Supplemental File F

GRADE Ratings and meta-analyses for neurodevelopmental outcomes

Table of contents

Summary of outcomes available for IQ/cognition

Study Type	Outcome	Data	# of studies
IQ/Cognition			
Exposure Studies (light, moderate, heavy, very heavy, any level, confirmed-unquantifiable)	Composite IQ – Infants (6 months-2 years of age)	Mean and SDs;	**7 studies:** 1 light, 4 moderate, 1 heavy, 2 very heavy, 0 any level, 2 confirmed-unquantifiable
		aOR and 95% CIs (low IQ)	**1 study:** 0 light, 0 moderate, 1 heavy, 0 very heavy, 0 any level, 0 confirmed-unquantifiable
	Full-Scale IQ – School-Age (4-17 years of age)	Mean and SDs; adjusted mean difference and 95% CIs; median and inter-quartile range	**16 studies:** 2 light, 5 moderate, 3 heavy, 2 very heavy, 1 any level, 9 confirmed-unquantifiable
		aOR and 95% CIs (low IQ)	**1 study:** 1 study with light, moderate and heavy
	Verbal IQ – School-Age (4-17 years of age)	Mean and SDs; adjusted mean difference and 95% CIs; median and inter-quartile range	**7 studies:** 2 light, 3 moderate, 3 heavy, 0 very heavy, 1 any level, 2 confirmed-unquantifiable
		aOR and 95% CIs (low verbal IQ)	**1 study:** light, moderate and heavy
	Performance IQ – School-Age (4-17 years of age) Non-Verbal IQ	Mean and SDs; adjusted mean difference and 95% CIs	**6 studies:** 2 light, 2 moderate, 2 heavy, 0 very heavy, 1 any level, 2 confirmed-unquantifiable
		aORs and 95% CIs (low performance IQ)	**1 study:** light, moderate and heavy
	Non-Verbal IQ – School-Age (4-17 years)	Mean and SDs; adjusted mean difference and 95% CIs; median and inter-quartile range	**6 studies:** 0 light, 2 moderate, 3 heavy, 1 very heavy, 0 any level, 2 confirmed-unquantifiable
		aORs and 95% CIs (low non-verbal IQ)	**1 study:** with moderate and heavy
Diagnosed Studies (FASD, FAS, pFAS, Other FASDs) (3yrs – 22 yrs)	Full-Scale IQ	Mean and SDs	**23 studies:** 16 FASD, 7 FAS, 7 pFAS, 7 Other FASDs
	Verbal IQ	Mean and SDs	**12 studies: 4** FASD, 8 FAS, 5 pFAS, 4 Other FASDs
	Performance IQ	Mean and SDs	**9 studies: 4** FASD, 4 FAS, 1 pFAS, 2 Other FASDs
	Non-Verbal IQ	Mean and SDs	**18 studies:** 7 FASD, 8 FAS, 7 pFAS, 4 Other FASDs
	General Ability Percentile	Mean and SDs	**5 studies:** 3 FASD, 2 FAS, 2 pFAS, 1 Other FASDs
	Verbal Ability Percentile	Mean and SDs	**5 studies:** 2 FASD, 2 FAS, 2 pFAS, 1 Other FASDs
	Non-Verbal Ability Percentile	Mean and SDs	**5 studies:** 3 FASD, 2 FAS, 2 pFAS, 1 Other FASDs

GRADE ratings for IQ/cognition

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)[1]	Certainty
		Certainty assessment				№ of patients		Effect		Certainty
EXPOSURE STUDIES										
Composite IQ – Infants (6 months–2 years of age)										
Light prenatal alcohol exposure (1-20g/w in at least one trimester)										
1	serious[a]	not serious	serious[c]	serious[d,f]	none	68	213	-	**SMD 0.09 lower** (0.37 lower to 0.18 higher)	⊕◯◯◯ Very Low
Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)										
4	serious[a]	serious[b]	not serious	serious[d,e]	none	182	918	-	**SMD 0.06 lower** (0.37 lower to 0.26 higher)	⊕◯◯◯ Very Low
Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)										
1	serious[a]	not serious	not serious	serious[d]	none	186	525	-	**SMD 0.06 higher** (0.11 lower to 0.22 higher)	⊕⊕◯◯ Low
Very heavy prenatal alcohol exposure (201g+/w in at least one trimester)										
2	serious[a]	serious[b]	not serious	serious[e,f]	none	46	268	-	**SMD 0.89 lower** (1.76 lower to 0.01 lower)	⊕◯◯◯ Very Low
Any level prenatal alcohol exposure (Exposure dichotomized yes/no) – no studies										
Confirmed prenatal alcohol exposure-Level Unquantifiable										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	40	57	-	**SMD 0.66 lower** (1.45 lower to 0.13 higher)	⊕◯◯◯ Very Low
Full-Scale IQ – School-Age (4-17 yrs)										
Light prenatal alcohol exposure (1-20g/w in at least one trimester)										
2	serious[a]	not serious	not serious	serious[d]	none	2471	2688	-	**SMD 0.04 higher** (0.01 lower to 0.10 higher)	⊕⊕◯◯ Low
Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)										
5	serious[a]	serious[b]	not serious	serious[d,e]	none	1183	3126	-	**SMD 0.1 lower** (0.47 lower to 0.11 higher)	⊕◯◯◯ Very Low
Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)										
3	serious[a]	serious[b]	not serious	serious[d,e]	none	374	1095	-	**SMD 0.98 higher** (0.46 lower to 2.42 higher)	⊕◯◯◯ Very Low
Very heavy prenatal alcohol exposure (201g+/w in at least one trimester)										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	36	69	-	**SMD 0.12 higher** (1.30 lower to 1.53 higher)	⊕◯◯◯ Very Low
Any level prenatal alcohol exposure (exposure dichotomized to yes/no)										

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Exposed	Control		Effect (SMD)	Certainty
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	28	28	-	**SMD 0.01 higher** (0.52 lower to 0.53 higher)	⊕◯◯◯ Very Low
Confirmed prenatal alcohol exposure-Level Unquantifiable										
9	serious[a]	serious[b]	not serious	serious[e]	none	785	942	-	**SMD 1.05 lower** (1.32 lower to 0.79 lower)	⊕◯◯◯ Very Low
Verbal IQ – School-Age (4-17 years of age)										
Light prenatal alcohol exposure (1-20g/w in at least one trimester)										
2	serious[a]	not serious	not serious	serious[d]	none	2471	2688	-	**SMD 0.04 higher** (0.01 lower to 0.10 higher)	⊕⊕◯◯ Low
Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)										
3	serious[a]	not serious	not serious	serious[d]	none	1120	2977	-	**SMD 0** (0.10 lower to 0.09 higher)	⊕⊕◯◯ Low
Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)										
3	serious[a]	serious[b]	not serious	serious[d,e]	none	523	1073	-	**SMD 0.32 lower** (0.66 lower to 0.02 higher)	⊕◯◯◯ Very Low
Very heavy prenatal alcohol exposure (201+g/w in at least one trimester) – 0 studies										
Any level prenatal alcohol exposure (exposure dichotomized to yes/no)										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	28	28	-	**SMD 0.14 lower** (0.67 lower to 0.38 higher)	⊕◯◯◯ Very Low
Confirmed prenatal alcohol exposure-Level unquantifiable										
2	serious[a]	serious[b]	not serious	serious[e,f]	none	143	90	-	**SMD 0.90 lower** (2.21 lower to 0.40 lower)	⊕◯◯◯ Very Low
Performance IQ – School-Age (4-17 years of age)										
Light prenatal alcohol exposure (1-20g/w in at least one trimester)										
2	serious[a]	not serious	not serious	serious[d]	none	2471	2688	-	**SMD 0.02 higher** (0.03 lower to 0.07 higher)	⊕⊕◯◯ Low
Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)										
2	serious[a]	not serious	not serious	serious[d]	none	236	2688	-	**SMD 0.05 lower** (0.19 lower to 0.09 higher)	⊕⊕◯◯ Low
Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)										

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N1	N2	Relative (OR)	Absolute (SMD)	Certainty
2	serious a	serious b	not serious	serious d,e	none	189	784	-	**SMD 0.60 lower** (1.63 lower to 0.43 higher)	⊕◯◯◯ Very Low

Very heavy prenatal alcohol exposure (201g+/w in at least one trimester) – 0 studies

Any level prenatal alcohol exposure (exposure dichotomized to yes/no)

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N1	N2	Relative (OR)	Absolute (SMD)	Certainty
1	serious a	not serious	not serious	very serious d,e,f	none	28	28	-	**SMD 0.25 higher** (0.28 lower to 0.77 higher)	⊕◯◯◯ Very Low

Confirmed prenatal alcohol exposure-Level unquantifiable

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N1	N2	Relative (OR)	Absolute (SMD)	Certainty
2	serious a	serious b	not serious	serious e,f	none	143	90	-	**SMD 0.52 lower** (1.09 lower to 0.05 lower)	⊕◯◯◯ Very Low

Non-Verbal IQ – School-Age (4-17 years of age)

Light prenatal alcohol exposure (1-20g/w in at least one trimester) – no studies

Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N1	N2	Relative (OR)	Absolute (SMD)	Certainty
2	serious a	serious b	not serious	not serious	none	968	1831	-	**SMD 0.30 higher** (0.08 higher to 0.53 higher)	⊕⊕◯◯ Low

Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N1	N2	Relative (OR)	Absolute (SMD)	Certainty
3	serious a	serious b	not serious	serious d,e	none	481	2004	-	**SMD 0.03 lower** (0.32 lower to 0.25 higher)	⊕◯◯◯ Very Low

Very heavy prenatal alcohol exposure (201g+/w in at least one trimester)

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N1	N2	Relative (OR)	Absolute (SMD)	Certainty
1	serious a	not serious	not serious	very serious d,e,f	none	25	21	-	**SMD 0.55 lower** (1.14 lower to 0.04 higher)	⊕◯◯◯ Very Low

Any level prenatal alcohol exposure (exposure dichotomized to yes/no) – no studies

Confirmed prenatal alcohol exposure-Level Unquantifiable

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N1	N2	Relative (OR)	Absolute (SMD)	Certainty
2	serious a	not serious	not serious	serious e,f	none	82	82	-	**SMD 0.91 lower** (1.25 lower to 0.58 lower)	⊕⊕◯◯ Low

Low IQ (MDI<85)

Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N1	N2	Relative (OR)	Absolute (SMD)	Certainty
1	serious a	not serious	serious c	serious f	none	243	323	OR 2.11 (1.49 to 2.99)	-	⊕◯◯ ◯ Very Low

Light, Moderate, Very Heavy, Any Level, Confirmed-Unquantifiable – no studies

Low Full-Scale IQ (< 1 SD)

Light prenatal alcohol exposure (1-20g/w in at least one trimester)

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	N1	N2	Relative (OR)	Absolute (SMD)	Certainty
1	serious a	not serious	not serious	serious d,f	none	675	758	OR 1.10 (0.70 to 1.73)	-	⊕⊕◯◯ Low

Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)

1	serious[a]	not serious	not serious	serious[d,f]	none	175	758	**OR 1.10** (0.50 to 2.42)	-	⊕⊕◯◯ Low

Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)

1	serious[a]	not serious	not serious	serious[e,f]	none	20	758	**OR 4.60** (1.20 to 17.63)	-	⊕⊕◯◯ Low

Very Heavy, Any Level, Confirmed-Level unquantifiable – no studies

Low Verbal IQ (< 1 SD)

Light prenatal alcohol exposure (1-20g/w in at least one trimester)

1	serious[a]	not serious	not serious	serious[d,f]	none	675	758	**OR 0.90** (0.50 to 1.62)	-	⊕⊕◯◯ Low

Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)

1	serious[a]	not serious	not serious	serious[d,f]	none	175	758	**OR 1.30** (0.60 to 2.82)	-	⊕⊕◯◯ Low

Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)

1	serious[a]	not serious	not serious	serious[e,f]	none	20	758	**OR 5.90** (1.40 to 24.86)	-	⊕⊕◯◯ Low

Very Heavy, Any Level, Confirmed-Level Unquantifiable – no studies

Low Performance IQ (< 1 SD)

Light prenatal alcohol exposure (1-20g/w in at least one trimester)

1	serious[a]	not serious	not serious	serious[d,f]	none	675	758	**OR 1.00** (0.60 to 1.67)	-	⊕⊕◯◯ Low

Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)

1	serious[a]	not serious	not serious	serious[d,f]	none	175	758	**OR 1.20** (0.60 to 2.40)	-	⊕⊕◯◯ Low

Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)

1	serious[a]	not serious	not serious	very serious[d,e,f]	none	20	758	**OR 2.70** (0.80 to 9.11)	-	⊕◯◯◯ Very Low

Very Heavy, Any Level, Confirmed-Level Unquantifiable – no studies

Low Non-Verbal IQ (< 85)

Light prenatal alcohol exposure (1-20g/w in at least one trimester) – no studies

Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)

1	serious[a]	not serious	not serious	serious[d,f]	none	84	1542	**OR 0.70** (0.30 to 1.63)	-	⊕⊕◯◯ Low

Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)

1	serious[a]	not serious	not serious	serious[d,f]	none	39	1542	**OR 0.80** (0.40 to 1.60)	-	⊕⊕◯◯ Low

