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META-ANALYSIS

ALCOHOLISM CLINICAL & EXPERIMENTAL RESEARCH

A meta-analytic review of adaptive functioning in fetal alcohol spectrum disorders, and the effect of IQ, executive functioning, and age

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Abstract

Introduction: Fetal alcohol spectrum disorders (FASD) are highly prevalent developmental disabilities associated with prenatal alcohol exposure. In addition to varied strengths and unique talents, people with FASD experience significant challenges, including in adaptive functioning. Adaptive functioning refers to skills related to everyday life such as communication, practical skills, and social skills. For the current review, we aimed to understand how adaptive functioning in FASD compares to that of alcohol nonexposed individuals and those with attention deficit-hyperactivity disorder (ADHD). Additionally, we investigated how this relationship may change based on IQ, executive functioning, and age.

Method: The current review was registered in the International Prospective Register of Systematic Reviews. Studies were eligible for inclusion if they measured adaptive functioning and included an FASD group and at least one eligible comparison group. Articles available in May 2021 in PubMed, PsycInfo, Scopus, and ProQuest Dissertations were searched. Publication bias was assessed using Egger's regression and three-level random effects models were computed for all domains of adaptive functioning. Possible moderation by IQ, executive functioning, and age were investigated when heterogeneity analyses were significant. A *post hoc* moderation analysis of recruitment method was also completed.

Results: Thirty studies were included. Individuals with FASD had significantly lower adaptive functioning than other groups, with effect sizes ranging from 1.04 to 1.35 compared to alcohol nonexposed groups and from 0.30 to 0.43 compared to ADHD groups. No significant moderating effects were found for IQ or age; executive functioning significantly moderated communication skills in FASD compared to the alcohol nonexposed group. Recruitment method significantly affected this relationship, with larger effect sizes on average found for clinically identified samples than at-risk or population samples.

Conclusions: Individuals with FASD have impairments in adaptive functioning relative to alcohol nonexposed and ADHD groups, regardless of IQ, executive functioning, or age. Limitations of the review include small sample sizes in some comparisons and a limited age range.

Registration: This protocol was registered at PROSPERO and can be found at the following link: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020203072

KEYWORDS
adaptive functioning, FASD, fetal alcohol spectrum disorder, meta-analysis, prenatal alcohol exposure

INTRODUCTION

Fetal alcohol spectrum disorders (FASD) is an umbrella term referring to a range of developmental disabilities including physical and neurobehavioral differences associated with prenatal alcohol exposure (PAE; Hoyme et al., 2016; Mattson et al., 2019). Rates of FASD have been estimated at 2 to 5% of children in the United States using active case ascertainment methods (May et al., 2018). Individuals face many barriers to obtaining a diagnosis and accessing needed services, including stigma, lack of awareness, and lack of resources (Kapasi, 2015; Mukherjee et al., 2013; Petrenko et al., 2014; Ryan et al., 2006). As a result, rates of mental health problems and adverse life experiences (e.g., trouble with the law, school disruption, confinement) are elevated in people with FASD (McLachlan et al., 2020; Streissguth et al., 2004).

Early intervention and disabilities services have been shown to have significant positive effects on the functioning of individuals with FASD (Bertrand & ICFASDR Consortium, 2009; Streissguth et al., 1996), further emphasizing the need for increased access to care, greater awareness of the disorder, and reduced stigma. Recognizing and supporting the strengths of people with FASD is also critical for interventions designed to improve quality of life (Petrenko & Kautz-Turnbull, In press). While they face many challenges, people with FASD have important strengths and unique talents, especially in social motivation and prosocial behaviors (Currie et al., 2016; Knorr & McIntyre, 2016). Furthermore, individuals with FASD can show great resilience, a true protective factor for their overall well-being (Pei et al., 2016; Price et al., 2017; Tait et al., 2017).

Adaptive functioning

Adaptive functioning, defined as personal and social skills necessary to cope with the demands of one's environment and everyday life (Sparrow et al., 2005), has particular relevance for quality of life and accessing important services. In addition to global indices of adaptive functioning, subdomains are also often considered, including conceptual skills, such as receptive and expressive language; practical skills, such as self-care and community living; and social skills, including interpersonal skills (AAIDD, 2008). Measures of adaptive functioning, such as the Vineland Adaptive Behavior Scales (Sparrow et al., 2005), Scales of Independent Behavior (SIB; Bruininks et al., 1985), and Adaptive Behavior Assessment System (ABAS; Harrison & Oakland, 2015) provide domain scores largely corresponding to these areas.

Deficits in adaptive functioning are commonly seen in FASD (Mattson et al., 2019), but current literature has not delineated the magnitude of impairment in adaptive functioning for people with FASD and PAE. Individuals with FASD have been shown to have poorer adaptive functioning than typically developing controls (Doyle et al., 2018, 2019; Kerns et al., 2016). Individuals with attention deficit hyperactivity disorder (ADHD), a persistent pattern of behavior including hyperactivity, impulsivity, and inattention, experience similar executive functioning and attention deficits as those with FASD, although to a lesser degree (American Psychiatric Association, 2013; Khoury & Milligan, 2019; Nanson & Hiscock, 1990; Peadon & Elliott, 2010; Vaurio et al., 2008). Therefore, people with ADHD are a well-suited comparison group to explore functioning in FASD relative to that of a similar disability. Some studies show greater deficits in adaptive functioning in people with FASD compared to those with ADHD (Ware et al., 2012), while others show comparable levels of adaptive functioning across groups (Crocker et al., 2009; Rasmussen et al., 2010; Someki, 2011). An additional complicating factor is the high rate of comorbid ADHD in FASD, with some suggesting as high as 95% in clinical samples (Fryer et al., 2007). Further research is needed to clarify the relationship of adaptive functioning in FASD and ADHD.

Potential moderators

Adaptive functioning has been associated with cognitive ability, executive functioning, and age in developmental disabilities including autism (Clark et al., 2002; Klin et al., 2007; Pugliese et al., 2016), but the strength of these relationships in FASD remains unclear.

A recent meta-analysis estimated the population correlation of adaptive functioning and IQ at 0.51 (Alexander & Reynolds, 2020), but some studies suggest that a relationship between adaptive functioning and IQ is weaker or does not exist in FASD (Carr et al., 2010; Doyle et al., 2019; Whaley et al., 2001). FASD diagnosis alone often does not qualify an individual for developmental disability services, and it can be easier to obtain needed supports with a low IQ (Greenspan et al., 2016; Petrenko et al., 2014). Therefore, it is important to investigate the effect of IQ on the relationship of alcohol exposure and adaptive functioning.

Executive functioning has been theorized as a core mechanism supporting adaptive functioning (Calkins & Marcovitch, 2010); however, with the exception of social skills (McGee et al., 2008; Schonfeld et al., 2006), the relationship of overall adaptive functioning and executive functioning in FASD has not been extensively investigated. This gap in the literature is surprising given results suggesting a strong relationship between the two constructs in other developmental disabilities such as autism (Gilotty et al., 2002; Udhnani et al., 2020). Furthermore, as FASD is characterized by deficits in executive functioning, a connection between the two areas would be especially meaningful.

Finally, understanding how adaptive functioning changes across development is essential to long-term planning and supports for individuals with FASD. Some literature suggests the level of impairment in FASD becomes greater with age relative to typically developing peers, suggesting a plateau in development (Crocker et al., 2009; Thomas et al., 1998; Whaley et al., 2001). Adaptive deficits may also increase with age in ADHD but to a somewhat lesser degree than in FASD (Thomas et al., 1998; Whaley et al., 2001). However, studies showing this effect are largely cross-sectional, and may not give an accurate sense of functioning in this population.

