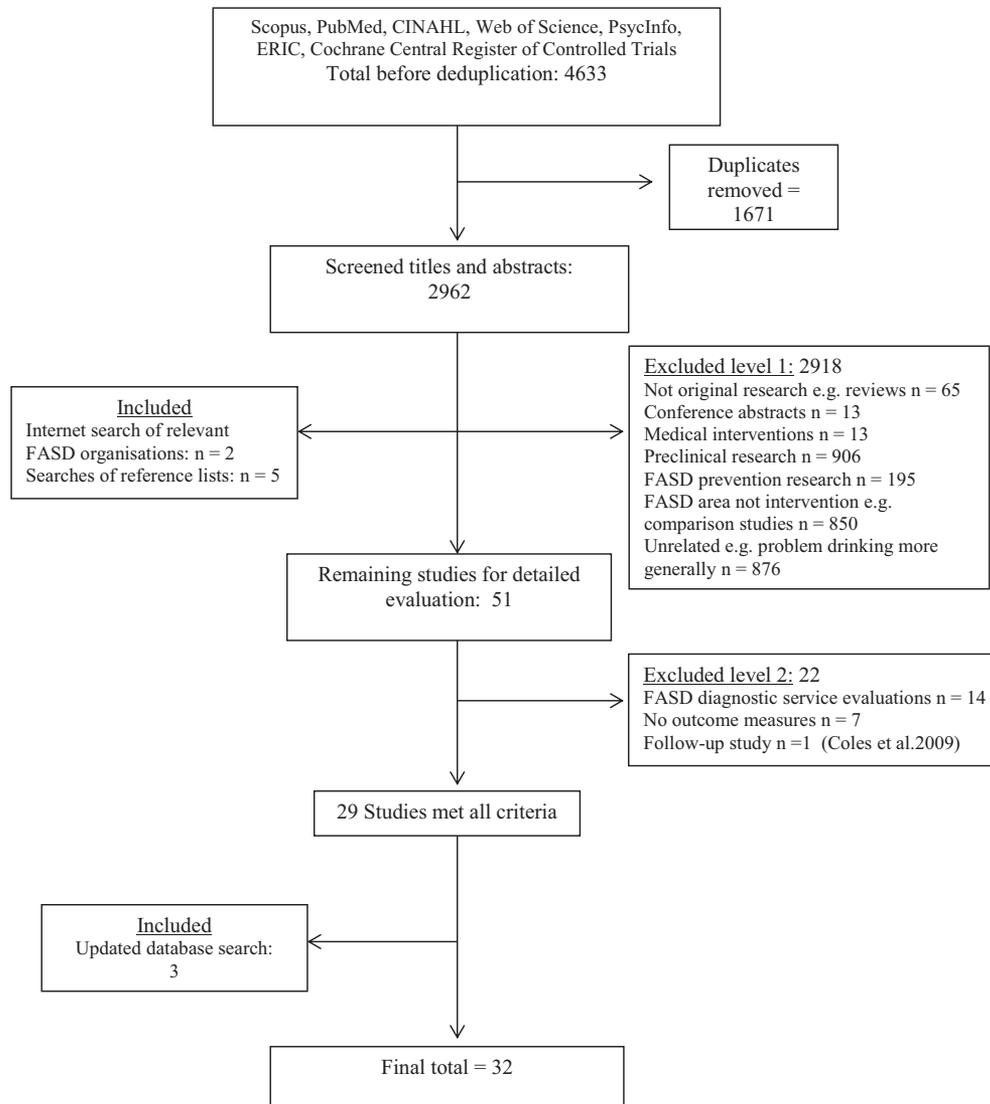


Fig. 1. Study selection flow chart.

Specific Skills. Nine studies focused on remediation of specific skills. Three demonstrated that children were able to benefit from a mathematical skills program specifically designed for children with FASDs. The first intervention trial carried out by Kable and colleagues (2007) found that 6 weeks of The Math Interactive Learning Experience (MILE) program resulted in significant gains in both math knowledge and parent reports of problem behavior, which were maintained at 6 months compared to control children (Coles et al., 2009). More recently, Kable and colleagues (2015) conducted a community translation of the MILE program and found that compared to a parent instruction group, children in the intervention groups (center-based or community-based) showed more positive gains in math skills immediately posttest. Finally, findings from a case study ($n = 5$) provide preliminary evidence for the use of components of the MILE program to improve nonverbal reasoning, reading comprehension, and mathematics reasoning in chil-

dren and in adolescents aged 10 to 13 years (Millians and Coles, 2014).