Very Heavy, Any Level, Confirmed-Level Unquantifiable – no studies

DIAGNOSED STUDIES

Full-Scale IQ

FASD

16	serious[a]	serious[b]	not serious	serious[e]	none	750	543	-	**SMD 1.71 lower** (2.11 lower to 1.31 lower)	⊕◯◯◯ Very Low
FAS										
7	serious[a]	serious[b]	not serious	serious[e]	none	193	621	-	**SMD 2.19 lower** (3.18 lower to 1.20 lower)	⊕◯◯◯ Very Low
pFAS (pFAS or pFAS/FAS or dysmorphic)										
7	serious[a]	serious[b]	not serious	serious[e]	none	194	440	-	**SMD 1.98 lower** (2.82 lower to 1.13 lower)	⊕◯◯◯ Very Low
Other FASDs (ARND, ND-AE, SE-AE, Non-syndromal)										
7	serious[a]	serious[b]	not serious	serious[e]	none	203	256	-	**SMD 2.91 lower** (4.04 lower to 1.78 lower)	⊕◯◯◯ Very Low
Verbal IQ										
FASD										
4	serious[a]	serious[b]	not serious	serious[e,f]	none	172	122	-	**SMD 3.02 lower** (4.56 lower to 1.48 lower)	⊕◯◯◯ Very Low
FAS										
8	serious[a]	serious[b]	serious[c]	serious[e]	none	362	883	-	**SMD 1.75 lower** (2.44 lower to 1.05 lower)	⊕◯◯◯ Very Low
pFAS (pFAS or pFAS/FAS or dysmorphic)										
5	serious[a]	not serious	serious[c]	serious[e]	none	199	668	-	**SMD 0.62 lower** (0.88 lower to 0.36 lower)	⊕◯◯◯ Very Low
Other FASDs (ARND, ND-AE, SE-AE, Non-syndromal)										
4	serious[a]	serious[b]	not serious	serious[e]	none	145	399	-	**SMD 1.89 lower** (3.00 lower to 0.78 lower)	⊕◯◯◯ Very Low
Performance IQ										
FASD										
4	serious[a]	serious[b]	not serious	serious[e,f]	none	172	122	-	**SMD 2.81 lower** (4.30 lower to 1.33 lower)	⊕◯◯◯ Very Low
FAS										
4	serious[a]	serious[b]	not serious	serious[e]	none	143	334	-	**SMD 2.65 lower** (4.29 lower to 1.01 lower)	⊕◯◯◯ Very Low
pFAS (pFAS or pFAS/FAS or dysmorphic)										
1	serious[a]	not serious	not serious	serious[e,f]	none	23	56	-	**SMD 0.95 lower** (1.45	⊕⊕◯◯ Low

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	№	№	Relative	Absolute (SMD)	Certainty
									lower to 0.44 lower)	
Other FASDs (ARND, ND-AE, SE-AE, Non-syndromal) - 2 studies										
2	serious [a]	serious [b]	not serious	serious [e,f]	none	69	106	-	**SMD 2.88 lower** (6.01 lower to 0.25 lower)	⊕◯◯◯ Very Low
Non-Verbal IQ										
FASD										
7	serious [a]	serious [b]	not serious	serious [e]	none	229	216	-	**SMD 1.16 lower** (1.57 lower to 0.75 lower)	⊕◯◯◯ Very Low
FAS										
8	serious [a]	serious [b]	serious [c]	not serious	none	290	714	-	**SMD 0.93 lower** (1.16 lower to 0.70 lower)	⊕◯◯◯ Very Low
pFAS (pFAS or pFAS/FAS or dysmorphic)										
7	serious [a]	not serious	serious [c]	not serious	none	218	771	-	**SMD 0.57 lower** (0.75 lower to 0.40 lower)	⊕⊕◯◯ Low
Other FASDs (ARND, ND-AE, SE-AE, Non-syndromal)										
4	serious [a]	not serious	serious [c]	not serious	none	103	383	-	**SMD 0.76 lower** (1.03 lower to 0.49 lower)	⊕⊕◯◯ Low
General Ability Percentile										
FASD										
3	serious [a]	not serious	not serious	not serious	none	91	843	-	**SMD 0.58 lower** (0.80 lower to 0.37 lower)	⊕⊕⊕◯ Moderate
FAS										
2	serious [a]	not serious	not serious	serious [e]	none	43	1034	-	**SMD 0.61 lower** (0.93 lower to 0.29 lower)	⊕⊕◯◯ Low
pFAS (pFAS or pFAS/FAS or dysmorphic)										
2	serious [a]	not serious	not serious	not serious	none	82	1034	-	**SMD 0.46 lower** (0.69 lower to 0.23 lower)	⊕⊕⊕◯ Moderate
Other FASDs (ARND, ND-AE, SE-AE, Non-syndromal)										
1	serious [a]	not serious	not serious	serious [d]	none	44	761	-	**SMD 0.19 lower** (0.50 lower to 0.11 higher)	⊕⊕◯◯ Low
Verbal Ability Percentile										
FASD										
3	serious [a]	not serious	not serious	not serious	none	91	843	-	**SMD 0.58 lower** (0.83 lower to 0.32 lower)	⊕⊕⊕◯ Moderate

FAS										
2	serious[a]	not serious	not serious	serious[d,e]	none	43	1034	-	**SMD 0.31 lower** (0.63 lower to 0.01 higher)	⊕⊕◯◯ Low
pFAS (pFAS or pFAS/FAS or dysmorphic)										
2	serious[a]	not serious	not serious	not serious	none	82	1034	-	**SMD 0.27 lower** (0.50 lower to 0.04 lower)	⊕⊕⊕◯ Moderate
Other FASDs (ARND, ND-AE, SE-AE, Non-syndromal)										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.05 lower** (0.35 lower to 0.25 higher)	⊕⊕◯◯ Low
Non-Verbal Ability Percentile										
FASD										
3	serious[a]	not serious	not serious	not serious	none	91	843	-	**SMD 0.40 lower** (0.61 lower to 0.18 lower)	⊕⊕⊕◯ Moderate
FAS										
2	serious[a]	not serious	not serious	serious[e]	none	43	1034	-	**SMD 0.61 lower** (1.07 lower to 0.15 lower)	⊕⊕◯◯ Low
pFAS (pFAS or pFAS/FAS or dysmorphic)										
2	serious[a]	not serious	not serious	not serious	none	82	1034	-	**SMD 0.38 lower** (0.60 lower to 0.15 lower)	⊕⊕⊕◯ Moderate
Other FASDs (ARND, ND-AE, SE-AE, Non-syndromal)										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.22 lower** (0.52 lower to 0.09 higher)	⊕⊕◯◯ Low

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.

Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I^2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CI for overall estimate crossed the line of no effect; e) wide 95% CIs for overall estimate; f) optimal information size criteria were not met

Meta-analyses for IQ/cognition

Exposure studies

INFANTS (6 MONTHS – 2 YEARS OF AGE)

Composite IQ

Light PAE and Composite IQ (1 study)

Study or Subgroup	Light PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bandoli et al 2019 (6 months; BSID-II MDI)	90.2	7.9	68	90.9	7.4	213	100.0%	-0.09 [-0.37, 0.18]		— (red)
Total (95% CI)			68			213	100.0%	-0.09 [-0.37, 0.18]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.67 (P = 0.51)

Scale: -10, -5, 0, 5, 10 — Light PAE   Control

Risk of bias legend
(A) Overall Risk of Bias

Moderate PAE and Composite IQ (4 studies)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
2.1.1 Low-Moderate Risk of Bias										
Bakhireva et al 2018 (6months; BSID-III Cog)	102.4	7.5	39	101.3	9.3	54	23.2%	0.13 [-0.29, 0.54]		? (yellow)
Subtotal (95% CI)			39			54	23.2%	0.13 [-0.29, 0.54]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.60 (P = 0.55)										
2.1.2 High Risk of Bias										
Bandoli et al 2019 (6 months; BSID-II MDI)	85.1	7.5	14	90.9	7.4	213	17.8%	-0.78 [-1.33, -0.23]		— (red)
Halliday et al 2017 (24months; BSID-III Cog)	106	11.9	74	105.3	12.2	126	29.3%	0.06 [-0.23, 0.34]		— (red)
McCormack et al 2018 (11-16months; BSID-III Cog)	107.95	11.2726	55	106.72	10.5399	525	29.7%	0.12 [-0.16, 0.39]		— (red)
Subtotal (95% CI)			143			864	76.8%	-0.13 [-0.55, 0.29]		
Heterogeneity: Tau² = 0.10; Chi² = 8.66, df = 2 (P = 0.01); I² = 77%										
Test for overall effect: Z = 0.63 (P = 0.53)										
Total (95% CI)			182			918	100.0%	-0.06 [-0.37, 0.26]		

Heterogeneity: Tau² = 0.07; Chi² = 9.04, df = 3 (P = 0.03); I² = 67%
Test for overall effect: Z = 0.37 (P = 0.71)
Test for subgroup differences: Chi² = 0.76, df = 1 (P = 0.38), I² = 0%

Scale: -10, -5, 0, 5, 10 — Moderate PAE   Control

Risk of bias legend
(A) Overall Risk of Bias

Heavy PAE and Composite IQ (1 study)

Study or Subgroup	Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McCormack et al 2018 (11-16months; BSID-III Cog)	107.32	11.3197	186	106.72	10.5399	525	100.0%	0.06 [-0.11, 0.22]		— (red)
Total (95% CI)			186			525	100.0%	0.06 [-0.11, 0.22]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.65 (P = 0.51)

Scale: -10, -5, 0, 5, 10 — Heavy PAE   Control

Risk of bias legend
(A) Overall Risk of Bias

Very Heavy PAE and Composite IQ (2 studies)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bandoli et al 2019 (6 months; BSID-II MDI)	80.4	11.7	20	90.9	7.4	213	50.0%	-1.33 [-1.81, -0.86]		— (red)
Coles et al 1987 (6 months; BSID MDI)	102.9	23.48	26	111.03	15.43	55	50.0%	-0.44 [-0.91, 0.03]		— (red)
Total (95% CI)			46			268	100.0%	-0.89 [-1.76, -0.01]		

Heterogeneity: Tau² = 0.34; Chi² = 6.89, df = 1 (P = 0.009); I² = 85%
Test for overall effect: Z = 1.98 (P = 0.05)

Scale: -10, -5, 0, 5, 10 — Very Heavy PAE   Control

Risk of bias legend
(A) Overall Risk of Bias

Any Level PAE and Composite IQ (0 studies)

-

Confirmed PAE-Level Unquantifiable (2 studies)

Study or Subgroup	Confirmed-Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Donald et al 2016 (6 months; BSID-III Cog)	97.5	8.76	28	101.09	11.48	45	60.4%	-0.34 [-0.81, 0.14]		🔴
Golden et al 1982 (6-20months; BSID MDI)	86	20	12	105	10	12	39.6%	-1.16 [-2.04, -0.28]		🔴
Total (95% CI)			40			57	100.0%	**-0.66 [-1.45, 0.13]**		

Heterogeneity: Tau² = 0.21; Chi² = 2.61, df = 1 (P = 0.11); I² = 62%
Test for overall effect: Z = 1.65 (P = 0.10)

Risk of bias legend
(A) Overall Risk of Bias

SCHOOL-AGE (4-17 YEARS OF AGE)

Full-Scale IQ

Light PAE and Full-Scale IQ (2 studies)

Study or Subgroup	Light PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
1.2.1 Mean and/or SD estimated - Low-Moderate Risk of Bias^										
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R)	105.5	17.3535	675	104.9	17.3535	758	27.7%	0.03 [-0.07, 0.14]		🟡
Subtotal (95% CI)			675			758	27.7%	**0.03 [-0.07, 0.14]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.65 (P = 0.51)										
1.2.2 High Risk of Bias										
Alati et al 2008 (8yrs; WISC-III)	106.4	16.3	1796	105.7	16.2	1930	72.3%	0.04 [-0.02, 0.11]		🔴
Subtotal (95% CI)			1796			1930	72.3%	**0.04 [-0.02, 0.11]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 1.31 (P = 0.19)										
Total (95% CI)			2471			2688	100.0%	**0.04 [-0.01, 0.10]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.89); I² = 0%
Test for overall effect: Z = 1.46 (P = 0.14)
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.89), I² = 0%
Risk of bias legend
(A) Overall Risk of Bias

Note: Falgreen Eriksen et al 2012 = mean and SD estimated from adjusted mean difference and 95% CI.

Moderate PAE and Full-Scale IQ (5 studies)

Study or Subgroup	Moderate PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
2.2.2 High Risk of Bias										
Alati et al 2008 (8yrs; WISC-III)	104.6	15.2	61	105.7	16.2	1930	21.2%	-0.07 [-0.32, 0.19]		🔴
Burden et al 2011 (11yrs; WISC-IV)	95.3	12	38	92.6	12.7	101	17.8%	0.21 [-0.16, 0.59]		🔴
Subtotal (95% CI)			99			2031	39.1%	**0.04 [-0.23, 0.31]**		
Heterogeneity: Tau² = 0.01; Chi² = 1.50, df = 1 (P = 0.22); I² = 33%										
Test for overall effect: Z = 0.28 (P = 0.78)										
2.2.3 Meand and/or SD estimated - Low-Moderate Risk of Bias^										
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R)	104.5	17.0342	175	104.9	17.0342	758	23.5%	-0.02 [-0.19, 0.14]		🟡
Larroque et al 1998 (4.5 yrs, McCarthy GCI)	96.8	1.9056	25	99.7	1.9056	48	13.4%	-1.51 [-2.05, -0.96]		🟡
Subtotal (95% CI)			200			806	36.8%	**-0.74 [-2.19, 0.71]**		
Heterogeneity: Tau² = 1.06; Chi² = 26.07, df = 1 (P < 0.00001); I² = 96%										
Test for overall effect: Z = 1.00 (P = 0.32)										
2.2.4 Mean and/or SD estimated - High Risk of Bias^										
Maher et al 2022 (5 yrs; K-BIT)	104	8.15	884	104	8.89	289	24.1%	0.00 [-0.13, 0.13]		🔴
Subtotal (95% CI)			884			289	24.1%	**0.00 [-0.13, 0.13]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.00 (P = 1.00)										
Total (95% CI)			1183			3126	100.0%	**-0.18 [-0.47, 0.11]**		

Heterogeneity: Tau² = 0.09; Chi² = 30.01, df = 4 (P < 0.00001); I² = 87%
Test for overall effect: Z = 1.24 (P = 0.22)
Test for subgroup differences: Chi² = 1.08, df = 2 (P = 0.58), I² = 0%
Risk of bias legend
(A) Overall Risk of Bias

Note: Falgreen Eriksen et al 2012 and Larroque et al 1998 = mean and SD estimated from adjusted mean difference and 95% CI; Maher et al 2022 = mean and SD estimated from median and inter-quartile range.