Aims

Existing literature has demonstrated adaptive functioning deficits in FASD compared to nonexposed individuals and those with ADHD. However, research has not yet provided an overall effect size of the deficits in adaptive functioning in FASD and PAE. Synthesis across different study designs and methods, as well as conclusions based on a large sample, will serve to provide an overall estimate of this effect. Constructs including IQ, executive functioning, and age which may affect these relationships have yet to be explored. Therefore, the current study aimed to

1. estimate adaptive functioning deficits in FASD and PAE by
    a. comparing the adaptive functioning of individuals with FASD or PAE and those who were not prenatally exposed to alcohol
    b. comparing the adaptive functioning of individuals with FASD or PAE and those with ADHD
2. investigate whether deficits in adaptive functioning in FASD differ based on age, executive functioning, or IQ

METHODS

Literature search and retrieval

The current meta-analytic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO; https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=203072). Four databases were searched: PubMed, Scopus, PsycInfo, and ProQuest Dissertations and Theses Global. The search string used was the following: '("fetal alcohol" OR "prenatal alcohol") AND "adaptive"', and was restricted to the title and abstract. Published studies and dissertations available online in May 2021 were eligible for review. A total of 385 abstracts were retrieved and reviewed. Additionally, any literature review that was retrieved was searched for relevant citations, leading to an additional 99 studies (see Figure 1).

Articles were eligible for the current review if they (1) were original empirical studies measuring adaptive functioning using one of the following measures: Vineland Scales of Adaptive Behavior (Sparrow et al., 1984), SIB (Bruininks et al., 1985), ABAS (Harrison & Oakland, 2015), or Behavior Assessment for Children (BASC; Merenda, 1996) and (2) the study population included individuals with FASD or confirmed PAE and at least one control group of nonexposed individuals or individuals with ADHD. For the current review, comorbidities within groups were not considered exclusionary; that is, studies that included individuals with comorbid FASD and ADHD in the FASD group were eligible.

Full-text review

The abstract of each study was reviewed by the first author to determine whether the full article would be examined. Fifty-six articles

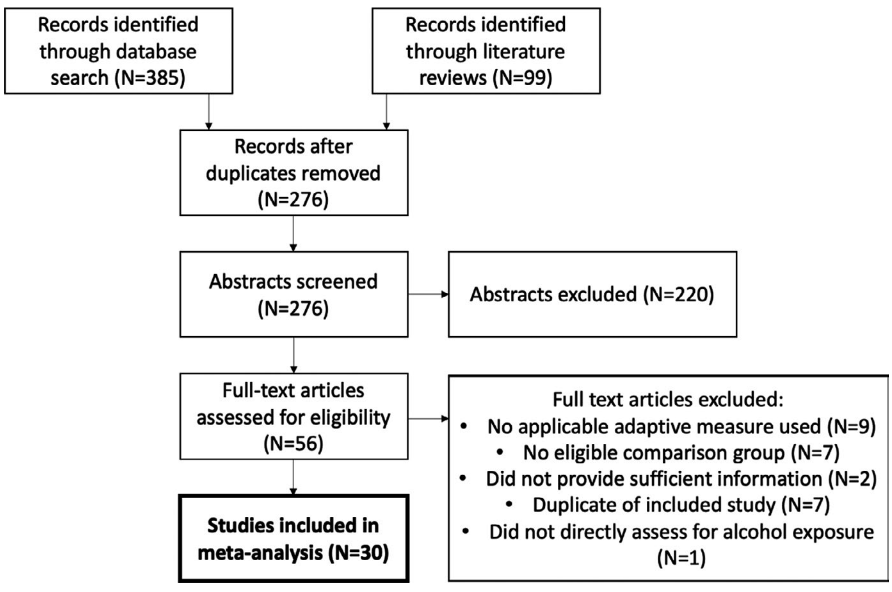

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

underwent full-text review to determine eligibility. Upon review, it was determined that an additional 17 studies were ineligible under the inclusion and exclusion criteria described above. Studies were also carefully reviewed for duplication; seven studies were noted to be duplicates of included studies (e.g., a dissertation that was later published, studies examining additional constructs using the same sample). In the case of duplicates, the study that presented the most complete data was included. Finally, two studies did not provide sufficient information to be included, and authors either could not be reached or were unable to provide information; therefore, these were excluded.

Coding

Eligible studies were then coded by the first author for the following:

General study characteristics: Authors, title, year, journal, and publication status were coded.

Study design: The number of groups and sample size of each group were coded. Additionally, each included group type was coded based on description and/or diagnosis; for example, FASD, ADHD, typically developing controls.

Study population: Demographics of the study population were coded by group, including gender, and mean and standard deviation of age.

Data: Data were coded by construct; namely, adaptive functioning, IQ, and executive functioning. Codes included a measure of the construct and mean and standard deviation per group.

Adaptive functioning

The Vineland, SIB, ABAS, and BASC were eligible and coded in the current review. The Vineland provides an overall adaptive functioning measure called the Adaptive Behavior Composite as well as three domain scores labeled Communication, Daily Living, and Socialization. The SIB also provides an overall adaptive functioning score, called the Broad Independence Score, and three domain scores: Social/Communication, Personal Living, and Community Living. The ABAS provides an overall measure of adaptive functioning called the General Adaptive Composite, as well as three domains: Conceptual, Social, and Practical. Finally, the BASC provides an Adaptive Skills Composite score, as well as Social Skills, Leadership, Activities of Daily Living, Adaptability, and Functional Communication scores.

Cognitive functioning

Any measure of cognitive functioning that provided an overall measure of functioning, such as the full-scale IQ (Wechsler, 1955) or General Conceptual Ability (Elliott et al., 1990) was coded in the current meta-analysis. Domains or subdomains (such as verbal or nonverbal intelligence) were not coded as this was considered outside the scope of the review.

Executive functioning

Two measures of executive functioning were coded in the current review: A Developmental Neuropsychological Assessment (NEPSY; Brooks et al., 2009), and the Delis-Kaplan Executive Function System (D-KEFS; Delis et al., 2001). These performance-based measures were coded at the subtest level.

Data analytic plan

Descriptive analyses were conducted using SPSS and meta-analyses were conducted using the "metafor" and "weightr" packages in R (Coburn & Vevea, 2017; Viechtbauer, 2010). Age was measured in years, IQ was measured using standard scores with a population mean of 100 and standard deviation of 15, and executive functioning scores were converted to z scores with a population mean of 0 and standard deviation of 1.

A random-effects model was used to account for a distribution of effect sizes attributable to this variation in study design, diagnosis, and construct measures. Nested models were used to take into account dependency introduced by studies which may have overlapping samples or methods (Konstantopoulos, 2011). Additionally, several studies included in the current review stemmed from two large, multisite studies; these were the Collaborative Initiative on FASD or CIFASD (Mattson et al., 2010), and the Collaboration on FASD Prevalence or CoFASP (Warren, 2020). Thus, meta-analyses conducted were three-level random-effects models. Models were estimated using Restricted Maximum Likelihood.