Two studies (Coles et al., 2007; Padgett et al., 2006) demonstrated that children with FAS or pFAS were able to learn a sequence of safety commands after playing computer games designed to teach safety skills relating to either fire or street safety. Adnams and colleagues (2007) tested the effectiveness of a classroom-based literacy training intervention of 38 hours of therapy over a 9-month period. Children with FASDs improved in specific language and literacy skills, although no parallel improvements in general scholastic skills were found compared to control children.

Loomes and colleagues (2008) found short-term improvements in digit span in children receiving rehearsal training across 10 days, while Gryiec and colleagues (2004) found improvements in the number of words spelt correctly, following 6 weeks of practicing a “cover, copy, and compare” spelling procedure by a 7-year-old child. Finally, Keiver and

Table 2. Intervention Studies Across the Life Span

Author and design	Sample size and population	Approach and follow-up	Results
Developmental outcome in infants			
Karlin and colleagues (2002) CCT	65 home visiting advocacy service, 31 controls; women reported heavy substance use during pregnancy. Recruited within 1 month of delivery; children tested at 3 years	3-year home visitation program to assist mothers with drug/alcohol treatment and support	No differences between the groups although all children performed below developmental age
Yazdani and colleagues (2009) Retrospective case-file analysis	28 children primary PAE and 15 no alcohol use recruited. All mothers reported use of cocaine. Children tested at 2/3 years	Intensive home visiting program with liaison with ancillary services, addiction, parenting	No differences between groups. All children scored in normal range
Self-regulation and attentional control			
Nash and colleagues (2015) CCT	14 treatment, 15 delayed; pFAS & ARND; Canadian Guidelines or 4-digit code. Mean age 10 years (8 to 12 range)	ALERT program for self-regulation; 12 weeks; individual 1-hour sessions. Pre/post and 6-month follow-up	Significant improvement for treatment compared to delayed on the Inhibition-Naming & Affect Recognition (NEPSY-II) and the BRIEF
Wells and colleagues (2012) RCT	40 treatment, 38 control; FAS or ARND; Canadian Guidelines or 4-digit code. Mean age 8 years (6 to 11 range)	ALERT; 12 weeks, 75-minute group sessions for children and parents run separately. Pre/post and 2/3-month follow-up	Treatment group showed significant improvement compared to control group on the BRIEF and the RATC
Soh and colleagues (2015) CCT	20 treatment, 18 delayed; 27 control FAS, pFAS, ARND; Canadian Guidelines or 4-digit code. Mean age 9 years (8 to 12 range)	ALERT 12 weeks; individual 1.5 hourly sessions; pre/post-testing; 2 weeks after treatment	Improvements on BRIEF and NEPSY-II for treatment group. Some evidence of increase in gray matter for treatment relative to delayed treatment
Kerns and colleagues (2010) Cohort	10 children previous diagnosis of FASD (diagnostic categories/criteria not stated). Mean age 12 years (8 to 15 range)	The Computerised Progressive Attention Program; 16 hours over 9 weeks at school; pre/post-testing	Significant decrease in reaction times and distractibility; significant improvement in auditory sustained attention and math and reading fluency
Vernescu (2008) CCT	10 treatment, 10 control; pFAS & FAS; Canadian guidelines. Mean age 9 years (6 to 11 range)	Activities from the pay attention training protocol and additional visual search tasks; 12 daily individual 30-minute sessions; pre/post-testing	Intervention group showed: Significant improvements in nonverbal reasoning, auditory and visual sustained attention. Trend for improved performance on alternating attention
Adnams et al. reported in Riley and colleagues (2003) CCT	5 treatment; 5 control; identified from previous study (<i>n</i> = 64) diagnosed with FAS criteria not stated. Mean age 8 years	Cognitive control therapy 1-hour session each week for 10 school-term months; pre/post-testing	Improvement in behavior ratings in intervention group. No differences on neuropsychological tests
Specific skills			
Kable and colleagues (2007) CCT	28 treatment; 26 comparison. FAS or pFAS using IOM criteria or significant alcohol-related dysmorphism. Mean age 6 years (3 to 10 range)	All parents attended 2 × 2 hours workshops on FASD. All children received individual learning plan; treatment group received adapted tuition for maths MILE program. Pre/post-testing	Significant gains in caregiver knowledge of FAS, behavior regulation and advocacy; decrease in problem behaviors. Significant higher gains found for intervention group on maths knowledge
Kable and colleagues (2015) CCT	20 centre-based treatment; 19 community treatment; 21 parent instruction group, FAS or pFAS; IOM criteria or significant alcohol-related dysmorphism. Mean age 6 years	All parents attended 2 × 2 hours workshops on FASD and provided manual on math learning (parent instruction group received no further intervention). Community translation of the MILE program expanded to 15 weeks and incorporated metacognitive control techniques. Pre/post-testing Individualized interventions using the MILE program adapted for use with older children. Pre/post-testing	Participants in both the MILE groups showed greater gains in math skills at posttest compared to parent instruction group
Millians and Coles (2014) Case study	5; affected or suspected of PAE in foster care; 2 FAS; 1 no diagnosis, 1 deferred, 1 pFAS, IOM criteria. Ten to 13 years	Played a virtual reality game of fire safety and street safety. Pre/post-testing and follow-up test at 1 week	Three of 5 adolescents made gains in 1 cognitive domain although these differed for each child. Two showed no changes
Coles and colleagues (2007) CCT	16 children allocated to street safety and 16 to fire safety computer games, FAS or pFAS; IOM criteria. Mean age 7 years (4 to 10 range)		Posttest children showed significant greater knowledge of fire and street safety; 1 week posttest children who played the fire safety game showed significant knowledge gain while street safety did not; majority of children in both groups were able to demonstrate the skills they learnt immediately and after 1 week