Heavy PAE and Full-Scale IQ (3 studies)

Study or Subgroup	Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
3.2.1 Mean and/or SD estimated - Low-Moderate Risk of Bias^										
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R)	99.4	18.6935	20	104.9	18.6935	758	33.7%	-0.29 [-0.74, 0.15]		?
Larroque et al 1998 (4.5 yrs, McCarthy GCI)	106.3	1.9162	20	99.7	1.9162	48	31.6%	3.41 [2.62, 4.19]		?
Subtotal (95% CI)			40			806	65.3%	1.54 [-2.08, 5.17]		
Heterogeneity: Tau² = 6.73; Chi² = 64.33, df = 1 (P < 0.0001); I² = 98%										
Test for overall effect: Z = 0.83 (P = 0.40)										
3.2.2 Mean and/or SD estimated - High Risk of Bias^										
Maher et al 2022 (5 yrs; K-BIT)	104	8.15	334	104	8.89	289	34.7%	0.00 [-0.16, 0.16]		●
Subtotal (95% CI)			334			289	34.7%	0.00 [-0.16, 0.16]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.00 (P = 1.00)										
Total (95% CI)			374			1095	100.0%	0.98 [-0.46, 2.42]		
Heterogeneity: Tau² = 1.55; Chi² = 72.24, df = 2 (P < 0.00001); I² = 97%										
Test for overall effect: Z = 1.33 (P = 0.18)										
Test for subgroup differences: Chi² = 0.69, df = 1 (P = 0.41), I² = 0%										

Risk of bias legend
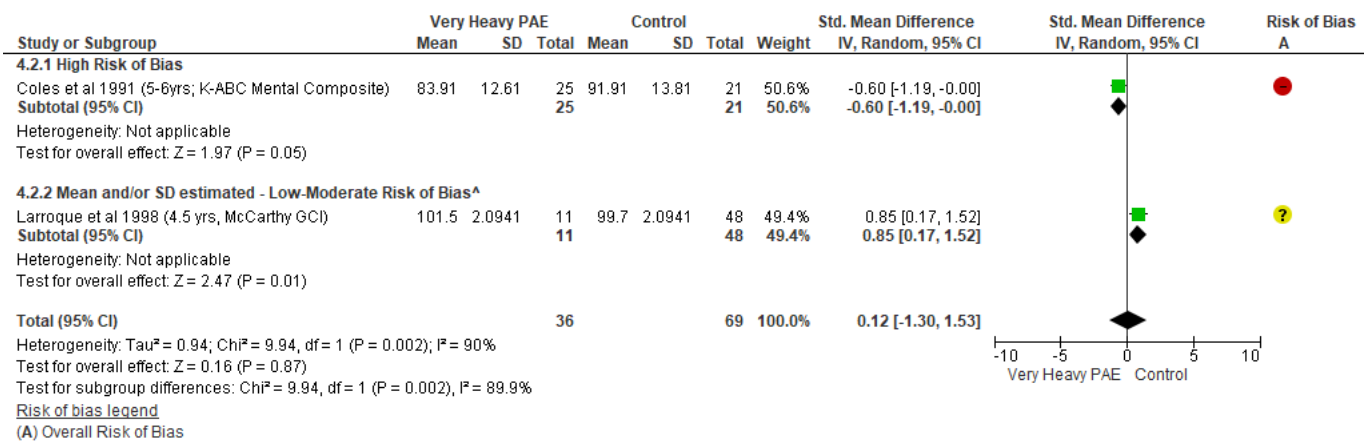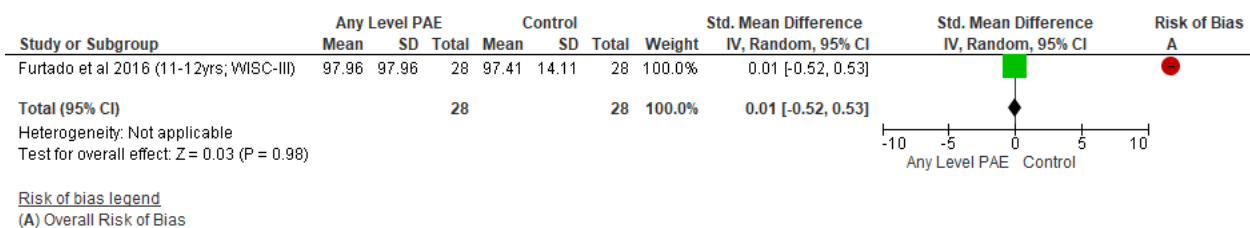(A) Overall Risk of Bias

Note: Falgreen Eriksen et al 2012 and Larroque et al 1998 = mean and SD estimated from adjusted mean difference and 95% CI; Maher et al 2022 = mean and SD estimated from median and IQR.

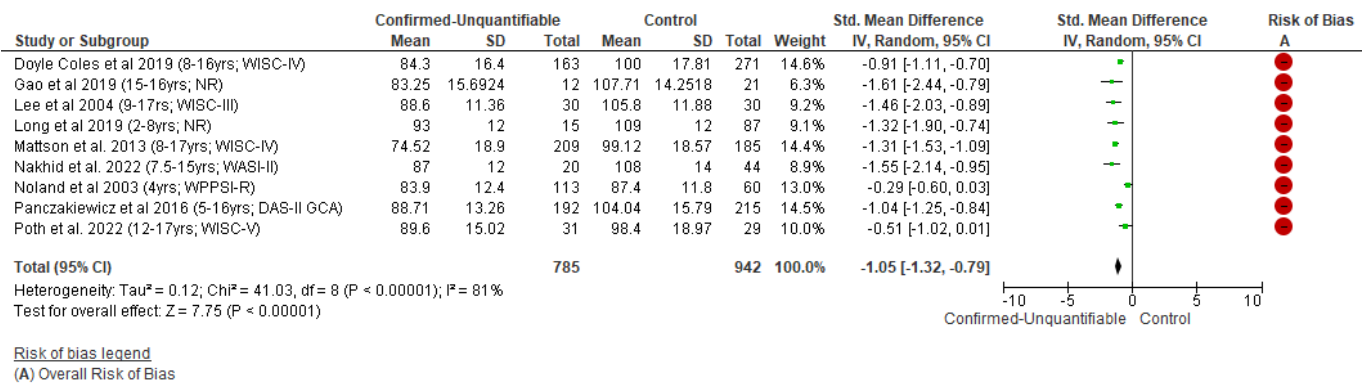## Very Heavy PAE and Full-Scale IQ (2 studies)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
4.2.1 High Risk of Bias										
Coles et al 1991 (5-6yrs; K-ABC Mental Composite)	83.91	12.61	25	91.91	13.81	21	50.6%	-0.60 [-1.19, -0.00]		●
Subtotal (95% CI)			25			21	50.6%	-0.60 [-1.19, -0.00]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 1.97 (P = 0.05)										
4.2.2 Mean and/or SD estimated - Low-Moderate Risk of Bias^										
Larroque et al 1998 (4.5 yrs, McCarthy GCI)	101.5	2.0941	11	99.7	2.0941	48	49.4%	0.85 [0.17, 1.52]		?
Subtotal (95% CI)			11			48	49.4%	0.85 [0.17, 1.52]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 2.47 (P = 0.01)										
Total (95% CI)			36			69	100.0%	0.12 [-1.30, 1.53]		
Heterogeneity: Tau² = 0.94; Chi² = 9.94, df = 1 (P = 0.002); I² = 90%										
Test for overall effect: Z = 0.16 (P = 0.87)										
Test for subgroup differences: Chi² = 9.94, df = 1 (P = 0.002), I² = 89.9%										

Risk of bias legend
(A) Overall Risk of Bias

Note: Falgreen Eriksen et al 2012 and Larroque et al 1998 = mean and SD estimated from adjusted mean.

Any Level PAE AND Full-Scale IQ (1 study)

Study or Subgroup	Any Level PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Furtado et al 2016 (11-12yrs; WISC-III)	97.96	97.96	28	97.41	14.11	28	100.0%	0.01 [-0.52, 0.53]		●
Total (95% CI)			28			28	100.0%	0.01 [-0.52, 0.53]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.03 (P = 0.98)										

Risk of bias legend
(A) Overall Risk of Bias

Confirmed PAE-Level Unquantifiable and Full-Scale IQ (9 studies)

Study or Subgroup	Confirmed-Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total			
Doyle Coles et al 2019 (8-16yrs; WISC-IV)	84.3	16.4	163	100	17.81	271	14.6%	-0.91 [-1.11, -0.70]	🔴
Gao et al 2019 (15-16yrs; NR)	83.25	15.6924	12	107.71	14.2518	21	6.3%	-1.61 [-2.44, -0.79]	🔴
Lee et al 2004 (9-17rs; WISC-III)	88.6	11.36	30	105.8	11.88	30	9.2%	-1.46 [-2.03, -0.89]	🔴
Long et al 2019 (2-8yrs; NR)	93	12	15	109	12	87	9.1%	-1.32 [-1.90, -0.74]	🔴
Mattson et al. 2013 (8-17yrs; WISC-IV)	74.52	18.9	209	99.12	18.57	185	14.4%	-1.31 [-1.53, -1.09]	🔴
Nakhid et al. 2022 (7.5-15yrs; WASI-II)	87	12	20	108	14	44	8.9%	-1.55 [-2.14, -0.95]	🔴
Noland et al 2003 (4yrs; WPPSI-R)	83.9	12.4	113	87.4	11.8	60	13.0%	-0.29 [-0.60, 0.03]	🔴
Panczakiewicz et al 2016 (5-16yrs; DAS-II GCA)	88.71	13.26	192	104.04	15.79	215	14.5%	-1.04 [-1.25, -0.84]	🔴
Poth et al. 2022 (12-17yrs; WISC-V)	89.6	15.02	31	98.4	18.97	29	10.0%	-0.51 [-1.02, 0.01]	🔴
Total (95% CI)			**785**			**942**	**100.0%**	**-1.05 [-1.32, -0.79]**	

Heterogeneity: Tau² = 0.12; Chi² = 41.03, df = 8 (P < 0.00001); I² = 81%
Test for overall effect: Z = 7.75 (P < 0.00001)

Risk of bias legend
(A) Overall Risk of Bias

Verbal IQ

Light PAE and Verbal IQ (2 studies)

Study or Subgroup	Light PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total			
1.3.1 Mean and/or SD estimated - Low-Moderate Risk of Bias^									
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R)	105.2	14.4613	675	104.3	14.4613	758	27.7%	0.06 [-0.04, 0.17]	❓
Subtotal (95% CI)			675			758	27.7%	0.06 [-0.04, 0.17]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.18 (P = 0.24)									
1.3.2 High Risk of Bias									
Alati et al 2008 (8yrs; WISC-III)	109.2	16.7	1796	108.6	16.5	1930	72.3%	0.04 [-0.03, 0.10]	🔴
Subtotal (95% CI)			1796			1930	72.3%	0.04 [-0.03, 0.10]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.10 (P = 0.27)									
Total (95% CI)			**2471**			**2688**	**100.0%**	**0.04 [-0.01, 0.10]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 1 (P = 0.68); I² = 0%
Test for overall effect: Z = 1.56 (P = 0.12)
Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.68), I² = 0%

Risk of bias legend
(A) Overall Risk of Bias

Note: Falgreen Eriksen et al 2012 = mean and SD estimated from adjusted mean difference and 95% CI.