Data were examined for outliers using Cook's distance (Cook, 1977). If studies with a Cook's distance falling above the general rule of thumb (4/n) were present, leave-one-out analyses were performed to determine the effect of the outliers on the estimate. Data presented by specific diagnosis or classification (e.g., FAS, pFAS, PAE without FAS) were combined using weighted means and combined standard deviations in order to create one FASD group. Although some studies have demonstrated differential effects based on specific diagnosis (e.g., Carr et al., 2010), analyses based on FASD diagnosis were considered outside the scope of the current review given differences in diagnostic criteria and low agreement across systems (Coles et al., 2016). Likewise, for the executive functioning moderator, individual aspects of executive functioning such as inhibition or attention were not investigated separately as this was also considered outside the scope of the current review.

Cohen's d was used to obtain an estimate of the magnitude of impairment in adaptive functioning for people with FASD compared to the nonexposed and ADHD groups. Using the rules of thumb established by Cohen (Cohen, 1988), effect sizes of 0.2 were considered small, 0.5 medium, and 0.8 large. Moderation analyses were conducted if a significant amount of heterogeneity was present, denoted by a significant Q statistic, which tests the null hypothesis that all studies share a common effect size (Borenstein et al., 2011). Studies did not need to provide data for all three moderators to be included, and studies with missing data were excluded listwise. Moderation analyses were completed if two or more studies provided data; as few as two data points are thought to be acceptable for moderation in meta-analyses, although more are preferred (Pincus et al., 2011).

Publication bias

Publication bias refers to bias introduced by the increased likelihood of publication for studies with positive effects, especially large effects. The presence of publication bias was investigated using Egger's regression (Egger et al., 1997), a test which regresses a study's effect size onto its standard error, weighted by its inverse variance.

Recruitment method moderation

Although not an a priori comparison, the question was considered relevant of whether recruitment method (i.e., active case ascertainment in populations samples, screening of at-risk populations, or clinically identified samples) would have an effect on the results. Due to low awareness of FASD, stigma, and limited access to diagnostic clinics and informed providers, it is likely that individuals with milder symptoms of FASD may not be referred to a specialized clinic. Therefore, results may differ based on whether they utilized active case ascertainment in a population, screened an at-risk sample, or incorporated a clinically identified sample (e.g., self-referred or professionally referred to a diagnostic clinic or medical center). To test this, a post hoc moderation analysis was conducted in order to investigate the effect of study design on adaptive functioning deficits in FASD and PAE. Due to the exploratory nature of the analysis, the significance level was Bonferroni corrected and set at 0.004.

RESULTS

Descriptive statistics

The 30 studies in the current meta-analysis included a total of 6038 participants: 2272 in the FASD group, 3294 in the nonexposed group, and 472 in the ADHD group. In the original study inclusion criteria, four adaptive functioning measures were eligible: the Vineland, SIB, ABAS, and BASC. However, the majority of studies included in the current review ($k = 26$, 86.2%) utilized the Vineland, with two studies each utilizing the ABAS and SIB. Although one study utilized the BASC (de Water et al., 2021), it also included the Vineland; therefore, the Vineland was used for simplicity. To stay true to a priori inclusion criteria, all measures were included in the analysis by combining effect sizes calculated from conceptually similar domains. For simplicity, in the current review, adaptive functioning domains are labeled using the corresponding Vineland domain names. Notably, the Social Interaction & Communication domain on the SIB could fall under both the social and conceptual areas (Pearson, 2011), but for the current review was included only under the communication domain to reduce effect size inflation. See Table 1 for corresponding domains and correlations in existing literature in populations with and without developmental disabilities (Dupuis et al., 2020; Lotz, 2019; Pearson, 2011; Sparrow et al., 2005).

Study characteristics for studies included in the FASD/nonexposed comparison are presented in Table 2; those included in the FASD/ADHD comparison are presented in Table 3. Some studies met the inclusion criteria but did not present complete data for one or more effect sizes (e.g., presented only data for one domain of adaptive functioning); in these cases, authors were contacted for the remaining data.

Overall participant demographics by group are presented in Table 4. Independent *t*-tests indicated that the FASD group did not significantly differ from the nonexposed group on gender or age. The ADHD group did have significantly more males on average than did the FASD group. The average adaptive functioning scores, IQ, and executive functioning scores in the FASD group were significantly lower than those in the nonexposed group. In contrast, the FASD group was not significantly different than the ADHD group on adaptive functioning and IQ.

Moderators

For the three proposed moderators, data were combined across groups using weighted averages. Age was measured in years, IQ was measured in standard scores, and executive functioning was measured in *z* scores. For each study which presented multiple subtests measuring executive functioning, subtests were converted to *z* scores and averaged separately for the FASD and nonexposed groups. Subtests included in the executive functioning composite from the NEPSY were Animal Sorting ($k = 1$), Inhibition ($k = 7$), and Word Generation ($k = 2$), and from the DKEFS were Tower ($k = 2$), Color-Word Interference ($k = 2$), Trail-making ($k = 2$), Verbal Fluency ($k = 2$); Design Fluency ($k = 1$) and Twenty Questions ($k = 1$). The majority of these subtests measured inhibitory control ($k = 11$), with others measuring cognitive flexibility ($k = 7$), problem solving ($k = 1$), and set-shifting ($k = 1$). Studies including an ADHD group were limited ($k = 5$); consequently, data for moderating variables in this group were limited. Only one study provided executive functioning data for the ADHD group; therefore, executive functioning was not investigated in the ADHD group.

Random effects models

Adaptive functioning in FASD was first compared to that of nonexposed individuals, then to that of individuals with ADHD. Three-level

TABLE 1 Vineland domains, corresponding SIB and ABAS domains, and correlations from existing literature

Vineland domains	ABAS[a,b,c]	SIB[d]
Communication		
Corresponding Domain	Conceptual	Social Interaction & Communication
r	0.68 to 0.83	0.89
Daily living skills		
Corresponding domain	Practical	Community Living
r	0.70 to 0.86	0.84
Socialization		
Corresponding domain	Social	N/A
r	0.60 to 0.75	N/A
General adaptive composite		
Corresponding domain	Adaptive behavior composite	N/A
r	0.78 to 0.86	N/A

Abbreviations: ABAS, Adaptive Behavior Assessment System; SIB, Scales of Independent Behavior.
[a]Dupuis et al. (2020).
[b]Lotz (2019).
[c]Sparrow et al. (2005).
[d]Pearson (2011).

random effects models were computed for overall adaptive functioning and all domains of adaptive functioning separately. If analyses indicated a significant amount of heterogeneity, moderators were then explored.

FASD/Nonexposed comparison

First, adaptive functioning in FASD was compared to that of the nonexposed group. Results showed that the FASD group had significantly lower adaptive functioning than the nonexposed group in all domains, with extremely large effect sizes (see Table 5). Forest plots for each domain are presented in Figure 2. One outlier was identified for each model, with two outliers identified in the communication model. However, no outliers significantly affected the estimate based on leave-one-out analyses, so they were retained. For the overall and communication models, all effect sizes were positive, indicating the nonexposed group had higher scores than the FASD group. One effect size in the daily living model and two in the socialization model were negative. Results of Egger's regression were nonsignificant (*ps* > 0.13), indicating a low effect of publication bias for all models. Tests for heterogeneity revealed a large amount of heterogeneity for all models, indicating moderation would be appropriate (see Table 5).

FASD/Nonexposed comparison: moderation analyses

Results of moderation analyses for IQ, executive functioning, and age are presented in Table 6. Multilevel models were used for all moderation analyses as it was deemed important to correct for the multilevel structure given lower sample sizes in moderation analyses. All analyses for IQ and age were nonsignificant (*ps* > 0.29), indicating the overall effect size does not vary based on the average IQ or age of the FASD group. Executive functioning significantly moderated the effect size for Communication, $p = 0.01$.