Continued.

Table 2. (Continued)

Author and design	Sample size and population	Approach and follow-up	Results
Padgett and colleagues (2006) Case study	5 children; FAS or pFAS; IOM criteria. Five to 7 years	Played a virtual reality game of fire/street safety. Pre/post-testing and 1-week follow-up	All 5 children reached 100% accuracy on the fire safety game; at 1 week posttest able to perform steps in the correct sequence
Adams and colleagues (2007) CCT	18 exposed treatment; 18 exposed control; 23 nonexposed control; FAS pFAS or "deferred diagnosis category;" revised IOM criteria. Mean age 10 years (9 to 10 range)	Language and literacy intervention, 1 hour per week in groups of 5 children; 38 hours of therapy over 9 months; pre/post-testing	Treatment group significant improved on preliteracy, reading, and spelling; no significant difference between intervention and control on general scholastic tests; scores of exposed children (intervention and control) remained lower than nonexposed children
Loomes and colleagues (2008) CCT	17 Experimental, 16 controls; previously diagnosed with ARND, neurobehavioral, or static encephalopathy. Mean age 7 years (4 to 11 range)	Experimental group-rehearsal training across 10 days. Pre/post-testing	Experimental group showed significant increase in digit span scores over the 3 sessions compared to the control group who showed no significant increase
Gryiec and colleagues (2004) Interrupted time series	1 child; 7-year-old girl; diagnosed with FAS (criteria not stated) and learning disabled	Cover, copy, and compare spelling procedure; 6 weeks with 2 to 3 sessions per week; 10 to 20 minutes per session; multiple baselines and measures at each session	Increase in number of words spelled correctly
Keiver and colleagues (2015) CCT	24 FASD, 32 control, ARND, pFAS & FAS; 4-digit code & Canadian Guidelines. Mean age 10 years (6 to 13 range)	FAST Club 8-week group motor skills intervention—Two 1.5-hour sessions per week for 8 weeks. Pre/post-testing	Cortisol levels were higher in children with FASD compared to control children in the afternoon and evening; the program did not significantly affect cortisol levels in children with FASD
Social skills interventions			
Timler and colleagues (2005) Case Study	1 child; girl aged 9 years 8 months, previous diagnosis of FASD (diagnostic category not stated); 4-digit code	Social communication intervention 6 weeks—2 weeks of individual sessions (1 hour each) and 4 weeks of group sessions with 2 peers (2 hours each). Pre/post-testing	Increased use of mental state verbs (e.g., know, thought). Increased knowledge of social script strategies that were used during the intervention (e.g., plan and take action)
O'Connor and colleagues (2006) CCT	51 treatment, 49 delayed, FAS, pFAS & ARND, 4-digit code & IOM criteria. Mean age 8 years (6 to 12 range)	CFT; 12 sessions, 90 minutes and separate concurrent parent sessions. Pre/post and 3-month follow-up	CFT group showed significant improvement in social skills and decreased problem behaviors compared to delayed CFT at posttreatment and follow-up
Keil and colleagues (2010) CCT	51 treatment, 49 delayed; FAS, pFAS or ARND; 4-digit code & IOM criteria. Mean age 8 years (6 to 12 range)	CFT 12 sessions, 90 minutes, separate concurrent parent sessions. Pre/post and 3-month follow-up	CFT group made fewer hostile attributions in the peer group entry scenarios than delayed treatment group; maintained at follow-up
O'Connor and colleagues (2012) CCT	41 treatment, 44 standard care, PAE ($n = 32$) FAS, pFAS, ARND, 4-digit code & IOM criteria; 53 control children without PAE. Mean age 8 years (6 to 12 range)	CFT in a community setting 12 sessions, 90 minutes, and separate concurrent parent sessions. Pre/post and 3-month follow-up	CFT group significant improvement on test of social skills knowledge and self-esteem compared to standard care. CFT equally effective for children with PAE as for those without
Meyer (1998) Case Study	4 children identified with FAE. Mean age 8 years	Required to imitate a 4-minute videotape of a block building task. Pre/post-observation	None of the children were able to imitate the block building task
Sparks-Keeney and colleagues (2011) Cohort	11 children with FASDs (diagnostic categories not stated); 4 digit code. Seven to 12 years	Community-based social skills group 90-minute sessions for 7 weeks, concurrent sessions with parents. Pre/post-testing	8 of the 11 children's parents completed an adapted 25-item SSRS at pre- and post-testing. Of those, 7 showed improved ratings
Parenting skills			
Olson et al. reported in Bertrand (2009) RCT	26 treatment; 26 standard care diagnosed with FASD (diagnostic categories not stated) 4-digit code, all had significant challenging behaviors. Five to 11 years	Families moving forward (FMF) behavioral consultation fortnightly sessions of 90 minutes for 9 to 11 months. Pre/post-testing	Improved parental self-efficacy, parental self-care, and parent report of child behavior problems in FMF compared to standard care; no differences in child-related parental stress
Gurwitch et al. reported in Bertrand (2009) RCT	23 treatment and 23 comparison; diagnosed with FASD (diagnostic categories not stated); modified IOM criteria and 4-digit code. Three to 7 years	Group adaptation of PCIT; Comparison—parent-only support and management; Both weekly 1-hour sessions × 14 weeks; pre-, mid- and post-testing	Approximately 50% attrition for both groups within the 14 weeks of treatment; No group differences observed, although reductions found across both groups on parenting stress and child behavioral problems