Moderate PAE and Verbal IQ (3 studies)
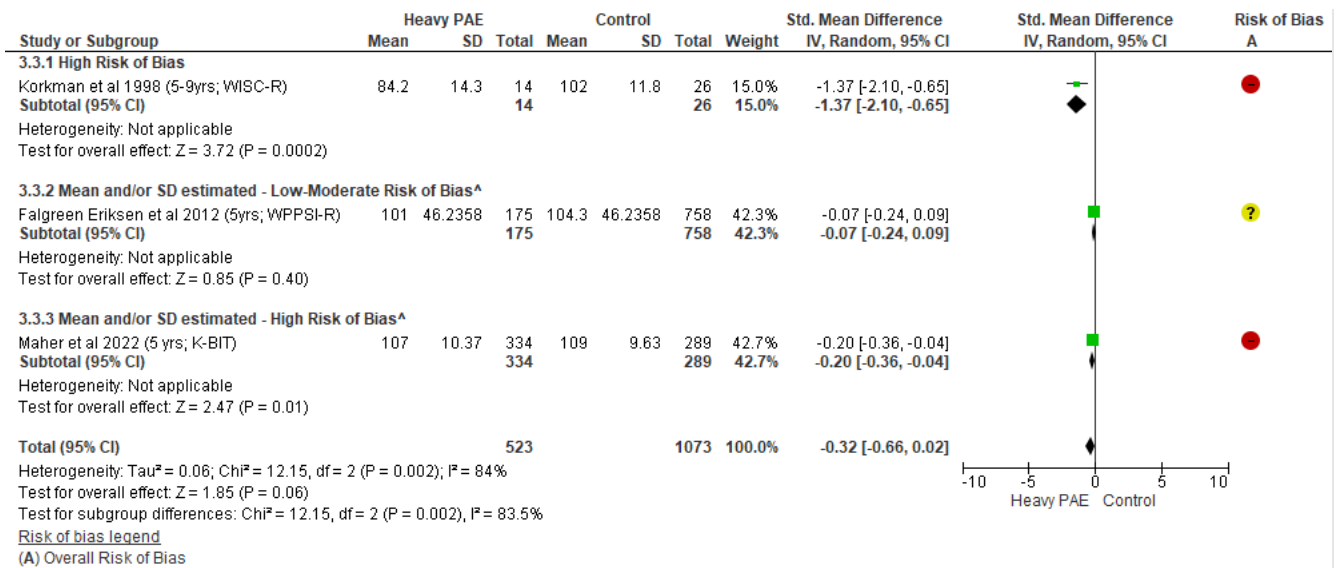
Study or Subgroup	Moderate PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total			
2.3.1 High Risk of Bias									
Alati et al 2008 (8yrs; WISC-III)	108.8	17.2	61	108.6	16.5	1930	14.1%	0.01 [-0.24, 0.27]	🔴
Subtotal (95% CI)			61			1930	14.1%	0.01 [-0.24, 0.27]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.09 (P = 0.93)									
2.3.2 Mean and/or SD estimated - High Risk of Bias^									
Maher et al 2022 (5 yrs; K-BIT)	109	9.63	884	109	9.63	289	52.0%	0.00 [-0.13, 0.13]	🔴
Subtotal (95% CI)			884			289	52.0%	0.00 [-0.13, 0.13]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.00 (P = 1.00)									
2.3.3 Mean and/or SD estimated - Low-Moderate Risk of Bias^									
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R)	104	13.9789	175	104.3	17.0342	758	33.9%	-0.02 [-0.18, 0.15]	❓
Subtotal (95% CI)			175			758	33.9%	-0.02 [-0.18, 0.15]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.22 (P = 0.83)									
Total (95% CI)			**1120**			**2977**	**100.0%**	**-0.00 [-0.10, 0.09]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 2 (P = 0.98); I² = 0%
Test for overall effect: Z = 0.09 (P = 0.93)
Test for subgroup differences: Chi² = 0.05, df = 2 (P = 0.98), I² = 0%

Risk of bias legend
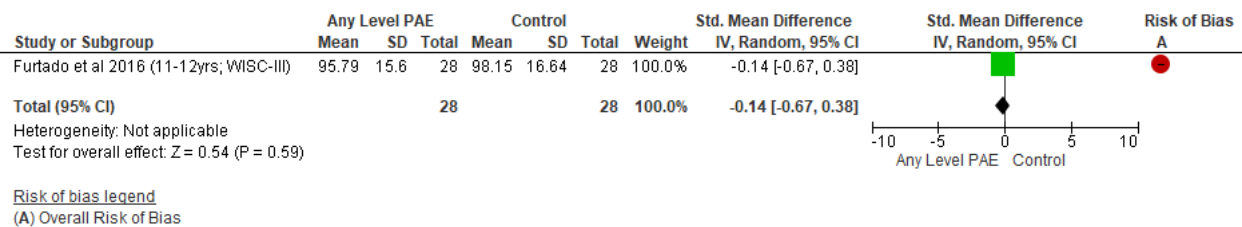(A) Overall Risk of Bias

Note: Falgreen Eriksen et al 2012 = mean and SD estimated from adjusted mean difference and 95% CI; Maher et al 2022 = mean and SD estimated from median and IQR.
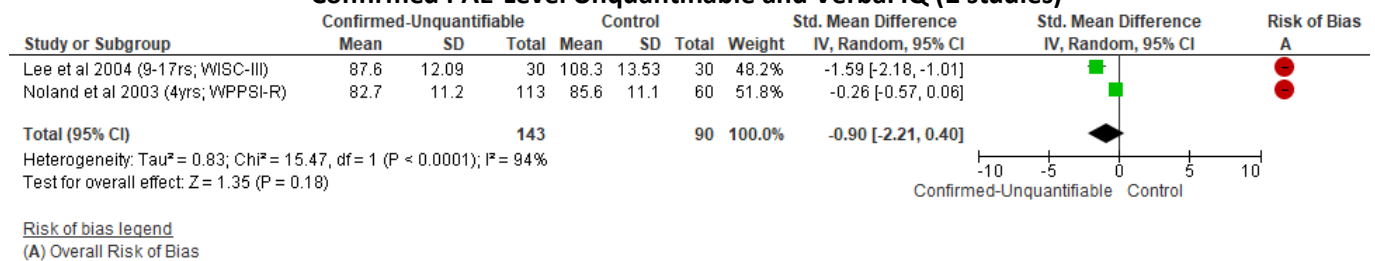
Heavy PAE and Verbal IQ (3 studies)
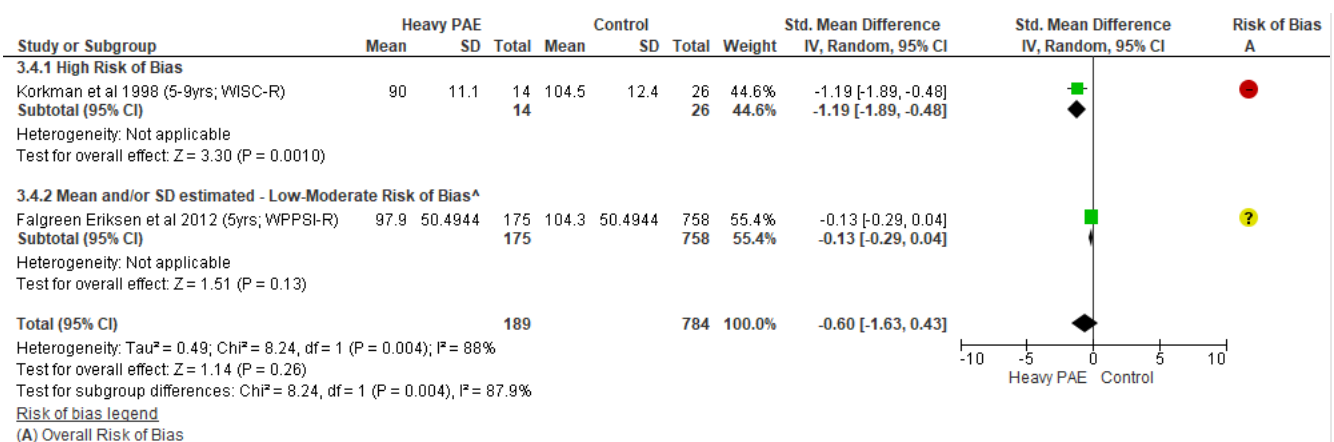
Study or Subgroup	Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
3.3.1 High Risk of Bias									
Korkman et al 1998 (5-9yrs; WISC-R)	84.2	14.3	14	102	11.8	26	15.0%	-1.37 [-2.10, -0.65]	🔴
Subtotal (95% CI)			14			26	15.0%	-1.37 [-2.10, -0.65]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.72 (P = 0.0002)									
3.3.2 Mean and/or SD estimated - Low-Moderate Risk of Bias^									
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R)	101	46.2358	175	104.3	46.2358	758	42.3%	-0.07 [-0.24, 0.09]	❓
Subtotal (95% CI)			175			758	42.3%	-0.07 [-0.24, 0.09]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.85 (P = 0.40)									
3.3.3 Mean and/or SD estimated - High Risk of Bias^									
Maher et al 2022 (5 yrs; K-BIT)	107	10.37	334	109	9.63	289	42.7%	-0.20 [-0.36, -0.04]	🔴
Subtotal (95% CI)			334			289	42.7%	-0.20 [-0.36, -0.04]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.47 (P = 0.01)									
Total (95% CI)			523			1073	100.0%	-0.32 [-0.66, 0.02]	
Heterogeneity: Tau² = 0.06; Chi² = 12.15, df = 2 (P = 0.002); I² = 84%									
Test for overall effect: Z = 1.85 (P = 0.06)									
Test for subgroup differences: Chi² = 12.15, df = 2 (P = 0.002), I² = 83.5%									

Risk of bias legend
(A) Overall Risk of Bias

Note: Falgreen Eriksen et al 2012 = mean and SD estimated from adjusted mean difference and 95% CI; Maher et al 2022 = mean and SD estimated from median and IQR.

Very Heavy PAE and Verbal IQ (0 studies)
-

Any Level PAE and Verbal IQ (1 study)

Study or Subgroup	Any Level PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Furtado et al 2016 (11-12yrs; WISC-III)	95.79	15.6	28	98.15	16.64	28	100.0%	-0.14 [-0.67, 0.38]	🔴
Total (95% CI)			28			28	100.0%	-0.14 [-0.67, 0.38]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.54 (P = 0.59)									

Risk of bias legend
(A) Overall Risk of Bias

Confirmed PAE-Level Unquantifiable and Verbal IQ (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lee et al 2004 (9-17rs; WISC-III)	87.6	12.09	30	108.3	13.53	30	48.2%	-1.59 [-2.18, -1.01]	🔴
Noland et al 2003 (4yrs; WPPSI-R)	82.7	11.2	113	85.6	11.1	60	51.8%	-0.26 [-0.57, 0.06]	🔴
Total (95% CI)			143			90	100.0%	-0.90 [-2.21, 0.40]	
Heterogeneity: Tau² = 0.83; Chi² = 15.47, df = 1 (P < 0.0001); I² = 94%									
Test for overall effect: Z = 1.35 (P = 0.18)									

Risk of bias legend
(A) Overall Risk of Bias

Performance IQ

Light PAE and Performance IQ (2 studies)

Note: Falgreen Eriksen et al 2012 = mean and SD estimated from adjusted mean difference and 95% CI.

Moderate PAE and Performance IQ (2 studies)

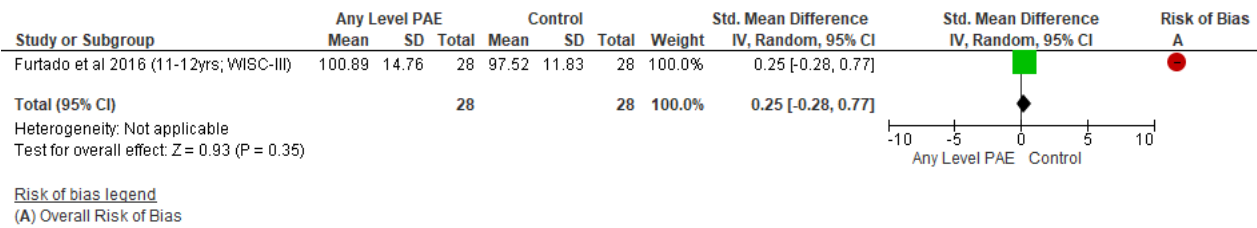*Note:* Falgreen Eriksen et al 2012 = mean and SD estimated from adjusted mean difference and 95% CI.
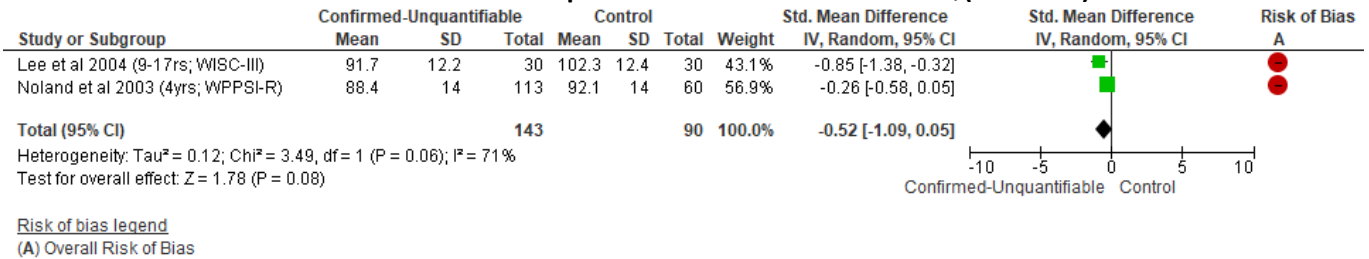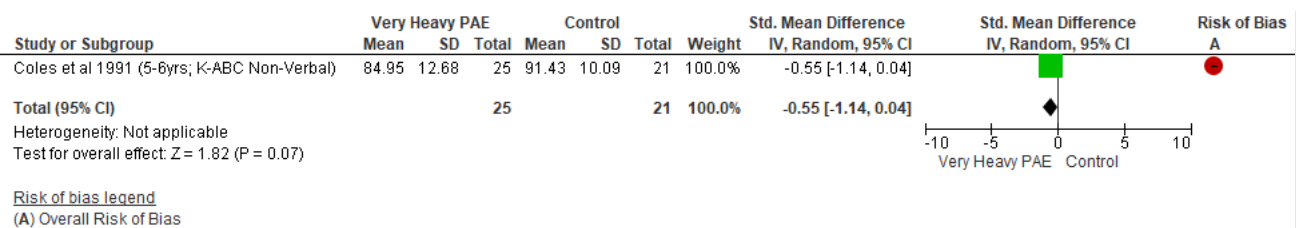
Heavy PAE and Performance IQ (2 studies)

Note: Falgreen Eriksen et al 2012 = mean and SD estimated from adjusted mean difference and 95% CI.