Post hoc exploratory moderation analysis

Finally, a post hoc moderation was conducted to ascertain whether the degree of impairment in adaptive functioning in FASD relative to nonexposed controls differed by recruitment method. Some CIFASD studies ($k = 3$) were excluded from this moderation as studies combined across sites, and some sites utilized active case ascertainment while others utilized referrals (Mattson et al., 2010). Moderation results are presented in Table 7. Results indicated that compared to those utilizing active case ascertainment or at-risk screening methods, studies utilizing a clinically identified sample had significantly larger effect sizes relative to nonexposed controls. That is, people with FASD were significantly more impaired in adaptive functioning relative to controls in clinical samples than were population-based or at-risk screening samples. Effect sizes in studies using active case ascertainment and at-risk populations did not significantly differ from each other. Random-effects models were conducted for each recruitment method separately to investigate adaptive functioning in FASD compared to the nonexposed group to determine whether groups differed in each recruitment type. In all domains, the FASD group had significantly lower adaptive functioning than the nonexposed group ($p < 0.05$) with the exception of the daily living skills ($p = 0.052$) and socialization ($p = 0.064$) domains in the at-risk group. It should

TABLE 2 Characteristics of studies included in the FASD/nonexposed comparison

First author (year)	FASD N	Nonexposed N	Measure/Version	Composite ES	Communication ES	Daily living ES	Social ES	Mean IQ	Mean executive function	Mean age
Arviso (1993)[c]	15	15	VABS-R I	nr	2.09	0.38	2.21	87.70	N/A	10.05
Ase (2012)	73	40	VABS I	2.17	1.74	1.50	1.66	89.24	N/A	13.29
Astley (2009)	64	16	VABS I	2.10	nr	nr	1.79	92.83	−0.44	12.42
Bower (2018)	2	7	VABS I	nr	0.27	0.12	0.25	N/A	N/A	nr
Brusati (2015) [c]	63	53	VABS I	nr	2.27	nr	1.91	96.22	N/A	12.55
Chambers (2019) [b]	93	761	VABS I	0.42	0.4	0.31	0.43	N/A	−0.25	7.12
Crawford (2020)	39	29	VABS-2 I	2.79	2.74	2.71	2.31	81.42	−0.76	9.57
Crocker (2009)	22	20	VABS I	nr	1.41	1.7	1.25	100.62	N/A	10.15
de Water[a] (2021)	41	43	VABS-3	nr	nr	nr	2.12	103.77	N/A	11.75
Doyle (2018)[a]	142	160	VABS-2 SF	nr	1.84	nr	nr	95.69	−0.67	13.22
Doyle (2019)[a]	163	274	VABS-2 SF	1.13	1.12	0.89	0.85	94.14	N/A	12.29
Fago (2012)[c]	28	32	ABAS-2 SF	0.82	nr	0.38	nr	N/A	N/A	9.47
Goh (2016)[a,c]	227	254	VABS-2 SF	1.72	nr	nr	nr	96.19	N/A	10.81
Howell (2006)	128	53	VABS I	0.19	0.31	0.16	−0.02	76.39	N/A	14.95
Jirikowic (2008)	25	23	SIB-R SF	1.31	1.28	1.13	nr	99.73	N/A	6.74
Kalberg (2006)	22	11	VABS-2 SF	1.54	0.81	0.96	1.01	N/A	N/A	3.48
Kerns (2016)	22	22	VABS-2 SF	2.37	3.00	1.66	1.7	97.40	N/A	11.20
Lynch (2015)	113	57	ABAS-2 SF	0.22	0.35	−0.09	−0.07	82.71	N/A	22.62
May (2014)	31	74	VABS-2 SF	nr	0.95	1.4	0.56	N/A	N/A	6.94
May (2015)	26	186	VABS-2 SF	1.03	1.13	0.59	0.68	104.84	N/A	7.08
May (2020c)[b]	24	150	VABS-2 SF	0.4	0.82	0.32	0.29	N/A	−0.29	6.80
May (2020a)[b]	32	292	VABS-2 SF	0.47	0.64	0.87	0.34	N/A	−0.10	6.82
May (2020b)[b]	35	194	VABS-2 SF	0.33	0.57	0.29	0.59	N/A	−0.29	6.92
Panczakiewicz (2016)[a]	190	209	VABS-2 I	nr	1.66	1.4	1.58	96.74	−0.30	10.93
Quattlebaum (2013)	97	28	VABS SF	nr	1.37	1.34	0.91	99.52	N/A	8.53
Ware (2012)[a]	142	133	VABS-2 SF	1.7	nr	nr	nr	N/A	−0.14	12.25
Ware (2014)[a]	110	125	VABS-2 SF	nr	1.94	1.29	1.45	98.33	N/A	12.54
Whaley (2001)	33	33	VABS I	0.12	0.13	0.23	0.21	83.40	N/A	6.15

Abbreviations: ABAS, Adaptive Behavior Assessment System; I, Interview; SF, Survey Form; SIB, Scales of Independent Behavior; VABS-R, Vineland Adaptive Behavior Scales, Revised; VABS-2, Vineland Adaptive Behavior Scales, second Edition; VABS-3, Vineland Adaptive Behavior Scales, third Edition.

[a]CIFASD study.

[b]CoFASP study.

[c]Unpublished thesis; nr = not reported; ES = effect size. Age is provided in years, IQ in standard score with population mean of 100 and SD of 15, and executive functioning in *z* score with population mean of 0 and SD of 1.

TABLE 3 Characteristics of studies included in the FASD/ADHD comparison

First author (year)	FASD N	ADHD N	Measure/ Version	Composite ES	Communication ES	Daily living ES	Social ES	Mean IQ	Mean executive function	Mean age
Boseck (2015)	81	147	VABS I	0.30	0.26	0.34	0.19	N/A	N/A	9.84
Crocker (2009)	22	23	VABS I	nr	0.49	0.60	0.13	98.84	N/A	8.62
Someki (2011)[a]	189	149	SIB-R SF	nr	0.35	0.49	nr	94.49	N/A	11.25
Ware (2012)[b]	142	82	VABS-2 SF	0.43	nr	nr	nr	N/A	8.94	12.01
Ware (2014)[b]	110	71	VABS-2 SF	nr	0.38	0.46	0.48	87.25	N/A	12.29

Abbreviations: ABAS, Adaptive Behavior Assessment System; I, Interview; SF, Survey Form; SIB, Scales of Independent Behavior; VABS, Vineland Adaptive Behavior Scales; VABS-2, Vineland Adaptive Behavior Scales, second Edition.

[a]Unpublished thesis; nr = not reported; ES = effect size. Age is provided in years, IQ in standard score with population mean of 100 and SD of 15, and executive functioning in *z* score with population mean of 0 and SD of 1.

[b]CIFASD study.

be noted that analyses at this level had smaller sample sizes and so should be interpreted with caution.

FASD/ADHD comparison

Next, adaptive functioning in FASD was compared to that in ADHD. All effect sizes were positive, indicating the ADHD group had higher scores than the FASD group.

Random-effects models revealed that the FASD group had significantly lower adaptive functioning relative to the ADHD group, with small to medium effect sizes (see Table 8). Egger's regression was not significant in any model ($ps > 0.43$), indicating a low effect of publication bias (note: Egger's regression was not conducted in the overall adaptive functioning model due to low sample size). Heterogeneity analyses were nonsignificant for all models ($ps > 0.32$), indicating that any variance is likely due to error and moderation analyses would not be appropriate. Forest plots are presented in Figure 3.