Continued.

Table 2. (Continued)

Author and design	Sample size and population	Approach and follow-up	Results
Kable and colleagues (2012) CCT	24 community standard; 23 workshop; 29 Internet training parents of a child with FAS or pFAS; IOM criteria or significant alcohol-related dysmorphism. Mean age 7 years	Information only (community standard), workshop or Internet support 2 × 2 hour sessions covering behavior, information, and advocacy. Pre/post-testing	All groups reported improvement in knowledge of behavioral learning principles; Internet and workshop significant improvement in knowledge of FASD and parent advocacy; Some indication that significant differences reported on child behavior in community and workshop groups but not Internet group
Support, education & advocacy Leenaars and colleagues (2012) Retrospective case-file analysis Pelech and colleagues (2013) Cohort analytic	186 families parenting at least 1 child with FASD (diagnostic categories not stated); 4-digit code. Mean age 10 years (1 to 23 range) 98 intervention 84 comparison; out-of-home-care; diagnosed (categories or criteria not stated) or suspected (i.e., documented PAE). Mean age 11 years	Coaching families program provides support, education and advocacy for families with a child with FASD. Program length not stated. Pre/post-testing Promising practices enhanced child welfare practices to improve placement stability. Tracked placement changes during 15-month period prior and compared to placement changes during project implementation	Reduction in numbers of daily needs and parenting stress. Length of time in program associated with a greater reduction in needs and number of goals met Significant decline in number of placement changes among children in the intervention group
Clark and colleagues (2014) CCT	6 teachers and 7 children treatment; 6 teachers and 6 children comparison group; and their classroom teachers; FAS, Gestalt diagnostic guidelines. Mean age 7 years (6 to 12 range)	Professional development for teachers focused on classroom environment. Over 1 school year. Included 2 full-day and 4 half-day workshops and weekly mentor-teacher meetings. Pre-, mid- and post-testing	Significant improvements in adaptive skills and significant decreases in school problems (both measured by the BASC-2 completed by teachers) reported for the intervention group; no significant changes found for the comparison group; no significant changes in academic achievement for intervention students
Hume and colleagues (2009) Cohort	81 parents/caregivers completed both intake and exit questionnaires; Families with children or youth with FASDs (diagnostic categories not stated); 0 to 19 years	“Key worker” program assist parents/caregivers and service providers understand child’s deficits and help develop environmental accommodations program length not stated. Pre/post-testing	Trends in direction of increased parenting confidence, parents experiencing less stress, reduction in parent/caregiver challenges; childcare were significant; changes reported in parent/caregivers’ ratings of child problem behaviors—overall no statistical difference from pre to post
Supporting parents who have FASD Denys and colleagues (2011) Retrospective case-file analysis	24 Parents with FASD or suspected FASD (1 male, 23 female) (diagnostic categories/guidelines not stated). Mean age 30 years (19 to 47 range)	Step-by-step—3-year program; mentors work with families to help access support and services. Pre/post-testing	Significant reduction in client’s needs (e.g., housing, financial issues, mental health issues, addiction) significant increase in client’s goals (e.g., parenting, personal skills management, assessment, self-care and health)
Grant and colleagues (2004) Cohort	19; women diagnosed with or suspected FASDs; years enrolled in standard PCAP for women at risk of giving birth to a child with FASD with at least 1 year remaining in the program; 4-digit code. Mean age 22 years (14 to 36 range)	12-month pilot of PCAP-home visitation case management program modified to accommodate clients with FASDs. Pre/post-testing	Decreased alcohol and drug use. Increased use of contraception, medical, and mental health care services. Increases in obtaining stable housing