Very Heavy PAE and Performance IQ (0 studies)

-

Any Level PAE and Performance IQ (1 study)

Study or Subgroup	Any Level PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Furtado et al 2016 (11-12yrs; WISC-III)	100.89	14.76	28	97.52	11.83	28	100.0%	0.25 [-0.28, 0.77]	🔴
Total (95% CI)			28			28	100.0%	**0.25 [-0.28, 0.77]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.93 (P = 0.35)

Risk of bias legend
(A) Overall Risk of Bias

Confirmed PAE-Level Unquantifiable and Performance IQ (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lee et al 2004 (9-17rs; WISC-III)	91.7	12.2	30	102.3	12.4	30	43.1%	-0.85 [-1.38, -0.32]	🔴
Noland et al 2003 (4yrs; WPPSI-R)	88.4	14	113	92.1	14	60	56.9%	-0.26 [-0.58, 0.05]	🔴
Total (95% CI)			143			90	100.0%	**-0.52 [-1.09, 0.05]**	

Heterogeneity: Tau² = 0.12; Chi² = 3.49, df = 1 (P = 0.06); I² = 71%
Test for overall effect: Z = 1.78 (P = 0.08)

Risk of bias legend
(A) Overall Risk of Bias

Non-Verbal IQ

Light PAE and Non-Verbal IQ (0 studies)

-

Moderate PAE and Non-Verbal IQ (2 studies)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
2.5.1 Mean and/or SD estimated - Low-Moderate Risk of Bias^									
O'Callaghan et al 2007 (14yrs; Ravens Non-Verbal)	102.5	14.5372	84	99.9	15.2	1542	42.7%	0.17 [-0.05, 0.39]	🟡
Subtotal (95% CI)			84			1542	42.7%	**0.17 [-0.05, 0.39]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.53 (P = 0.13)									
2.5.2 Mean and/or SD estimated - High Risk of Bias^									
Maher et al 2022 (5 yrs; K-BIT)	100	7.41	884	97	7.41	289	57.3%	0.40 [0.27, 0.54]	🔴
Subtotal (95% CI)			884			289	57.3%	**0.40 [0.27, 0.54]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 5.93 (P < 0.00001)									
Total (95% CI)			968			1831	100.0%	**0.30 [0.08, 0.53]**	

Heterogeneity: Tau² = 0.02; Chi² = 3.16, df = 1 (P = 0.08); I² = 68%
Test for overall effect: Z = 2.64 (P = 0.008)
Test for subgroup differences: Chi² = 3.16, df = 1 (P = 0.08), I² = 68.3%
Risk of bias legend
(A) Overall Risk of Bias

Note: O'Callaghan et al 2017 = mean and SD estimated from adjusted mean difference and 95% CI; Maher et al 2022 = mean and SD estimated from median and IQR.

Heavy PAE and Non-Verbal IQ (3 studies)

Study or Subgroup	Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
3.5.1 High Risk of Bias										
Coles et al 2021 (4yrs; DAS-II Non-verbal Composit	96.44	16.67	108	100.93	13.19	173	33.2%	-0.31 [-0.55, -0.06]		➖
Subtotal (95% CI)			108			173	33.2%	-0.31 [-0.55, -0.06]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 2.48 (P = 0.01)										
3.5.2 Mean and/or SD estimated - Low-Moderate Risk of Bias^										
O'Callaghan et al 2007 (14yrs; Ravens Non-Verbal)	100.8	14.4562	39	99.9	15.2	1542	28.3%	0.06 [-0.26, 0.38]		❓
Subtotal (95% CI)			39			1542	28.3%	0.06 [-0.26, 0.38]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.37 (P = 0.71)										
3.5.3 Mean and/or SD estimated - High Risk of Bias^										
Maher et al 2022 (5 yrs; K-BIT)	98	7.69	334	97	7.41	289	38.5%	0.13 [-0.03, 0.29]		➖
Subtotal (95% CI)			334			289	38.5%	0.13 [-0.03, 0.29]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 1.64 (P = 0.10)										
Total (95% CI)			481			2004	100.0%	-0.03 [-0.32, 0.25]		

Heterogeneity: Tau² = 0.05; Chi² = 8.97, df = 2 (P = 0.01); I² = 78%
Test for overall effect: Z = 0.23 (P = 0.81)
Test for subgroup differences: Chi² = 8.97, df = 2 (P = 0.01), I² = 77.7%

-10 -5 0 5 10
Heavy PAE   Control

Risk of bias legend
(A) Overall Risk of Bias

Note: O'Callaghan et al 2017 = mean and SD estimated from adjusted mean difference and 95% CI; Maher et al 2022 = mean and SD estimated from median and IQR.

Very Heavy PAE and Non-Verbal IQ (1 study)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 1991 (5-6yrs; K-ABC Non-Verbal)	84.95	12.68	25	91.43	10.09	21	100.0%	-0.55 [-1.14, 0.04]		➖
Total (95% CI)			25			21	100.0%	-0.55 [-1.14, 0.04]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.82 (P = 0.07)

-10 -5 0 5 10
Very Heavy PAE   Control

Risk of bias legend
(A) Overall Risk of Bias

Any Level PAE and Non-Verbal IQ (0 studies)

-

Confirmed PAE- Level Unquantifiable and Non-Verbal IQ (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Glass et al 2014 (12yrs; Leiter-R Brief IQ)	96.4	16.25	44	109.6	12.08	22	39.1%	-0.87 [-1.40, -0.33]		➖
Mattson et al 2010 (7-21yrs; Leiter-R)	96	15.05	38	108.9	12.52	60	60.9%	-0.94 [-1.37, -0.52]		➖
Total (95% CI)			82			82	100.0%	-0.91 [-1.25, -0.58]		

Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = 0.83); I² = 0%
Test for overall effect: Z = 5.37 (P < 0.00001)

-10 -5 0 5 10
Confirmed-Unquantifiable   Control

Risk of bias legend
(A) Overall Risk of Bias

Low IQ (MDI<85)

Light PAE and Low IQ (MDI<85) (0 studies)

-

Moderate Level PAE and Low IQ (MDI<85) (0 studies)

-

Heavy PAE and Low IQ (MDI<85) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Heavy PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Bandoli et al 2022 (6-12months; BSID-II MD less85)	0.746	0.1786	243	323	100.0%	2.11 [1.49, 2.99]		🔴
Total (95% CI)			243	323	100.0%	2.11 [1.49, 2.99]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.18 (P < 0.0001)

Risk of bias legend
(A) Overall Risk of Bias

Very Heavy PAE and Low IQ (MDI<85) (0 studies)
-

Any Level PAE and Low IQ (MDI<85) (0 studies)
-

Confirmed PAE- Level Unquantifiable and IQ (MDI<85) (0 studies)

Low Full-Scale IQ (< 1 SD)

Light PAE and Low Full-Scale IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Light PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	0.0953	0.2306	675	758	100.0%	1.10 [0.70, 1.73]		❓
Total (95% CI)			675	758	100.0%	1.10 [0.70, 1.73]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.41 (P = 0.68)

Risk of bias legend
(A) Overall Risk of Bias

Moderate PAE and Low Full-Scale IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Moderate PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	0.0953	0.4023	175	758	100.0%	1.10 [0.50, 2.42]		❓
Total (95% CI)			175	758	100.0%	1.10 [0.50, 2.42]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)

Risk of bias legend
(A) Overall Risk of Bias

Heavy PAE and Low Full-Scale IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Heavy PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	1.5261	0.6856	20	758	100.0%	4.60 [1.20, 17.63]		❓
Total (95% CI)			20	758	100.0%	4.60 [1.20, 17.63]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.23 (P = 0.03)

Risk of bias legend
(A) Overall Risk of Bias

Very Heavy PAE and Low Full-Scale IQ (0 studies)
-

Any Level PAE and Low Full-Scale IQ (0 studies)
-

Confirmed PAE- Level Unquantifiable and Low Full-Scale IQ (0 studies)
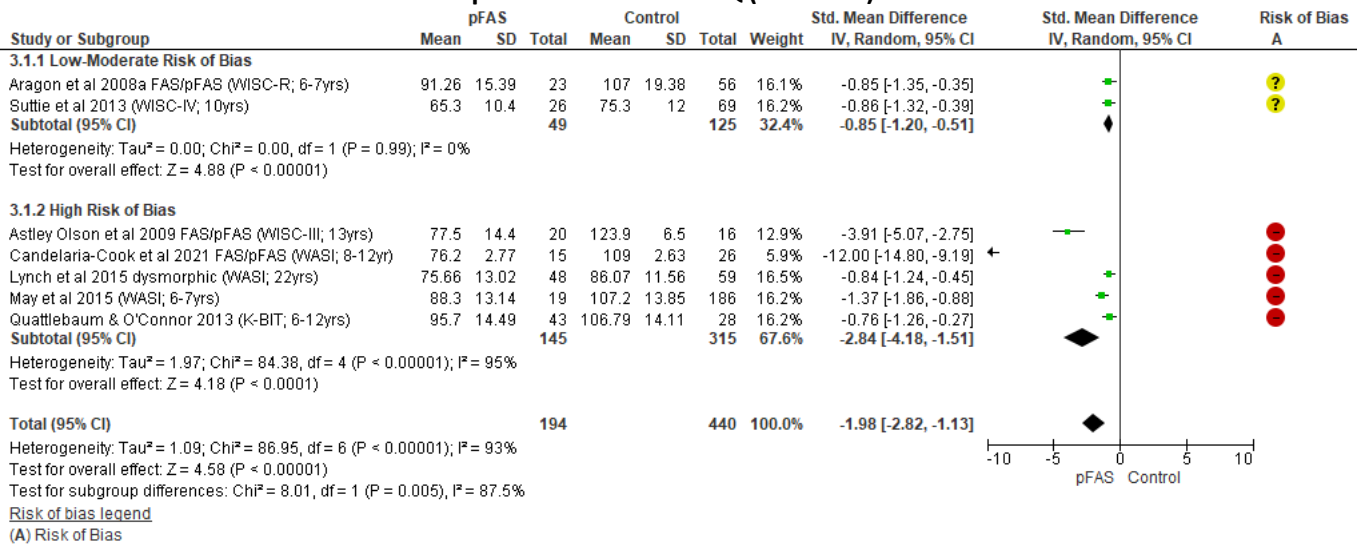
-

Low Verbal IQ (< 1 SD)

Light PAE and Low Verbal IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Light PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	-0.1054	0.2999	675	758	100.0%	0.90 [0.50, 1.62]		?
Total (95% CI)			675	758	100.0%	0.90 [0.50, 1.62]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.35 (P = 0.73)

Risk of bias legend
(A) Overall Risk of Bias

Moderate PAE and Low Verbal IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Moderate PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	0.2624	0.3945	175	758	100.0%	1.30 [0.60, 2.82]		?
Total (95% CI)			175	758	100.0%	1.30 [0.60, 2.82]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.67 (P = 0.51)

Risk of bias legend
(A) Overall Risk of Bias

Heavy PAE and Low Verbal IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Heavy PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	1.775	0.7339	20	758	100.0%	5.90 [1.40, 24.86]		?
Total (95% CI)			20	758	100.0%	5.90 [1.40, 24.86]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.42 (P = 0.02)

Risk of bias legend
(A) Overall Risk of Bias

Very Heavy PAE and Low Verbal IQ (0 studies)

-

Any Level PAE and Low Verbal IQ (0 studies)

-

Confirmed PAE- Level Unquantifiable and Low Verbal IQ (0 studies)

-

Low Performance IQ (< 1 SD)

Light PAE and Low Performance IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Light PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	0	0.2606	675	758	100.0%	1.00 [0.60, 1.67]		?
Total (95% CI)			**675**	**758**	**100.0%**	**1.00 [0.60, 1.67]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

Risk of bias legend
(A) Overall Risk of Bias

Moderate PAE and Low Performance IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Moderate PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	0.1823	0.3537	175	758	100.0%	1.20 [0.60, 2.40]		?
Total (95% CI)			**175**	**758**	**100.0%**	**1.20 [0.60, 2.40]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.52 (P = 0.61)

Risk of bias legend
(A) Overall Risk of Bias

Heavy PAE and Low Performance IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Heavy PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	0.9933	0.6206	20	758	100.0%	2.70 [0.80, 9.11]		?
Total (95% CI)			**20**	**758**	**100.0%**	**2.70 [0.80, 9.11]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.60 (P = 0.11)

Risk of bias legend
(A) Overall Risk of Bias

Very Heavy PAE and Low Performance IQ (0 studies)
-

Any Level PAE and Low Performance IQ (0 studies)
-

Confirmed PAE- Level Unquantifiable and Low Performance IQ (0 studies)
-

Low Non-Verbal (Raven < 85)

Light PAE and Low Non-Verbal IQ (0 studies)
-

Moderate PAE and Low Non-Verbal IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Moderate PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Callaghan etal 2007 (14yr; Ravens less85 NV)	-0.3567	0.4323	84	1542	100.0%	0.70 [0.30, 1.63]		?
Total (95% CI)			**84**	**1542**	**100.0%**	**0.70 [0.30, 1.63]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)

Risk of bias legend
(A) Overall Risk of Bias

Heavy PAE and Low Non-Verbal IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Heavy PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Callaghan etal 2007 (14yr; Ravens less85 NV)	-0.2231	0.3537	39	1542	100.0%	0.80 [0.40, 1.60]		?
Total (95% CI)			**39**	**1542**	**100.0%**	**0.80 [0.40, 1.60]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)