DISCUSSION

The current meta-analytic review sought to estimate adaptive functioning deficits in FASD by comparing adaptive functioning in people with FASD and PAE to both nonexposed and ADHD groups. Results indicated that people with FASD had significantly lower adaptive functioning than both of these groups, which is generally in line with current research (Crocker et al., 2009; Doyle et al., 2019; Mattson et al., 1997; Streissguth et al., 1991; Ware et al., 2012, 2014). These results suggest that deficits associated with PAE are immensely affecting these individuals' daily lives. Paired with widespread inability to access needed services (Greenspan et al., 2016), this underscores that individuals with FASD are significantly underserved.

Effect sizes compared to nonexposed individuals were extremely large, ranging from 1.04 to 1.35. In contrast, effect sizes compared to individuals with ADHD were smaller although still significant, ranging from 0.30 to 0.43. This is consistent with prior literature indicating that FASD and ADHD are similar in their associated symptoms (Nanson & Hiscock, 1990; Peadon & Elliott, 2010; Vaurio et al., 2008), but indicates that people with FASD are more impaired in adaptive functioning relative to those with similar attention and executive functioning deficits. This also implies that adaptive functioning deficits in FASD are impaired beyond the possible effect of symptoms such as hyperactivity or impulsivity.

Overall IQ of the FASD group did not moderate adaptive functioning deficits in FASD and PAE, indicating that impairment in adaptive functioning remains relatively constant regardless of IQ. This is consistent with literature suggesting that adaptive functioning in FASD may be more impaired than what would be suggested by IQ (Åse et al., 2012; Astley et al., 2009; Thomas et al., 1998). The majority of individuals with FASD do not have intellectual disabilities (Mattson et al., 2011), with mean IQ scores in FASD samples estimated at around 80 (Mattson et al., 1997). This estimate is in line with the average IQ of the FASD group in the current study, which was 85.94. IQ is a common measure of functioning especially when discerning eligibility for services (Greenspan et al., 2016; Petrenko et al., 2014). This may mean that individuals with higher IQs may not be receiving the services they need despite experiencing a similar magnitude of adaptive deficits as those with lower IQs.

Executive functioning did not moderate the magnitude of impairment for overall adaptive functioning, daily living, and socialization domains. It did significantly moderate the degree of impairment in communication skills; that is, as executive functioning in individuals with FASD increased, the difference in adaptive functioning decreased. However, given the limited number of studies in this comparison, it is difficult to determine whether this specific effect is theoretically meaningful. Future research should investigate whether certain domains of adaptive functioning may be differentially related to executive functioning.

The executive functioning constructs used in the current analysis may further complicate interpretation of results. Executive functioning is made up of diverse areas including working memory, attention, behavioral regulation, inhibition, and others (Delis et al., 2001), and some have found differing effects in FASD based on

TABLE 4 Overall participant demographics by diagnostic group

	FASD group	Nonexposed group	ADHD group	Independent *t* tests
Total participants (number of studies)	2272 (30)	3294 (28)	472 (5)	
Gender				
Males (%)	54.58	53.02	72.87	$t(52) = 0.37, p = 0.71$[1]
Range	39.00 to 77.00	39.00 to 81.80	60.90 to 75.17	$t(8) = -2.91, p = 0.02$[2]
Age				
Mean (SD)	11.51 (4.18)	9.08 (3.58)	10.82 (2.61)	$t(52) = 0.02, p = 0.99$[1]
Range	3.56 to 22.53	3.33 to 22.80	9.78 to 11.83	$t(8) = 0.79, p = 0.45$[2]
Adaptive composite				
Mean (SD)	83.57 (19.37)	102.92 (15.22)	77.61 (17.94)	$t(34) = -4.73, p < 0.001$[1]
Range	59.41 to 103.18	73.06 to 111.44	69.46 to 92.22	$t(3) = -0.25, p = 0.82$[2]
Communication				
Mean (SD)	82.95 (17.34)	103.62 (16.60)	80.84 (17.61)	$t(44) = -6.68, p < 0.001$[1]
Range	70.22 to 99.80	75.09 to 113.80	74.14 to 88.93	$t(6) = -1.51, p = 0.18$[2]
Daily living				
Mean (SD)	84.82 (21.10)	103.63 (15.34)	84.70 (19.45)	$t(40) = -4.18, p < 0.001$[1]
Range	62.47 to 104.30	78.21 to 112.66	75.62 to 98.50	$t(6) = -1.32, p = 0.23$[2]
Socialization				
Mean (SD)	84.55 (19.92)	102.76 (15.30)	79.95 (18.60)	$t(44) = -4.69, p < 0.001$[1]
Range	62.78 to 102.25	70.36 to 114.15	72.78 to 93.93	$t(4) = -0.67, p = 0.55$[2]
IQ				
Mean (SD)	85.94 (15.18)	102.50 (16.75)	95.65 (14.55)	$t(36) = -5.91, p < 0.001$[1]
Range	68.18 to 98.56	78.42 to 123.90	91.80 to 99.11	$t(4) = -0.93, p = 0.41$[2]
Executive functioning				
Mean *z* score	−0.73	−0.14	[a]	$t(16) = -5.25, p < 0.001$
Range	−1.46 to −0.40	−0.41 to 0.44		

Note: Age is provided in years, IQ in standard score with population mean of 100 and SD of 15, and executive functioning in *z* score with population mean of 0 and SD of 1.

[1]Independent *t* test comparing FASD and nonexposed groups.

[2]Independent *t* test comparing FASD and ADHD groups.

[a]Note: only one study provided executive functioning scores for participants with ADHD; therefore, independent *t* tests could not be calculated.

domain of executive functioning (e.g., Khoury et al., 2015). Although combining subtests of executive functioning measures is relatively common in order to make conclusions across domains or constructs (Crawford et al., 2020; Khoury et al., 2015, Khoury & Milligan, 2019), it is possible that the magnitude of impairment in adaptive functioning for people with FASD and PAE is moderated by one or more specific constructs. Only four domains of executive functioning were represented in the current analysis, and the majority of studies included results on inhibition, which likely drove results. When only inhibition subtests were included in the moderation, results showed a similar pattern; however, it was impossible to examine other domains separately given insufficient data.

Finally, age did not moderate this relationship, indicating that the magnitude of deficits in adaptive functioning is similar across childhood and early adolescence. These results are consistent with studies finding no effect of age on other constructs in FASD, such as executive functioning and behavior (Panczakiewicz et al., 2016). This supports a delay in development in contrast to a plateau in development (Crocker et al., 2009; Streissguth et al., 1991; Thomas et al., 1998; Whaley et al., 2001). Existing literature has largely been cross-sectional; that is, these studies show older individuals with FASD have lower adaptive scores than do younger individuals. However, given that adaptive skills are age-normed, this may not indicate a plateau, but that children with FASD are not showing the same rate of improvement as would typically developing children. In a larger, aggregated sample with more variation, these differences in rates of change no longer appear significant.

It is important to note that the age range in the current sample represents only childhood through young adulthood (mean ages 3.56 to 22.62), and only one study had an average age above 14. Therefore, results may not be generalizable to other developmental periods such as infancy, early childhood, and adulthood. More research, especially incorporating longitudinal designs, is needed to understand adaptive functioning in FASD across development.