CCT, Controlled clinical trial; RCT, randomized controlled trial; FAS, fetal alcohol syndrome; ARND, alcohol-related neurodevelopmental disorder; BRIEF, Behaviour Rating Inventory of Executive Function; RATC, The Roberts Apperception Test for Children; MILE, Math Interactive Learning Experience; CFT, Children’s Friendship Training; FAE, fetal alcohol effects—child displays characteristics of FAS but not full syndrome; PCIT, parent-child interaction therapy; SSRS, Social Skills Rating System; BASC-2, Behaviour Assessment System for Children Second Edition; FASD, fetal alcohol spectrum disorder; IOM, Institute of Medicine; PAE, prenatal alcohol exposure; PCAP, parent-child assistance program.

Table 3. Quality Assessment Results for Included Studies

Author/Date	Selection bias	Study design	Confounders	Blinding	Data collection methods	Withdrawals/Dropouts
Developmental outcomes in infants						
Kartin and colleagues (2002)	Moderate	Strong	Strong	Moderate	Strong	Strong
Yazdani and colleagues (2009)	Moderate	Weak	Strong	N/A	Strong	N/A
Self-regulation and attentional control						
Nash and colleagues (2015)	Weak	Strong	Strong	Moderate	Strong	Strong
Wells and colleagues (2012)	Moderate	Strong	Strong	Moderate	Strong	Strong
Soh and colleagues (2015)	Weak	Strong	Strong	Moderate	Strong	Moderate
Kerns and colleagues (2010)	Weak	Moderate	N/A	N/A	Strong	Strong
Vernescu (2008)	Moderate	Strong	Strong	Moderate	Strong	Strong
Adnams and colleagues (reported in Riley et al., 2003)	Moderate	Strong	Weak	Moderate	Strong	Strong
Specific skills						
Kable and colleagues (2007)	Weak	Strong	Strong	Moderate	Strong	Strong
Kable and colleagues (2012)	Weak	Strong	Strong	Moderate	Strong	Strong
Millians and Coles (2014)	Moderate	Weak	N/A	N/A	Strong	N/A
Coles and colleagues (2007)	Weak	Strong	Strong	Moderate	Moderate	Strong
Padgett and colleagues (2006)	Moderate	Weak	N/A	N/A	Moderate	N/A
Adnams and colleagues (2007)	Moderate	Strong	Strong	Moderate	Strong	Strong
Loomes and colleagues (2008)	Moderate	Strong	Strong	N/A	Strong	Strong
Gryiec and colleagues (2004)	Moderate	Moderate	N/A	N/A	Strong	N/A
Keiver and colleagues (2015)	Weak	Strong	Strong	N/A	Strong	Strong
Social skills						
Timler and colleagues (2005)	Moderate	Weak	N/A	N/A	Strong	N/A
O'Connor and colleagues (2006)	Weak	Strong	Strong	Moderate	Strong	Strong
Keil and colleagues (2010)	Weak	Strong	Strong	Moderate	Strong	Strong
O'Connor and colleagues (2012)	Moderate	Strong	Strong	Moderate	Strong	Moderate
Meyer (1998)	Weak	Weak	N/A	N/A	Strong	N/A
Sparks-Keeney and colleagues (2011)	Moderate	Moderate	N/A	N/A	Strong	Moderate
Parenting skills						
Olson and colleagues (reported in Bertrand, 2009)	Moderate	Strong	Weak	Moderate	Strong	Strong
Gurwitch and colleagues (reported in Bertrand, 2009)	Weak	Strong	Weak	Moderate	Strong	Weak
Kable and colleagues (2012)	Moderate	Strong	Weak	Moderate	Strong	Moderate
Support, education, and advocacy						
Leenaars and colleagues (2012)	Moderate	Weak	N/A	N/A	Moderate	N/A
Pelech and colleagues (2013)	Moderate	Moderate	Strong	Moderate	Strong	Moderate
Clark and colleagues (2014)	Moderate	Strong	Weak	Moderate	Strong	Strong
Hume and colleagues (2009)	Weak	Moderate	N/A	N/A	Moderate	Weak
Supporting parents who have FASD						
Denys and colleagues (2011)	Moderate	Weak	N/A	N/A	Moderate	N/A
Grant and colleagues (2004)	Moderate	Moderate	N/A	N/A	Strong	Strong

Confounders were not assessed for 1-group studies; blinding was not assessed for 1-group studies, case-file analyses or studies that did not require interaction with participants when collecting outcome assessments; withdrawals/dropouts were not assessed for case studies or retrospective case-file analyses.

colleagues (2015) embedded an evaluation of a motor skills program in a study of the regulation of the stress response in typically developing children and children with FASDs. Cortisol levels were found to be higher in children with FASDs in the afternoon and evening compared to that of control children. No changes were associated with participation in the motor skills program. Overall, these studies suggest that early cognitive remediation for school-aged children shows promise in improving some specific areas of difficulty for children with PAE.