Risk of bias legend
(A) Overall Risk of Bias

Very Heavy PAE and Low Non-Verbal IQ (0 studies)
-

Any Level PAE and Low Non-Verbal IQ (0 studies)
-

Confirmed PAE- Level Unquantifiable and Low Non-Verbal IQ (0 studies)
-

Diagnosed studies

Full-Scale IQ

FASD and Full-Scale IQ (16 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
1.1.1 Low-Moderate Risk of Bias										
Kaemingk et al 2003 (WISC-III; 6-16yrs)	66.1	2.41	20	97	2.15	20	1.4%	-13.26 [-16.38, -10.14]		?
Kerns et al 2016 (WASI; 8-14yrs)	84.7	8.3	22	110.1	10.8	22	5.8%	-2.59 [-3.41, -1.77]		?
Subtotal (95% CI)			42			42	7.2%	-7.82 [-18.27, 2.64]		
Heterogeneity: Tau² = 55.59; Chi² = 41.98, df = 1 (P < 0.00001); I² = 98%										
Test for overall effect: Z = 1.46 (P = 0.14)										
1.1.2 High Risk of Bias										
Agnihotri et al 2019 (WASI, 9-17yrs)	87.89	14.19	41	114.52	10.81	64	6.9%	-2.16 [-2.65, -1.67]		●
Crawford et al 2020 (WISC-IV/WASI; 8-12yrs)	86.18	9.82	39	97.86	14.12	29	6.8%	-0.98 [-1.48, -0.47]		●
de Water et al 2021 (NR, 8-16 yrs)	92	14.76	41	115	12.32	43	6.8%	-1.68 [-2.18, -1.18]		●
Fagerlund et al 2012 (WISC/WAIS-III; 13 yrs)	79.34	17.27	73	107.32	14.49	40	7.0%	-1.70 [-2.15, -1.25]		●
Inkelis et al 2020 (WAIS; 13-30yrs)	82.3	13.71	106	108	14.47	55	7.1%	-1.83 [-2.21, -1.45]		●
Kooistra et al 2009 (WISC-III; 8-9yrs)	98	15.5	30	117.7	10	39	6.7%	-1.54 [-2.08, -0.99]		●
Lidstone et al 2020 (WASI-II; 7-17yrs)	91	11.2	16	111	10	21	5.9%	-1.86 [-2.65, -1.07]		●
May et al 2006 (NR; 6-7yrs)	85.6	13.11	20	102.25	8.19	20	6.2%	-1.49 [-2.20, -0.78]		●
Nayak et al 2012 (MISIC; 6yrs)	72.65	6.33	26	80.93	6.37	27	6.5%	-1.28 [-1.88, -0.69]		●
Quattlebaum & O'Connor 2013 (K-BIT; 6-12yrs)	99.52	14.87	125	106.79	14.11	28	7.1%	-0.49 [-0.90, -0.08]		●
Spottiswoode et al 2011 (WISC-III; 9-13yrs)	62.8	9.3	13	76.6	12.1	12	5.6%	-1.24 [-2.11, -0.37]		●
Treit et al 2017 (WRIT; 5-32yrs)	87	18	45	112	13	74	7.0%	-1.65 [-2.07, -1.22]		●
Walthall et al 2008 (K-BIT; 6-12yrs)	97.24	14.83	100	106.57	13.69	30	7.1%	-0.64 [-1.05, -0.22]		●
Wozniak et al 2009 (WISC-IV/WAIS-III; 10-17yrs)	76.9	13.3	33	107.3	11.1	19	6.1%	-2.39 [-3.12, -1.65]		●
Subtotal (95% CI)			708			501	92.8%	-1.48 [-1.78, -1.17]		
Heterogeneity: Tau² = 0.25; Chi² = 61.03, df = 13 (P < 0.00001); I² = 79%										
Test for overall effect: Z = 9.54 (P < 0.00001)										
Total (95% CI)			**750**			**543**	**100.0%**	**-1.71 [-2.11, -1.31]**		

Heterogeneity: Tau² = 0.55; Chi² = 123.40, df = 15 (P < 0.00001); I² = 88%
Test for overall effect: Z = 8.31 (P < 0.00001)
Test for subgroup differences: Chi² = 1.41, df = 1 (P = 0.23), I² = 29.1%
Risk of bias legend
(A) Risk of Bias

Funnel Plot

Subgroups
○ Low-Moderate Risk of Bias   ◇ High Risk of Bias

FAS and Full-Scale IQ (7 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
2.1.1 Low-Moderate Risk of Bias										
Sullivan et al 2020 (WAIS-R; 13-37yrs)	80.05	13.45	57	109.37	13.81	59	15.0%	-2.14 [-2.60, -1.68]		?
Suttie et al 2013 (WISC-IV; 10yrs)	60.6	11.1	22	75.3	12	69	14.9%	-1.24 [-1.75, -0.72]		?
Subtotal (95% CI)			79			128	29.8%	-1.69 [-2.58, -0.81]		
Heterogeneity: Tau² = 0.34; Chi² = 6.56, df = 1 (P = 0.01); I² = 85%										
Test for overall effect: Z = 3.76 (P = 0.0002)										
2.1.2 High Risk of Bias										
Mattson et al 1997 (WPPSI-R/WISC-R; 8yrs)	75.38	5.2	34	109.25	2.99	47	11.9%	-8.26 [-9.64, -6.88]		●
Mattson et al 2013 (WISC-IV; 8-17yrs)	65.15	14.37	41	99.12	18.57	185	15.1%	-1.89 [-2.27, -1.51]		●
May et al 2015 (WASI; 6-7yrs)	87	8.25	7	107.2	13.85	186	14.1%	-1.47 [-2.24, -0.70]		●
Quattlebaum & O'Connor 2013 (K-BIT; 6-12yrs)	90.4	15.64	10	106.79	14.11	28	14.1%	-1.11 [-1.87, -0.34]		●
Suttie et al 2018 (DAS-II; 12-13yrs)	90.5	45.1	22	109.8	56.2	47	14.9%	-0.36 [-0.87, 0.15]		●
Subtotal (95% CI)			114			493	70.2%	-2.49 [-4.03, -0.94]		
Heterogeneity: Tau² = 2.93; Chi² = 116.52, df = 4 (P < 0.00001); I² = 97%										
Test for overall effect: Z = 3.15 (P = 0.002)										
Total (95% CI)			193			621	100.0%	-2.19 [-3.18, -1.20]		
Heterogeneity: Tau² = 1.64; Chi² = 123.59, df = 6 (P < 0.00001); I² = 95%										
Test for overall effect: Z = 4.34 (P < 0.0001)										
Test for subgroup differences: Chi² = 0.76, df = 1 (P = 0.38), I² = 0%										

Risk of bias legend
(A) Risk of Bias

pFAS and Full-Scale IQ (7 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
3.1.1 Low-Moderate Risk of Bias										
Aragon et al 2008a FAS/pFAS (WISC-R; 6-7yrs)	91.26	15.39	23	107	19.38	56	16.1%	-0.85 [-1.35, -0.35]		?
Suttie et al 2013 (WISC-IV; 10yrs)	65.3	10.4	26	75.3	12	69	16.2%	-0.86 [-1.32, -0.39]		?
Subtotal (95% CI)			49			125	32.4%	-0.85 [-1.20, -0.51]		
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.99); I² = 0%										
Test for overall effect: Z = 4.88 (P < 0.00001)										
3.1.2 High Risk of Bias										
Astley Olson et al 2009 FAS/pFAS (WISC-III; 13yrs)	77.5	14.4	20	123.9	6.5	16	12.9%	-3.91 [-5.07, -2.75]		●
Candelaria-Cook et al 2021 FAS/pFAS (WASI; 8-12yr)	76.2	2.77	15	109	2.63	26	5.9%	-12.00 [-14.80, -9.19]	←	●
Lynch et al 2015 dysmorphic (WASI; 22yrs)	75.66	13.02	48	86.07	11.56	59	16.5%	-0.84 [-1.24, -0.45]		●
May et al 2015 (WASI; 6-7yrs)	88.3	13.14	19	107.2	13.85	186	16.2%	-1.37 [-1.86, -0.88]		●
Quattlebaum & O'Connor 2013 (K-BIT; 6-12yrs)	95.7	14.49	43	106.79	14.11	28	16.2%	-0.76 [-1.26, -0.27]		●
Subtotal (95% CI)			145			315	67.6%	-2.84 [-4.18, -1.51]		
Heterogeneity: Tau² = 1.97; Chi² = 84.38, df = 4 (P < 0.00001); I² = 95%										
Test for overall effect: Z = 4.18 (P < 0.0001)										
Total (95% CI)			194			440	100.0%	-1.98 [-2.82, -1.13]		
Heterogeneity: Tau² = 1.09; Chi² = 86.95, df = 6 (P < 0.00001); I² = 93%										
Test for overall effect: Z = 4.58 (P < 0.00001)										
Test for subgroup differences: Chi² = 8.01, df = 1 (P = 0.005), I² = 87.5%										

-10 -5 0 5 10
pFAS Control

Risk of bias legend
(A) Risk of Bias

Other FASDs and Full-Scale IQ (7 studies)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
4.1.1 Low-Moderate Risk of Bias										
Sullivan et al 2020 FAE (WAIS-R; 13-37yrs)	83.12	14.4	56	109.37	13.81	59	15.7%	-1.85 [-2.29, -1.41]		?
Subtotal (95% CI)			56			59	15.7%	-1.85 [-2.29, -1.41]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 8.25 (P < 0.00001)										
4.1.2 High Risk of Bias										
Astley Olson 2009 ND/AE (WISC-III; 13yrs)	99.2	11.3	21	123.9	6.5	16	14.6%	-2.53 [-3.42, -1.64]		●
Candelaria-Cook et al 2021 ARND (WASI; 8-12yrs)	82.67	3.68	10	109	2.63	26	9.8%	-8.74 [-11.00, -6.48]	←	●
Lynch et al 2015 AE CogAffect (WASI; 22yrs)	73.62	8.37	37	86.07	11.56	59	15.7%	-1.18 [-1.63, -0.74]		●
Malisza et al 2012 ARND (WISC-IV; 10-14yrs)	74.38	11.69	22	107.81	13.08	21	14.8%	-2.65 [-3.49, -1.81]		●
Mattson et al 1997 Non-dys (WPPSI-R/WISC-R; 8yrs)	83.25	8.51	13	109.25	2.99	47	13.7%	-5.46 [-6.65, -4.28]		●
Quattlebaum & O'Connor 2013 ARND (K-BIT; 6-12yrs)	100.7	13.65	44	106.79	14.11	28	15.7%	-0.44 [-0.92, 0.04]		●
Subtotal (95% CI)			147			197	84.3%	-3.21 [-4.69, -1.73]		
Heterogeneity: Tau² = 3.11; Chi² = 115.52, df = 5 (P < 0.00001); I² = 96%										
Test for overall effect: Z = 4.25 (P < 0.0001)										
Total (95% CI)			203			256	100.0%	-2.91 [-4.04, -1.78]		
Heterogeneity: Tau² = 2.05; Chi² = 116.61, df = 6 (P < 0.00001); I² = 95%										
Test for overall effect: Z = 5.06 (P < 0.00001)										
Test for subgroup differences: Chi² = 2.99, df = 1 (P = 0.08), I² = 66.5%										

-10 -5 0 5 10
ARND/Other Control

Risk of bias legend
(A) Risk of Bias

Verbal IQ

FASD and Verbal IQ (4 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
1.2.1 Low-Moderate Risk of Bias										
Kaemingk et al 2003 (WISC-III; 6-16yrs)	64.5	2.46	20	92.1	2.15	20	15.1%	-11.71 [-14.48, -8.94]		?
Subtotal (95% CI)			20			20	15.1%	-11.71 [-14.48, -8.94]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 8.28 (P < 0.00001)										
1.2.2 High Risk of Bias										
Inkelis et al 2020 (WAIS; 13-30yrs)	82.1	12.74	106	107.5	12.5	55	28.9%	-2.00 [-2.39, -1.60]		●
Nayak et al 2012 (MISIC; 6yrs)	78.27	6.71	26	84.94	6.68	27	28.3%	-0.98 [-1.55, -0.41]		●
May et al 2006 (NR; 6-7yrs)	86.65	12.39	20	103.25	9.87	20	27.7%	-1.45 [-2.16, -0.75]		●
Subtotal (95% CI)			152			102	84.9%	-1.50 [-2.16, -0.85]		
Heterogeneity: Tau² = 0.25; Chi² = 8.51, df = 2 (P = 0.01); I² = 77%										
Test for overall effect: Z = 4.52 (P < 0.00001)										
Total (95% CI)			172			122	100.0%	-3.02 [-4.56, -1.48]		
Heterogeneity: Tau² = 2.09; Chi² = 58.68, df = 3 (P < 0.00001); I² = 95%										
Test for overall effect: Z = 3.85 (P = 0.0001)										
Test for subgroup differences: Chi² = 49.31, df = 1 (P < 0.00001), I² = 98.0%										

-20 -10 0 10 20
FASD Control

Risk of bias legend
(A) Risk of Bias

FAS and Verbal IQ (8 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
2.3.1 Low-Moderate Risk of Bias										
Sullivan et al 2020 (WAIS-R; 13-37yrs)	79.74	12.51	57	108.27	11.98	59	12.8%	-2.31 [-2.79, -1.84]		?
Subtotal (95% CI)			57			59	12.8%	-2.31 [-2.79, -1.84]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 9.58 (P < 0.00001)										
2.3.2 High Risk of Bias										
Mattson et al 1997 (WPPSI-R/WISC-R; 8yrs)	75.35	5.51	34	107.35	3.78	47	9.8%	-6.92 [-8.09, -5.74]		●
May et al 2000 (NR; 6-7yrs)	71.7	12.45	46	88.3	9.66	42	12.8%	-1.47 [-1.94, -0.99]		●
May et al 2007 (TROG; 6-7yrs)	10.9	15.72	55	24.1	21.46	133	13.3%	-0.66 [-0.98, -0.34]		●
May et al 2013a (TROG, 6-7yrs)	5.1	7.6	66	13.4	18.2	87	13.3%	-0.57 [-0.89, -0.24]		●
May et al 2015 (WASI; 6-7yrs)	84.3	10.19	7	108.1	14.14	186	11.7%	-1.69 [-2.46, -0.92]		●
May et al 2016 (TROG; 6-7yrs)	20.2	21.5	69	38.4	26.9	206	13.4%	-0.71 [-0.99, -0.43]		●
Viljoen et al 2005 (TROG; 6.5yrs)	68.3	6.5	28	82.5	15.2	123	13.0%	-1.01 [-1.43, -0.58]		●
Subtotal (95% CI)			305			824	87.2%	-1.65 [-2.36, -0.94]		
Heterogeneity: Tau² = 0.83; Chi² = 118.01, df = 6 (P < 0.00001); I² = 95%										
Test for overall effect: Z = 4.56 (P < 0.00001)										
Total (95% CI)			362			883	100.0%	-1.75 [-2.44, -1.05]		
Heterogeneity: Tau² = 0.92; Chi² = 148.34, df = 7 (P < 0.00001); I² = 95%										
Test for overall effect: Z = 4.94 (P < 0.00001)										
Test for subgroup differences: Chi² = 2.35, df = 1 (P = 0.13), I² = 57.4%										