TABLE 5 Results for FASD/nonexposed comparisons

Comparison	Number of studies	Unweighted ES mean	ES range	Total *N*	Egger's regression (SE)	Egger's regression 95% CI	Heterogeneity	ES (SE)	95% CI
Overall adaptive functioning	18	1.16	0.12 to 2.79	3783	*B* = 15.89 (10.43)	−4.56 to 36.33	Q(df = 17) = 264.67**	1.32 (0.25)**	0.83 to 1.82
Communication	23	1.25	0.13 to 3.00	4313	*B* = 0.32 (4.28)	−8.07 to 8.71	Q(df = 22) = 276.33**	1.35 (0.21)**	0.94 to 1.75
Daily living	21	0.91	−0.09 to 2.71	3895	*B* = 0.03 (3.95)	−7.72 to 7.77	Q(df = 20) = 192.30*	1.04 (0.18)**	0.68 to 1.40
Socialization	23	1.04	−0.07 to 2.31	4126	*B* = 1.98 (3.97)	−5.79 to 9.75	Q(df = 22) = 258.21**	1.12 (0.19)**	0.75 to 1.49

Abbreviations: CI = Confidence Interval; ES = Effect Size; SE = standard error.

*$p < 0.001$; **$p < 0.0001$

These results also emphasize the pervasive and chronic nature of FASD. Although the current analysis indicates that people with FASD are not declining in skills as they age relative to nonexposed people, they are also not narrowing the gap. Interventions targeting adaptive functioning have shown positive results in school-age children (Coles et al., 2018; Kable et al., 2016; Padgett et al., 2006) but systems barriers, lack of resources, and stigma prevent many families from accessing these interventions (Petrenko et al., 2014; Ryan et al., 2006).

The results of the post hoc recruitment method moderation suggest that individuals who are referred to clinics or medical centers for a diagnosis may be significantly more impaired than those who are diagnosed through either general or at-risk population screening. Studies recruiting subjects who have been referred (including self-referred) to a diagnostic clinic may be oversampling for lower-functioning individuals. In contrast, those using a wider screening process may be able to capture a wider range of functioning. Previous research has shown that the prevalence of FASD estimated using record review or clinic-based studies systematically underestimates prevalence, and may select for more severe cases (May et al., 2009). This also emphasizes the need for wider awareness of FASD and increased resources devoted to assessment, especially at-risk or population screening. A large number of individuals with PAE are "missed" and do not obtain a needed FASD diagnosis (Chasnoff et al., 2015), largely due to the significant lack of FASD-informed providers and resources nationwide (Eyal & O'Connor, 2011; Payne et al., 2005; Petrenko et al., 2020; Wedding et al., 2007). Despite the fact that some individuals who are being "missed" show decreased deficits relative to those who are being referred to a clinic, they are generally still functioning at a significantly lower level than their nonexposed peers. Furthermore, given the results of the current analysis indicating that adaptive functioning deficits remain similar across IQ and executive functioning, it is likely the adaptive functioning of these individuals lags behind what might be suggested by their other abilities, meaning they will likely not qualify for other supports and services. In the context of lack of moderation of age, these deficits will remain relatively constant throughout their lives, underscoring the persistent negative implications of underdiagnosis of FASD.

Implications and future directions

The current review has a number of implications for future research. Null moderation results for executive functioning, IQ, and age suggest that another mechanism may account for adaptive functioning deficits in FASD. It is possible that social cognition may moderate the deficits; one recent study found that social cognition was a significant predictor of adaptive functioning over and above the effects of executive functioning and IQ (Crawford et al., 2020). The current results also suggest executive functioning, or a specific aspect of executive functioning, may be a promising candidate given medium to large regression coefficients, although most did not reach

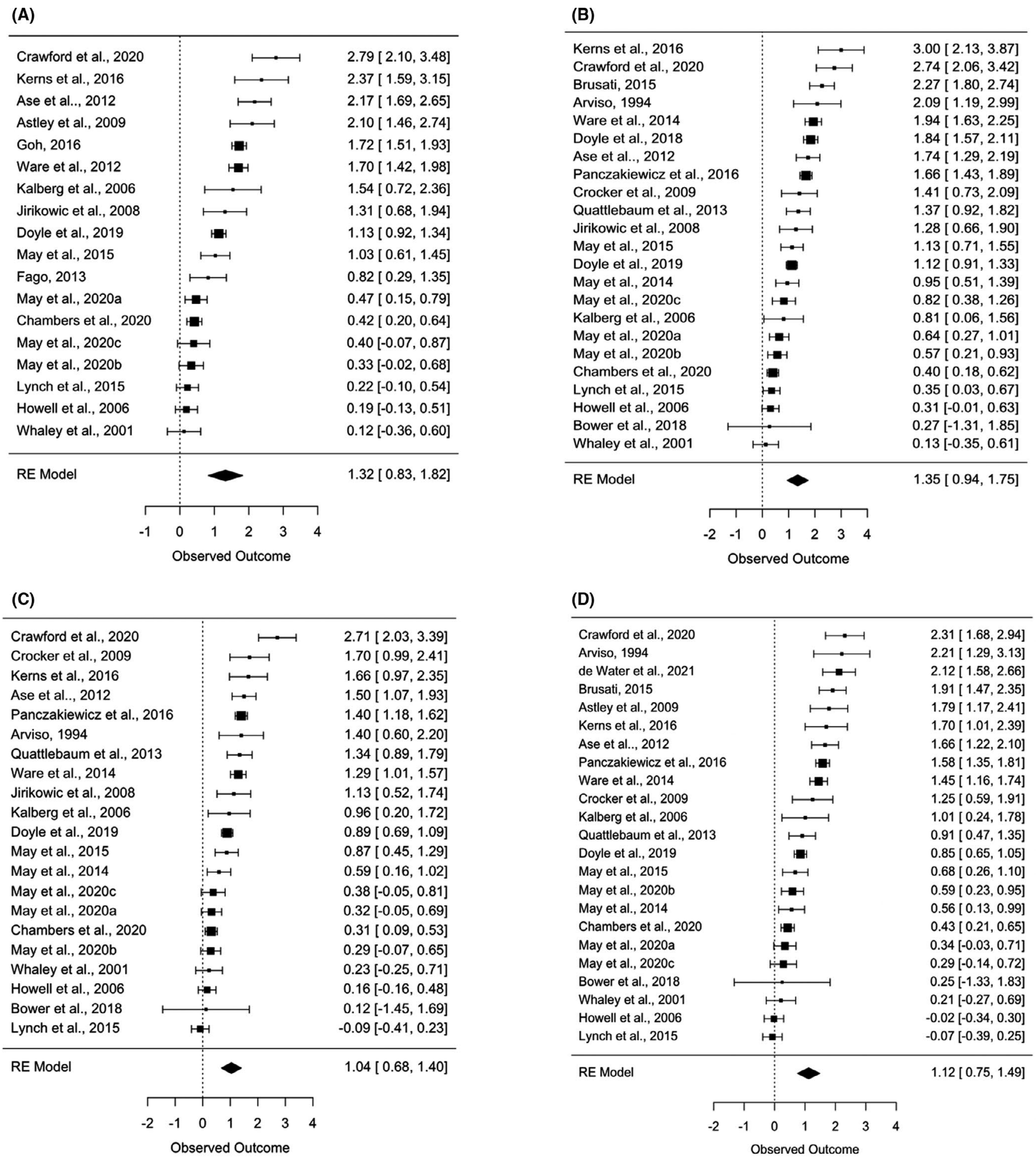

FIGURE 2 Forest plots for FASD/nonexposed comparison. (A) Overall adaptive functioning; (B) communication; (C) daily living skills; (D) socialization

significance. For example, interventions such as GoFAR (Coles et al., 2018) and the Families Moving Forward Program (Bertrand et al., 2009; Olson et al., 2009) improve adaptive functioning by teaching metacognition strategies and increasing behavior regulation, respectively. Variables not investigated in the current review may also have an effect on adaptive functioning in FASD. For example, the amount of alcohol exposure has been shown to be an important predictor of deficits (Alvik et al., 2013; Flak et al., 2014), as has early intervention and access to supports (Olson et al., 2009). Importantly, adverse life experiences such as trauma, maltreatment, exposure to other substances, and out-of-home placement changes may affect functioning (McKelvey et al., 2018).