Social Skills. In light of the well-established difficulties faced by children with FASDs in understanding social cues and problems in peer relationships, research has addressed whether interventions with a specific focus on social skills result in improvements. Six studies were identified, all

targeting children in the 3- to 12-year-age group. The earliest of these was a single case study showing improvements in social communication in the short term (Timler et al., 2005). Subsequently, 3 CCTs (Keil et al., 2010; O'Connor et al., 2006, 2012) evaluated an adaptation of the Child Friendship Training (CFT) program. Children were taught simple rules of social engagement, including modeling, which they rehearsed and practiced across settings while being coached by parents. In the first of these studies, O'Connor and colleagues (2006) found parents who received the intervention reported improvement in their children at postintervention, while parents in the wait list group did not. Importantly, an analysis of clinical significance indicated that children in the intervention group scored in the lower end of the normal range at follow-up. In a later study, Keil and colleagues (2010) found that the children in the

CFT group demonstrated improved social skills and lower rates of hostile attribution (as measured by a cartoon story task) compared to a delayed treatment group. Furthermore, these gains were maintained at a 3-month follow-up for the group receiving CFT first.

Last, O'Connor and colleagues (2012) found posttreatment gains in social skills and self-esteem for children who received CFT compared to a standard care condition in a community mental health setting. Notably, the intervention was equally effective for children with PAE compared to those without. Indicating that children with PAE can be treated effectively in community settings if interventions are suitably adapted and therapists are appropriately trained. Gains in parent-rated social skills were also seen in a small ($n = 11$) trial of a community-based social skills group (Sparks-Keeney et al., 2011). Conversely, a case study ($n = 4$) found that children with PAE were not able to imitate a block building task after viewing a videotape of a boy of a similar age completing the same task (Meyer, 1998). Taken together, these studies provide strong evidence for the utility of structured programs that include children and parents in helping to improve social skills.

Efficacy of Interventions that Support Parents, Caregivers, and Others

Parenting Skills. Three studies provided explicit instruction in parenting skills. Olson and colleagues (reported in Bertrand, 2009) found a significant improvement in parental self-efficacy, parent needs and parent self-care, and a reduction in child behavior problems in families receiving the families moving forward program. One study evaluating parent-child interaction therapy compared to a parent-only parenting support and management program found reductions in child behavioral problems and parenting stress. The observed changes for both programs were clinically significant with mean scores on child behavior problems moving from the clinical to the nonclinical range for both groups (Gurwitsch et al., reported in Bertrand, 2009).

Kable and colleagues (2012) carried out a controlled trial comparing parent education delivered in 3 formats: an information packet (i.e., community standard care), group workshops, and Internet training. All 3 groups showed increases in knowledge of behavioral learning principles. Some indication of differential improvement in behavior occurred across groups, with the workshop and the community group showing improvement but the Internet group showing none. Overall examination of the pattern of behavioral change found that approximately a quarter of the sample demonstrated clinically significant behavioral gains. In summary, the parent-based intervention studies provide promising evidence that parents and caregivers benefit from support in managing their children's behavior and that this improvement is accompanied by improvements in parent/caregiver well-being.

Support, Education, and Advocacy. Four studies have investigated the effectiveness of specially designed education, support, and advocacy services. Leenaars and colleagues (2012) conducted a retrospective case-file analysis of the coaching families (CF) program that provides support for families across childhood and adolescence. Significant decreases in needs (e.g., housing and transport) and caregiver stress, and increases in goals (e.g., improving parenting skills, self-care, and health) were found. The greater the duration of engagement with CF, the greater the goals attained and needs reduced.

In addition, promising practices, an intervention for children and youth suspected or diagnosed with FASDs in out-of-home-care (Pelech et al., 2013) found that specialized FASD training for workers and foster caregivers was associated with a significant decline in the number of placement changes compared to standard care. In a study of students with FASDs and their teachers, improvements were found in classroom behavior, although the finding was limited by a small sample size (Clark et al., 2014). Nonetheless, this adds to a body of literature that supports the role of training in advocacy and knowledge as a way of potentially improving outcomes for individuals with FASDs.