(scale: -10 -5 0 5 10, FAS Control)

Risk of bias legend
(A) Risk of Bias

pFAS and Verbal IQ (5 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
3.2.1 Low-Moderate Risk of Bias										
Aragon et al 2008a FAS/pFAS (WISC-R; 6-7yrs)	90.91	14.93	23	101.27	17.55	56	16.1%	-0.61 [-1.10, -0.11]		?
Subtotal (95% CI)			23			56	16.1%	-0.61 [-1.10, -0.11]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 2.41 (P = 0.02)										
3.2.2 High Risk of Bias										
May et al 2007 (TROG; 6-7yrs)	14	15.94	18	24.1	21.46	133	16.1%	-0.48 [-0.98, 0.01]		●
May et al 2013a (TROG, 6-7yrs)	5.7	10.2	51	13.4	18.2	87	22.8%	-0.49 [-0.84, -0.14]		●
May et al 2015 (WASI; 6-7yrs)	90.2	15.78	19	108.1	14.14	186	16.4%	-1.25 [-1.74, -0.76]		●
May et al 2016 (TROG; 6-7yrs)	26.4	23.2	88	38.4	26.9	206	28.6%	-0.46 [-0.72, -0.21]		●
Subtotal (95% CI)			176			612	83.9%	-0.64 [-0.95, -0.32]		
Heterogeneity: Tau² = 0.07; Chi² = 8.45, df = 3 (P = 0.04); I² = 65%										
Test for overall effect: Z = 3.90 (P < 0.0001)										
Total (95% CI)			199			668	100.0%	-0.62 [-0.88, -0.36]		
Heterogeneity: Tau² = 0.04; Chi² = 8.47, df = 4 (P = 0.08); I² = 53%										
Test for overall effect: Z = 4.72 (P < 0.00001)										
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.93), I² = 0%										

(scale: -10 -5 0 5 10, pFAS Control)

Risk of bias legend
(A) Risk of Bias

Other FASDs and Verbal IQ (4 studies)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
4.2.1 Low-Moderate Risk of Bias										
Sullivan et al 2020 FAE (WAIS-R; 13-37yrs)	82.55	13.47	58	108.27	11.98	59	25.9%	-2.01 [-2.45, -1.56]		?
Subtotal (95% CI)			58			59	25.9%	-2.01 [-2.45, -1.56]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 8.80 (P < 0.00001)										
4.2.2 High Risk of Bias										
Mattson et al 1997 Non-dys (WPPSI-R/WISC-R; 8yrs)	83.65	8.51	13	107.35	3.78	47	21.8%	-4.56 [-5.60, -3.52]		●
May et al 2013a ARND (TROG, 6-7yrs)	5.2	7.5	35	13.4	18.2	87	26.1%	-0.51 [-0.91, -0.11]		●
May et al 2016 ARND (TROG; 6-7yrs)	14.6	17.2	39	38.4	26.9	206	26.3%	-0.93 [-1.28, -0.57]		●
Subtotal (95% CI)			87			340	74.1%	-1.88 [-3.32, -0.44]		
Heterogeneity: Tau² = 1.51; Chi² = 50.59, df = 2 (P < 0.00001); I² = 96%										
Test for overall effect: Z = 2.55 (P = 0.01)										
Total (95% CI)			145			399	100.0%	-1.89 [-3.00, -0.78]		
Heterogeneity: Tau² = 1.18; Chi² = 66.05, df = 3 (P < 0.00001); I² = 95%										
Test for overall effect: Z = 3.34 (P = 0.0008)										
Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.87), I² = 0%										

(scale: -10 -5 0 5 10, ARND/Other Control)

Risk of bias legend
(A) Risk of Bias

Performance IQ

FASD and Performance IQ (4 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
1.3.1 Low-Moderate Risk of Bias									
Kaemingk et al 2003 (WISC-III; 6-16yrs)	73.2	2.46	20	103.4	2.17	20	13.4%	-12.76 [-15.77, -9.75]	?
Subtotal (95% CI)			20			20	13.4%	-12.76 [-15.77, -9.75]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 8.31 (P < 0.00001)									
1.3.2 High Risk of Bias									
Inkelis et al 2020 (WAIS; 13-30yrs)	86.4	15.9	106	107.5	16.15	55	29.6%	-1.31 [-1.67, -0.96]	(red)
May et al 2006 (NR; 6-7yrs)	86.9	13.8	20	101.45	11.06	20	28.3%	-1.14 [-1.81, -0.47]	(red)
Nayak et al 2012 (MISIC; 6yrs)	67.04	6.71	26	77.45	8.28	27	28.7%	-1.36 [-1.96, -0.76]	(red)
Subtotal (95% CI)			152			102	86.6%	-1.29 [-1.57, -1.01]	
Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 2 (P = 0.88); I² = 0%									
Test for overall effect: Z = 9.08 (P < 0.00001)									
Total (95% CI)			172			122	100.0%	-2.81 [-4.30, -1.33]	

Heterogeneity: Tau² = 1.90; Chi² = 55.55, df = 3 (P < 0.00001); I² = 95%
Test for overall effect: Z = 3.72 (P = 0.0002)
Test for subgroup differences: Chi² = 55.29, df = 1 (P < 0.00001), I² = 98.2%

Risk of bias legend
(A) Risk of Bias

FAS and Performance IQ (4 studies)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
2.4.1 Low-Moderate Risk of Bias									
Sullivan et al 2020 (WAIS-R; 13-37yrs)	84.29	15.47	56	108.8	15.44	59	26.0%	-1.58 [-2.00, -1.16]	?
Subtotal (95% CI)			56			59	26.0%	-1.58 [-2.00, -1.16]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 7.35 (P < 0.00001)									
2.4.2 High Risk of Bias									
Mattson et al 1997 (WPPSI-R/WISC-R; 8yrs)	75.35	5.51	34	108.3	3.78	47	23.1%	-7.12 [-8.33, -5.91]	(red)
May et al 2000 (NR; 6-7yrs)	74.1	11.13	46	94.2	13.56	42	25.9%	-1.61 [-2.10, -1.13]	(red)
May et al 2015 (WASI; 6-7yrs)	92.6	9.13	7	104.5	16.84	186	25.0%	-0.71 [-1.47, 0.05]	(red)
Subtotal (95% CI)			87			275	74.0%	-3.09 [-5.93, -0.26]	
Heterogeneity: Tau² = 6.08; Chi² = 82.53, df = 2 (P < 0.00001); I² = 98%									
Test for overall effect: Z = 2.14 (P = 0.03)									
Total (95% CI)			143			334	100.0%	-2.65 [-4.29, -1.01]	

Heterogeneity: Tau² = 2.64; Chi² = 84.12, df = 3 (P < 0.00001); I² = 96%
Test for overall effect: Z = 3.17 (P = 0.002)
Test for subgroup differences: Chi² = 1.08, df = 1 (P = 0.30), I² = 7.4%

Risk of bias legend
(A) Risk of Bias

pFAS and Performance IQ (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008a FAS/pFAS (WISC-R; 6-7yrs)	93.7	16.65	23	111.5	19.36	56	100.0%	-0.95 [-1.45, -0.44]	?
Total (95% CI)			23			56	100.0%	-0.95 [-1.45, -0.44]	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.65 (P = 0.0003)

Risk of bias legend
(A) Risk of Bias

Other FASDs and Performance IQ (2 studies)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
4.3.1 Low-Moderate Risk of Bias										
Sullivan et al 2020 FAE (WAIS-R; 13-37yrs)	87.84	16.18	56	108.8	15.44	59	51.2%	-1.32 [-1.72, -0.91]		?
Subtotal (95% CI)			56			59	51.2%	-1.32 [-1.72, -0.91]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 6.38 (P < 0.00001)										
4.3.2 High Risk of Bias										
Mattson et al 1997 Non-dys (WPPSI-R/WISC-R; 8yrs)	86.1	5.83	13	108.3	4.57	47	48.8%	-4.51 [-5.55, -3.47]		●
Subtotal (95% CI)			13			47	48.8%	-4.51 [-5.55, -3.47]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 8.53 (P < 0.00001)										
Total (95% CI)			69			106	100.0%	-2.88 [-6.01, 0.25]		

Heterogeneity: Tau² = 4.94; Chi² = 31.64, df = 1 (P < 0.00001); I² = 97%
Test for overall effect: Z = 1.80 (P = 0.07)
Test for subgroup differences: Chi² = 31.64, df = 1 (P < 0.00001), I² = 96.8%

Risk of bias legend
(A) Risk of Bias

Non-Verbal IQ

FASD and Non-Verbal IQ (7 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
1.4.1 Low-Moderate Risk of Bias										
Aragon et al 2008b (Leiter-R; 7-17yrs)	84.16	15.2	24	101.96	16.12	32	15.3%	-1.12 [-1.69, -0.54]		?
Subtotal (95% CI)			24			32	15.3%	-1.12 [-1.69, -0.54]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 3.83 (P = 0.0001)										
1.4.2 High Risk of Bias										
Doney et al 2016 (UNIT; 7-9yrs)	85	12.3	21	89.9	8.5	43	15.9%	-0.49 [-1.02, 0.04]		●
Fagerlund et al 2012 (LIPS-R BRIEF; 13yrs)	90.12	16.03	73	108.15	12.69	40	17.7%	-1.20 [-1.62, -0.78]		●
Hansen & Jirikowic 2013 (K-BIT 2; 5-11yrs)	91.56	18.84	11	115.83	11.36	12	10.1%	-1.52 [-2.47, -0.57]		●
Kalberg et al 2013 (Raven; yrs)	13	12.8	61	24.2	19.5	52	18.2%	-0.69 [-1.07, -0.30]		●
Lane et al 2014 (Leiter-R; 7-12yrs)	83.07	10.59	14	114.93	9.92	14	8.2%	-3.01 [-4.14, -1.89]		●
Jirikowic Olson et al 2008a (TONI-2; 5-8yrs)	91.2	15	25	109	14.1	23	14.5%	-1.20 [-1.82, -0.58]		●
Subtotal (95% CI)			205			184	84.7%	-1.19 [-1.68, -0.70]		
Heterogeneity: Tau² = 0.26; Chi² = 20.85, df = 5 (P = 0.0009); I² = 76%										
Test for overall effect: Z = 4.77 (P < 0.00001)										
Total (95% CI)			229			216	100.0%	-1.16 [-1.57, -0.75]		

Heterogeneity: Tau² = 0.20; Chi² = 21.01, df = 6 (P = 0.002); I² = 71%
Test for overall effect: Z = 5.52 (P < 0.00001)
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.84), I² = 0%

Risk of bias legend
(A) Risk of Bias

FAS and Non-Verbal IQ (8 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
2.2.1 Low-Moderate Risk of Bias										
Aragon et al 2008b (Leiter-R; 7-17yrs)	82.4	12.71	10	101.96	16.12	32	6.8%	-1.24 [-2.01, -0.48]		?
Subtotal (95% CI)			10			32	6.8%	-1.24 [-2.01, -0.48]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 3.20 (P = 0.001)										
2.2.2 High Risk of Bias										
Kodituwakku et al 2001 (Ravens; 7-19yrs)	76.6	11.57	10	101.45	12.89	20	5.1%	-1.94 [-2.86, -1.01]		●
Mattson et al 2010 (Leiter-R; 13yrs)	91.6	14.37	41	110	12.09	46	12.6%	-1.38 [-1.85, -0.91]		●
May et al 2013a (Ravens; 6-7yrs)	8.9	7.2	66	22.2	19.1	87	16.8%	-0.87 [-1.21, -0.54]		●
May et al 2006 (Ravens; 6-7yrs)	51.8	19.7	11	73.3	21.7	67	8.4%	-0.99 [-1.65, -0.34]		●
May et al 2007 (Ravens; 6-7yrs)	9.4	9.1	55	21.1	18.9	133	17.3%	-0.70 [-1.02, -0.38]		●
May et al 2016 (Ravens; 6-7yrs)	13	9	69	29.1	22.3	206	18.8%	-0.81 [-1.09, -0.53]		●
Viljoen et al 2005 (Ravens; 6.5yrs)	79.7	8.2	28	84.6	10	123	14.2%	-0.50 [-0.92, -0.09]		●
Subtotal (95% CI)			280			682	93.2%	-0.91 [-1.16, -0.67]		
Heterogeneity: Tau² = 0.06; Chi² = 14.02, df = 6 (P = 0.03); I² = 57%										
Test for overall effect: Z = 7.29 (P < 0.00001)										
Total (95% CI)			290			714	100.0%	-0.93 [-1.16, -0.70]		

Heterogeneity: Tau² = 0.05; Chi² = 14.99, df = 7 (P = 0.04); I² = 53%
Test for overall effect: Z = 7.86 (P < 0.00001)
Test for subgroup differences: Chi² = 0.67, df = 1 (P = 0.41), I² = 0%