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TABLE 6 Moderation results

Moderator	Adaptive functioning domain	Number of effect sizes	Total N	Unweighted average in FASD group	Range in FASD group	Results
IQ	Overall	11	1896	82.63	68.18 to 91.20	$B = -0.01$, SE = 0.04, $p = 0.73$
	Communication	16	2585	84.57	68.18 to 98.56	$B = -0.01$, SE = 0.03, $p = 0.64$
	Daily Living	14	2167	84.20	68.18 to 98.56	$B = 0.00$, SE = 0.03, $p = 0.78$
	Socialization	16	2399	84.45	68.18 to 98.56	$B = -0.03$, SE = 0.13, $p = 0.89$
Executive functioning	Overall	7	1938	−0.75	−1.46 to −0.40	$B = -0.20$, SE = 0.48, $p = 0.67$
	Communication	7	2346	−0.80	−1.46 to −0.40	$B = -0.96$, SE = 0.38, $p = 0.01$*
	Daily Living	6	2044	−0.78	−1.46 to −0.40	$B = -0.28$, SE = 0.50, $p = 0.58$
	Socialization	7	2124	−0.76	−1.46 to −0.40	$B = -0.24$, SE = 0.47, $p = 0.62$
Age	Overall	18	3783	10.05	3.56 to 22.53	$B = -0.01$, SE = 0.04, $p = 0.85$
	Communication	22	4304	10.02	3.56 to 22.53	$B = 0.02$, SE = 0.04, $p = 0.62$
	Daily Living	20	3886	9.75	3.56 to 22.53	$B = -0.03$, SE = 0.03, $p = 0.29$
	Socialization	22	4117	10.22	3.56 to 22.53	$B = 0.00$, SE = 0.04, $p = 0.95$

Note: IQ is provided in standard score with population mean of 100 and SD of 15, executive functioning in scaled score with population mean of 10 and SD of 3, and age in years.

*Significant at $p < 0.05$.

TABLE 7 Results of post hoc recruitment method moderation

Domain	*B* (SE)	*p*
ACA versus at-risk		
Overall	0.11 (0.46)	0.80
Communication	0.24 (0.34)	0.49
Daily living	0.02 (0.37)	0.96
Socialization	0.12 (0.29)	0.68
ACA versus clinic		
Overall	−1.35 (0.36)	0.0002*
Communication	−1.13 (0.30)	0.0002*
Daily living	−1.04 (0.26)	<0.0001*
Socialization	−1.27 (0.11)	<0.0001*
At-risk vs clinic		
Overall	−1.47 (0.34)	<0.0001*
Communication	−1.37 (0.32)	<0.0001*
Daily living	−1.06 (0.33)	0.001*
Socialization	−1.39 (0.23)	<0.0001*

Abbreviations: ACA, active case ascertainment.

*Significant at Bonferroni-corrected *p* value of 0.004.

Finally, the current review provides strong support for policy including FASD as a qualifying diagnosis for developmental disability services. Currently, in a number of US states, FASD are not seen as a qualifying developmental disability for services (Greenspan et al., 2016). According to the 2014 criteria for a condition to qualify as a developmental disability under the Developmental Disabilities Act section 102(8) one must have: "a severe, chronic disability of an individual that (i) is attributable to a mental or physical impairment or combination of mental and physical impairments; (ii) is manifested before the individual attains age 22; (iii) is likely to continue indefinitely; (iv) results in substantial functional limitations in three or more of the following areas of major life activity: self-care, receptive and expressive language, learning, mobility, self-direction, capacity for independent living, and economic self-sufficiency; and (v) reflects the individual's need for a combination and sequence of special, interdisciplinary, or generic services, individualized supports, or other forms of assistance that are of lifelong or extended duration and are individually planned and coordinated (Developmental Disabilities Assistance and Bill of Rights Act of 2000). Notably, the construct of adaptive functioning represents each of these domains of functional impairment. Results of the current review indicate most individuals with FASD will experience significant difficulty in these qualifying areas of everyday life with the exception of mobility, which was not investigated. Additionally, these impairments will persist across development and are not reflective of IQ. Eligibility for services, especially early diagnosis and intervention, is urgently needed in order to support these individuals and allow them to meet their full potential.

Limitations

The results of the current analysis should be interpreted in the context of a number of limitations. Although 30 studies were available for inclusion, the number of effect sizes for each domain varied due to missing data, and some comparisons had relatively few data points. The FASD/ADHD comparison was especially limited in its effect sizes, with as few as two effect sizes in specific domains. Therefore, these results should be thought of a preliminary estimate and lay the foundation for further investigation into this comparison.

As a consequence of the limited effect sizes, data for moderation analyses also varied across domains. Moderation results may, therefore, not be representative of true effects. Data for moderation were also limited in the FASD/ADHD comparison, but lack of

TABLE 8 Results for FASD/ADHD comparisons

Comparison	Number of studies	Unweighted ES mean	ES range	Total N	Egger's regression (SE)	Egger's regression 95% CI	Heterogeneity	ES (SE)	95% CI
Overall adaptive functioning	2	.37	0.30 to 0.43	452	N/A	N/A	Q(df = 1) = 0.43	0.36 (0.10)**	0.17 to 0.56
Communication	4	.37	0.26 to 0.49	664	*B* = 1.27 (1.98)	−2.62 to 5.15	Q(df = 3) = 0.64	0.34 (0.09)***	0.17 to 0.50
Daily Living	4	.47	0.34 to 0.60	661	*B* = 1.54 (1.97)	−2.32 to 5.39	Q(df = 3) = 0.87	0.43 (0.09)***	0.26 to 0.60
Socialization	3	.27	0.13 to 0.48	452	*B* = −0.97 (2.43)	−5.74 to 3.80	Q(df = 2) = 2.29	0.30 (0.12)*	0.07 to 0.53

Abbreviations: CI, Confidence Interval; ES, effect size; SE, standard error.

*$p < 0.05$; **$p < 0.001$; ***$p < 0.0001$.

heterogeneity indicated these analyses would not be appropriate. This may have been the case due to low power to detect heterogeneity as a consequence of the limited studies available, or due to other factors such as study design or population variables. Therefore, the question of whether IQ, executive functioning, or age moderate the comparison of FASD and ADHD was not able to be answered by the current review, and more research in this area is needed. It is possible that overall effects and lack of heterogeneity could be driven or exacerbated by comorbid ADHD in the FASD groups. Four of the thirty studies in the current review specifically included comorbid ADHD in the FASD group (Boseck et al., 2015; Kerns et al., 2016; Ware et al., 2012, 2014), and others may not have excluded or even assessed for ADHD. Although the real-world generalizability of these results is increased by including these studies given high rates of comorbid ADHD in FASD, future research may investigate these effects separately by comparing FASD with and without comorbid ADHD to nonexposed controls.