Hume and colleagues (2009) prepared a summative report for the British Columbia Ministry of Children and Family Development on the Key Worker and Parent Support Program. This program provided support, education, and liaison to existing intervention services for families with children or youth affected by FASDs. Qualitative findings provided evidence for improvements following the intervention (e.g., parents and caregivers reported that they had a better understanding of FASD, increased emotional and practical support). However, limited pre/post data were available on caregiver stress, parenting self-confidence, and child behavior, and no statistically significant changes were found, although trends toward improvements were noted.

Supporting Parents with FASDs. Two case management studies indicated a reduction in secondary disabilities in parents with FASDs. Step-by-step was a 3-year, goal-driven, mentoring program aimed at increasing parents' access to resources and support that targets parents affected or suspected of FASDs (i.e., the parents did not have access to an assessment during their time in the program to confirm the diagnosis). A retrospective case-file analysis conducted by Denys and colleagues (2011) found that following the program, parents reported significant reductions in needs (e.g., housing) and increases in goals (e.g., improving parenting skills). A second case management program that assisted mothers to address environmental difficulties and connect with available support services was implemented by Grant and colleagues (2004). This pilot intervention of the parent-child assistance program was modified to accommodate clients with FASDs. The participants were 19 women diagnosed with or suspected of having FASDs (i.e., "had characteristics of prenatal alcohol damage in the presence of

prenatal alcohol exposure"; Grant et al., 2004, p. 502). Following the intervention, the participants decreased their alcohol/drug use, increased use of contraception and health services, and were more likely to have obtained stable housing. These studies suggest that longer term case management during the transition to parenthood reduces the likelihood of secondary disabilities in young women with PAE.

DISCUSSION

This systematic review extended previous literature reviews (Kodituwakku, 2010; Paley and O'Connor, 2011; Petrenko, 2015) and the most recent systematic review (Peardon et al., 2009) by adopting a broader set of search criteria to capture studies that extended across the life span. Thirty-two studies were identified, and methodological quality was assessed. The studies were grouped according to the primary focus of the intervention to enable comparisons across studies to be made and conclusions regarding effectiveness to be drawn.

Four key findings from the assessment of study quality were found. The first point relates to selection bias. None of the reviewed studies randomly selected cases from a target population, so selection bias was rated as "moderate" (participants recruited from a clinic) or "weak" (self-referred participants). Future research should aim to select participants from geographical regions known to have high rates of FASDs in the general population rather than only clients who have attended FASD diagnostic clinics. Second, no studies were rated "strongly" with respect to "blinding," as none of the 2-group studies described blinding of both outcome assessors and study participants.

The third issue relates to the information required in order for a study to be classified as an RCT. While many of the studies classified as CCTs reported that randomization had taken place, many had not included information on how this had occurred. While this reduced the overall number of studies classified as RCTs, both RCTs and CCTs are rated as "strong," meaning that nearly two-thirds of the included studies were given a "strong" rating on study design. Last, one of the strongest findings to emerge was the rigor concerning outcome measurement. Twenty-seven studies received a rating of "strong" because they used reliable and valid measures.

Turning to the results of the studies, despite some studies with small samples and limited follow-up, the body of literature reviewed showed that it is possible to make improvements across many domains of functioning. In early infancy, mixed evidence was found for the potential to improve the developmental outcomes (Kartin et al., 2002; Yazdani et al., 2009), highlighting the importance of further systematic, rigorous research. Importantly, researchers need to consider measuring intervention effects using other tools in addition to standard developmental measures for infants and toddlers. If the focus of the intervention is to improve self-regulatory capacity and developmental outcome physiological

measures such as heart rate, heart rate variability, and salivary cortisol could be used, as there is evidence that infants with PAE show compromised autonomic nervous system development (Oberlander et al., 2010). In addition, measurement of the infant's environment that includes the quality of the caregiving relationship needs to be considered, given the evidence that a supportive warm relationship aids the development of self-regulatory skills (Calkins et al., 2008).

The importance of providing an optimal environment to promote development provides the impetus for early intervention (Dalziel and Segal, 2012) and is of particular relevance for children with FASDs whose early environmental experience is often less than optimal. Thus, program developers need to attend to the particular needs of families and children with FASDs and ensure that programs are adapted to suit the needs of this population.

Despite the mixed evidence for effectiveness in early infancy, the studies that focused on improving self-regulation and attentional control in early to middle childhood provided strong evidence for gains, demonstrated by improvement using parent/caregiver report, neuropsychological testing, and magnetic resonance imaging scans (Kerns et al., 2010; Nash et al., 2015; Soh et al., 2015; Wells et al., 2012). However, as the studies did not include, or only had a limited follow-up, the extent to which such changes are enduring has not been established.