Examining results by domain of executive functioning was not possible in the current analysis due to low sample size; thus, the executive functioning moderation may not represent true effects. Although current literature does combine across executive functioning domains (Crawford et al., 2020; Khoury et al., 2015, Khoury & Milligan, 2019), this may have obscured meaningful variation. The majority of participants in the current review were children or early adolescents, with only one study investigating young adults with FASD (Lynch et al., 2015). Therefore, results may not be generalizable to older individuals. Little research has been conducted with adults with FASD, and this is an area in urgent need of additional research. Additionally, although effect sizes from the SIB and ABAS were retained to be consistent with preregistration, studies using these measures were limited. Therefore, the adaptive functioning results are largely driven by scores on the Vineland. Moderation by adaptive functioning measure was tested and was not significant, although there was low power to detect differences. It is possible results could differ with greater representation of other adaptive functioning measures. Future research should continue to investigate the convergence of different adaptive functioning measures in FASD.

Additionally, differential effects by specific diagnosis (e.g., FAS, pFAS, etc.) and significant disparities in access to resources depending on race, ethnicity, income, and geographical location may have an influence on effect sizes and were not accounted for in the current review. Similarly, environmental and parenting variables, particularly maltreatment and out-of-home placements, are closely associated with adaptive and behavioral functioning and were not examined. These factors are likely mechanisms of challenges in people with FASD; however, literature is limited on maltreatment in FASD and rates of maltreatment in samples are not regularly reported. Studies with relevant comparison groups investigating adaptive functioning are also limited in the literature. Comparison of samples of children with maltreatment or foster care histories with and without FASD could yield important data to address these relative influences. Future research should continue to investigate possible differential or additive effects of FASD and maltreatment on child outcomes.

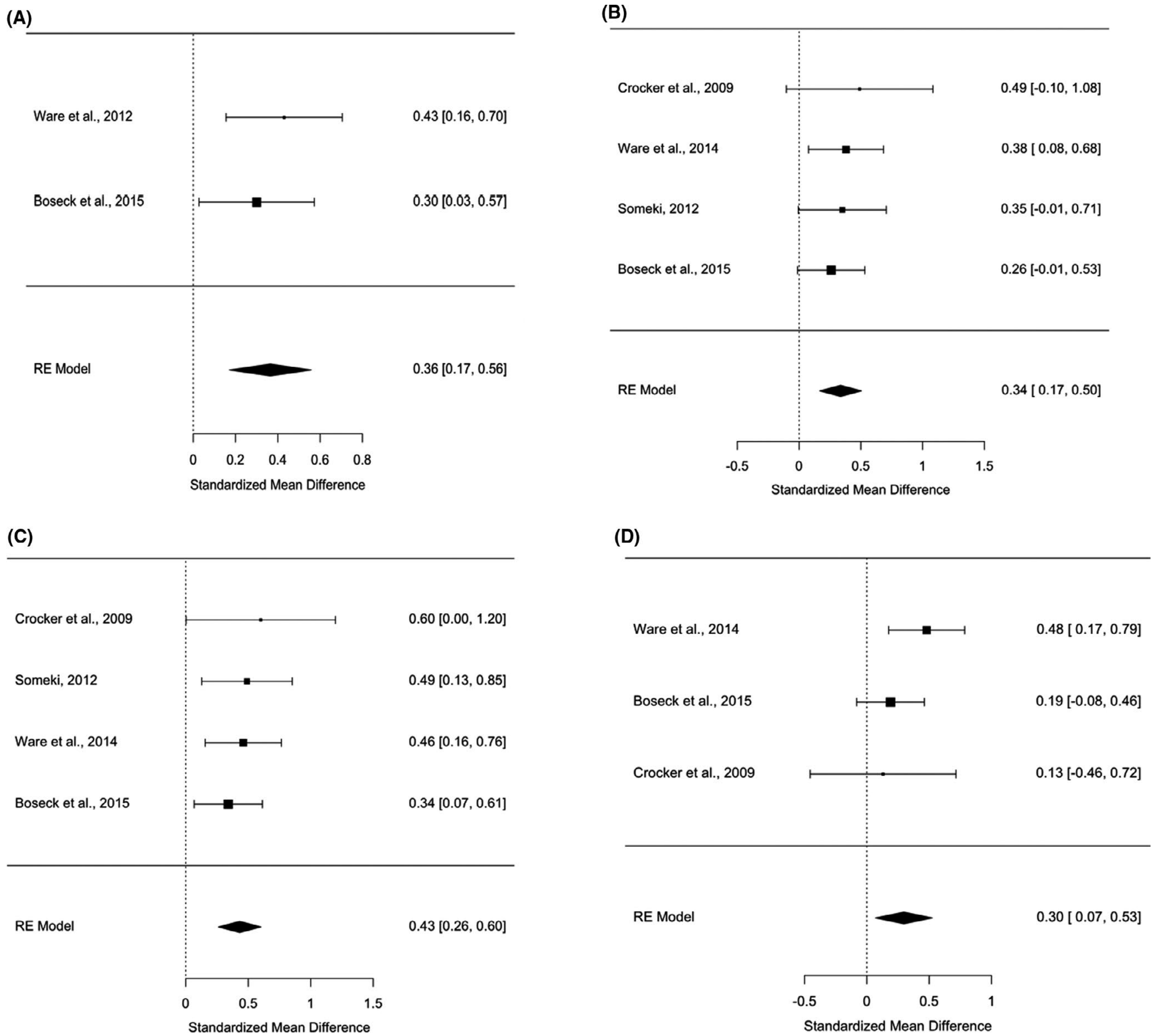

FIGURE 3 Forest plots for FASD/ADHD comparison. (A) overall adaptive functioning; (B) communication; (C) daily living skills; (D) socialization

CONCLUSION

The current study demonstrates that individuals with FASD show significant deficits in adaptive functioning compared to nonexposed individuals and those with ADHD. Moderation analyses were conducted in the nonexposed comparison, but could not be conducted in the ADHD comparison due to lack of data and nonsignificant heterogeneity. The effect in FASD compared to nonexposed samples was not moderated by IQ, executive functioning, or age, indicating deficits in adaptive functioning remain constant across levels of these constructs. Recruitment method did significantly moderate the effect; specifically, studies which used active case ascertainment or screened at-risk populations had lower effect sizes on average than did studies which utilized clinic referral or record review. These results suggest the presence of a group of individuals who may be functioning well enough to not be referred to a diagnostic clinic, yet are still impaired relative to their peers. In the context of lack of moderation of IQ and executive functioning, this implies that these people may not be functioning at the level of their other skills, meaning they may not qualify for needed supports. These deficits are likely to persist across development. Additional risk factors, such as maltreatment and out-of-home placement, may also affect the functioning of clinical samples, but were not able to be assessed due to a lack of studies with relevant comparisons.

These results emphasize the need for increased awareness of FASD and access to resources. Deficits in adaptive functioning cannot be predicted by IQ, executive functioning, or age, and so adaptive function must be assessed to get a sense of the individual's functioning in the real world. Interventions should be person-centered and strengths-based, and balance skill-building with environmental supports to improve adaptive functioning and increase quality of life (Petrenko & Kautz-Turnbull, In press). Widespread access to these interventions is imperative to improve outcomes for people with FASD.

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CONFLICT OF INTEREST

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