The evidence for changes in specific skills was more variable. Notably, only 1 study (Kable et al., 2007) had a follow-up period that extended beyond the posttreatment period. The greatest gains were found in the studies that evaluated the MILE program (Kable et al., 2007, 2015; Millians and Coles, 2014). Gains extended beyond math skills and included improvements in child behavior. The one study that investigated the stress response in children with FASDs found no changes in cortisol levels. The most plausible reason for this was that the level of exercise intensity (i.e., improving motor skills rather than fitness) was not sufficient to influence the stress response (Keiver et al., 2015). While the study did not achieve its aims, there are sound theoretical reasons for carrying out further research on the physiological underpinnings of PAE (Calkins et al., 2013). More research is needed to see whether interventions could lead to physiological changes, which importantly, may underlie some of the self-regulatory difficulties for individuals with FASDs.

The studies aimed at improving social skills showed consistently strong results. The controlled trials of the CFT program (Keil et al., 2010; O'Connor et al., 2006, 2012) were methodologically strong and importantly included a 3-month follow-up demonstrating some enduring benefit. Intervention at this developmental stage may help to prevent the development of further dysfunction, given that social skills deficits become more pronounced with age in young people with FASDs (Mattson et al., 1999; Whaley et al., 2001). Further research is required to evaluate the impact of

programs such as CFT with adolescents and adults. In summary, there is much to be optimistic about regarding the potential for improving aspects of children's functioning. However, currently, the lack of long-term follow-up limits any conclusions on whether the observed changes would endure over time.

Studies that included a specific focus on parenting skills found that helping parents understand and manage the complex set of behaviors they see in their children helped them feel less stressed (Gurwitsch et al., reported in Bertrand, 2009), and improve their well-being and perceived capacity to cope (Olson et al., reported in Bertrand, 2009). Notably, however, all studies targeted younger children and none had a follow-up beyond posttesting, so it is not possible yet to ascertain whether the programs provide the skills required to help parents revise their strategies in response to the changing needs of the developing child.

The evidence was mixed for studies that took a support, education, and advocacy focus or that targeted parents with FASDs. First, studies that employed a case management style approach found that supporting and educating families resulted in a reduction in needs (Leenaars et al., 2012) and reduced secondary disabilities in parents with FASDs (Denys et al., 2011; Grant et al., 2004). Second, an important emerging area of intervention research is targeting education and advocacy for people outside the family. For example, improving child welfare practices (Pelech et al., 2013) and assisting teachers to understand the cognitive deficits and make appropriate accommodations FASDs (Clark et al., 2014) resulted in improved outcomes for those with FASDs. Overall, considering the support, education, and advocacy interventions and parenting support interventions together, while interventions focused on case management were effective in improving outcomes for parents with FASDs, it remains unclear whether such interventions can result in improvements for children and youth who are affected by FASDs.

Implications for Research and Policy

The interventions included in the current review highlight both the potential for improving many different aspects of functioning for individuals with FASDs as well as methodological shortcomings. The majority of interventions are currently focused on improving outcomes for school-aged children. Future research is suggested to explore early intervention for infants and young children, ensuring that programs are informed by the evidence for clinical- and cost-effectiveness in high-risk families. Supporting adolescents and adults also needs to be considered as there is evidence that problems compound as children become older (Mattson et al., 1999; Whaley et al., 2001). It is also clearly evident that the difficulties facing individuals with FASDs do not lie in single domains of functioning. Thus, it would seem that the way forward for intervention research is to consider the dynamic interplay between individual characteristics and the

wider ecological context in which the individual lives. Consequently, the available evidence provides support for a proposed unified conceptual framework (Petrenko, 2015). Such a framework brings together models proposed by Koditwakku (2010) and Paley and O'Connor (2011) and takes into account the lived experiences of individuals and families with FASDs to guide intervention development. Taken together with the current review, this provides strong support for future interventions to address multiple domains of functioning for individuals with FASDs.

CONCLUSIONS

A number of interventions have been implemented with individuals and their families affected by PAE. The studies identified in this review differed considerably in their focus of the deficit(s) addressed. Further, there was considerable variability in their methodological rigor and the time frame for follow-up. Nonetheless, such attempts are critically important in propelling the field toward more rigorous and systematic intervention trials. We propose that considering the extensive deficits and the complexity of the life circumstances of many individuals, a deficit- or domain-specific focus for intervention is of limited utility. Rather, an approach that takes an ecological stance and looks at the multiple factors that may be at play will lead to more effective and enduring benefits. Ultimately, this is an empirical question and can only be answered by systematic and rigorous research trials.

CONFLICT OF INTEREST

None of the authors have a conflict of interest to report.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Data S1. Supplementary material.