Risk of bias legend
(A) Risk of Bias

pFAS and Non-Verbal IQ (7 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
3.4.1 Low-Moderate Risk of Bias									
Aragon et al 2008a FAS/pFAS (Ravens; 6-7yrs)	18.26	4.01	23	21.02	3.99	57	11.1%	-0.68 [-1.18, -0.19]	?
Aragon et al 2008b (Leiter-R; 7-17yrs)	84.07	17.02	14	101.96	16.12	32	6.3%	-1.07 [-1.74, -0.40]	?
Subtotal (95% CI)			37			89	17.5%	-0.82 [-1.22, -0.42]	
Heterogeneity: Tau² = 0.00; Chi² = 0.84, df = 1 (P = 0.36); I² = 0%									
Test for overall effect: Z = 4.04 (P < 0.0001)									
3.4.2 High Risk of Bias									
Kable et al 2021 FAS/pFAS (DAS-II; 3-4yrs)	86.6	24.5	5	92.9	15.6	70	3.5%	-0.38 [-1.29, 0.52]	−
May et al 2013a (Ravens; 6-7yrs)	14.4	12.1	51	22.2	19.1	87	20.8%	-0.46 [-0.81, -0.11]	−
May et al 2007 (Ravens; 6-7yrs)	10.7	9.6	18	21.1	18.9	133	11.1%	-0.57 [-1.07, -0.08]	−
May et al 2015 (WASI; 6-7yrs)	89	11.98	19	104.5	16.84	186	11.8%	-0.94 [-1.42, -0.46]	−
May et al 2016 (Ravens; 6-7yrs)	20.8	15.3	88	29.3	22.3	206	35.4%	-0.41 [-0.67, -0.16]	−
Subtotal (95% CI)			181			682	82.5%	-0.51 [-0.68, -0.34]	
Heterogeneity: Tau² = 0.00; Chi² = 3.81, df = 4 (P = 0.43); I² = 0%									
Test for overall effect: Z = 5.80 (P < 0.00001)									
Total (95% CI)			218			771	100.0%	-0.57 [-0.75, -0.40]	
Heterogeneity: Tau² = 0.01; Chi² = 6.62, df = 6 (P = 0.36); I² = 9%									
Test for overall effect: Z = 6.53 (P < 0.00001)									
Test for subgroup differences: Chi² = 1.97, df = 1 (P = 0.16), I² = 49.3%									

Risk of bias legend
(A) Risk of Bias

Other FASDs and Non-Verbal IQ (4 studies)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kable et al 2021 ARND (DAS-II; 3-4yrs)	85.5	19.1	19	92.9	15.6	70	21.9%	-0.45 [-0.96, 0.06]	−
Kodituwakku et al 2001 NonSyn (Ravens; 7-19yrs)	84.9	8.76	10	101.45	12.89	20	9.2%	-1.37 [-2.22, -0.53]	−
May et al 2013a ARND (Ravens; 6-7yrs)	7.7	4.5	35	22.2	19.1	87	30.8%	-0.88 [-1.29, -0.47]	−
May et al 2016 ARND (Ravens; 6-7yrs)	14.3	11.9	39	29.1	22.3	206	38.2%	-0.70 [-1.05, -0.35]	−
Total (95% CI)			103			383	100.0%	-0.76 [-1.03, -0.49]	
Heterogeneity: Tau² = 0.02; Chi² = 3.90, df = 3 (P = 0.27); I² = 23%									
Test for overall effect: Z = 5.57 (P < 0.00001)									

Risk of bias legend
(A) Risk of Bias

General Ability Percentile

FASD and General Ability Percentile (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020b (DAS-II; 6-7yrs)	35.6	23.8	49	51.1	26	444	53.7%	-0.60 [-0.90, -0.30]	−
May et al 2020c (DAS-II; 6-7yrs)	44.9	25.7	37	59.3	23.7	331	40.5%	-0.60 [-0.94, -0.26]	−
May et al 2021 (DAS-II; 7yrs)	37.4	34.2	5	45.7	27.1	68	5.7%	-0.30 [-1.21, 0.61]	−
Total (95% CI)			91			843	100.0%	-0.58 [-0.80, -0.37]	
Heterogeneity: Tau² = 0.00; Chi² = 0.40, df = 2 (P = 0.82); I² = 0%									
Test for overall effect: Z = 5.24 (P < 0.00001)									

Risk of bias legend
(A) Risk of Bias

FAS and General Ability Percentile (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (NR; 7yrs)	30.5	31.8	5	49	25.9	761	13.2%	-0.71 [-1.59, 0.17]	−
May et al 2020a (DAS-II; 6-7yrs)	44.7	30.8	38	59.7	24.5	273	86.8%	-0.59 [-0.93, -0.25]	−
Total (95% CI)			43			1034	100.0%	-0.61 [-0.93, -0.29]	
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.80); I² = 0%									
Test for overall effect: Z = 3.72 (P = 0.0002)									

Risk of bias legend
(A) Risk of Bias

pFAS and General Ability Percentile (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (NR; 7yrs)	39.7	26	44	49	25.9	761	55.9%	-0.36 [-0.66, -0.05]		
May et al 2020a (DAS-II; 6-7yrs)	44.7	30.8	38	59.7	24.5	273	44.1%	-0.59 [-0.93, -0.25]		
Total (95% CI)			82			1034	100.0%	**-0.46 [-0.69, -0.23]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.98, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 3.97 (P < 0.0001)

Risk of bias legend
(A) Risk of Bias

Other FASDs and General Ability Percentile (1 study)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 ARND (NR; 7yrs)	44	27.8	44	49	25.9	761	100.0%	-0.19 [-0.50, 0.11]		
Total (95% CI)			44			761	100.0%	**-0.19 [-0.50, 0.11]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.24 (P = 0.22)

Risk of bias legend
(A) Risk of Bias

Verbal Ability Percentile

FASD and Verbal Ability Percentile (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020b (DAS-II; 6-7yrs)	42.3	26.1	49	54	27.5	444	51.4%	-0.43 [-0.72, -0.13]		
May et al 2020c (DAS-II; 6-7yrs)	40.4	25.6	37	60.1	25	331	41.2%	-0.78 [-1.13, -0.44]		
May et al 2021 (DAS-II; 7yrs)	36.4	34.2	5	50.6	29.1	68	7.4%	-0.48 [-1.39, 0.43]		
Total (95% CI)			91			843	100.0%	**-0.58 [-0.83, -0.32]**		

Heterogeneity: Tau² = 0.01; Chi² = 2.42, df = 2 (P = 0.30); I² = 18%
Test for overall effect: Z = 4.47 (P < 0.00001)

Risk of bias legend
(A) Risk of Bias

FAS and Verbal Ability Percentile (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (NR; 7yrs)	46.5	27.6	5	48.2	29.5	761	13.0%	-0.06 [-0.94, 0.82]		
May et al 2020a (DAS-II; 6-7yrs)	49.3	33.1	38	58.6	25.7	273	87.0%	-0.35 [-0.69, -0.01]		
Total (95% CI)			43			1034	100.0%	**-0.31 [-0.63, 0.01]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.36, df = 1 (P = 0.55); I² = 0%
Test for overall effect: Z = 1.91 (P = 0.06)

Risk of bias legend
(A) Risk of Bias

pFAS and Verbal Ability Percentile (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (NR; 7yrs)	42	28.5	44	48.2	29.5	761	55.6%	-0.21 [-0.51, 0.09]		
May et al 2020a (DAS-II; 6-7yrs)	49.3	33.1	38	58.6	25.7	273	44.4%	-0.35 [-0.69, -0.01]		
Total (95% CI)			82			1034	100.0%	-0.27 [-0.50, -0.04]		

Heterogeneity: Tau² = 0.00; Chi² = 0.35, df = 1 (P = 0.56); I² = 0%
Test for overall effect: Z = 2.34 (P = 0.02)

Risk of bias legend
(A) Risk of Bias

Other FASDs and Verbal Ability Percentile (1 study)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 ARND (NR; 7yrs)	46.7	32.3	44	48.2	29.5	761	100.0%	-0.05 [-0.35, 0.25]		
Total (95% CI)			44			761	100.0%	-0.05 [-0.35, 0.25]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)

Risk of bias legend
(A) Risk of Bias

Non-Verbal Ability Percentile

FASD and Non-Verbal Ability Percentile (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020b (DAS-II; 6-7yrs)	32.4	27.1	49	44.3	26	444	53.7%	-0.46 [-0.75, -0.16]		
May et al 2020c (DAS-II; 6-7yrs)	42.3	25.5	37	50.3	24.5	331	40.6%	-0.32 [-0.67, 0.02]		
May et al 2021 (DAS-II; 7yrs)	34.4	26.7	5	44.1	27.3	68	5.7%	-0.35 [-1.26, 0.56]		
Total (95% CI)			91			843	100.0%	-0.40 [-0.61, -0.18]		

Heterogeneity: Tau² = 0.00; Chi² = 0.33, df = 2 (P = 0.85); I² = 0%
Test for overall effect: Z = 3.58 (P = 0.0003)

Risk of bias legend
(A) Risk of Bias

FAS and Non-Verbal Ability Percentile (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (NR; 7yrs)	22	14.1	5	46.4	23.4	761	22.6%	-1.04 [-1.92, -0.16]		
May et al 2020a (DAS-II; 6-7yrs)	43.1	28.1	38	56	26.4	273	77.4%	-0.48 [-0.83, -0.14]		
Total (95% CI)			43			1034	100.0%	-0.61 [-1.07, -0.15]		

Heterogeneity: Tau² = 0.04; Chi² = 1.35, df = 1 (P = 0.25); I² = 26%
Test for overall effect: Z = 2.61 (P = 0.009)

Risk of bias legend
(A) Risk of Bias

pFAS and Non-Verbal Ability Percentile (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (NR; 7yrs)	39.6	24.6	44	46.4	23.4	761	55.8%	-0.29 [-0.59, 0.01]		
May et al 2020a (DAS-II; 6-7yrs)	43.1	28.1	38	56	26.4	273	44.2%	-0.48 [-0.83, -0.14]		
Total (95% CI)			82			1034	100.0%	-0.38 [-0.60, -0.15]		

Heterogeneity: Tau² = 0.00; Chi² = 0.69, df = 1 (P = 0.41); I² = 0%
Test for overall effect: Z = 3.24 (P = 0.001)

Risk of bias legend
(A) Risk of Bias

Other FASDs and Non-Verbal Ability Percentile (1 study)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 ARND (NR; 7yrs)	41.3	23	44	46.4	23.4	761	100.0%	-0.22 [-0.52, 0.09]		🔴
Total (95% CI)			44			761	100.0%	-0.22 [-0.52, 0.09]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.40 (P = 0.16)

Risk of bias legend
(A) Risk of Bias

Summary of available outcomes for language

Language			
Study type	**Outcome**	**Data**	**# studies**
Exposure studies	2yrs: Ages & Stages	Frequency/OR	**1 study:** light & moderate
	<3yrs: Bayley Score of Infant Development (BSID)	mean/SD	**3 studies:** 2 moderate, 1 confirmed/unquantifiable
	3-5yrs: Clinical Evaluation of Language Fundamentals – Preschool (CELF-P)	mean/SD	**1 study:** 1 confirmed/unquantifiable
	>5yrs: Peabody Picture Vocabulary Test (PPVT-R)	mean/SD	**1 studies:** 1 confirmed/unquantifiable
	>5yrs, incl: NEPSY Word Generation, NEPSY Phonological Processing	mean/SD	**3 studies:** 3 confirmed/unquantifiable
	>5yrs: Evaluation of Language Fundamentals – 5 (CELF-5)	Frequency/OR	**1 study:** 1 confirmed/unquantifiable
	>5yrs: GFTA-3 speech sound	mean/SD	**1 study:** 1 confirmed/unquantifiable
	>5yrs: Children's Communication Checklist-2 – Parent	mean/SD	**1 study:** 1 confirmed/unquantifiable
Diagnosed studies	>5yrs: Evaluation of Language Fundamentals – 4 (CELF-4)	z-score	**1 study;** 1 FASD
	> 5 yrs: Peabody Picture Vocabulary Test (PPVT-R)	mean/SD	**3 studies:** 3 FASD
	> 5 yrs & 3-16 yrs: NEPSY Incl: Word Generation, Comprehension of Instructions	Mean/SD	**2 studies:** 2 FASD
	>5yrs Incl: Rustioni Test of Language Comprehension (qualitative), Rustioni Test of Language Comprehension (Errors) and Test of Language Competence, GMDS, TOLD-1:3, Oral Narrative (total different words),	Mean/SD	**7 studies:** 4 FASD, 1 FAS, 3 pFAS, 1 ARND/Others
	>5yrs: Connors Comprehensive Behaviour Rating Scale - Parent	T-score	**1 study:** 1 FASD

GRADE ratings for language

№ of studies	Risk of bias	Certainty assessment				№ of patients		Effect		Certainty
		Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	
EXPOSURE STUDIES										
2 years: Ages & Stages (Delayed Language as defined by the Communication Scales of the Ages & Stages)										
Light										
1	serious[a]	not serious	not serious	serious[d,f]	none	554	934	OR **0.97** (0.65 to 1.43)	-	⊕⊕◯◯ Low
Moderate										
1	serious[a]	not serious	not serious	serious[d,f]	none	202	934	OR **0.71** (0.40 to 1.27)	-	⊕⊕◯◯ Low
0 studies for heavy & very heavy										
< 3 yrs: Bayley Scales of Infant Development										
0 studies for light, heavy & very heavy										
Moderate										
2	serious[a]	not serious	not serious	serious[d,f]	none	113	180	-	SMD **0.05 higher** (0.19 lower to 0.29 higher)	⊕⊕◯◯ Low
Confirmed unquantifiable										
1	serious[a]	not serious	serious[c]	very serious[d,e,f]	none	28	45	-	SMD **0.16 higher** (0.31 lower to 0.64 higher)	⊕◯◯◯ Very Low
3 – 5 yrs: Clinical Evaluation of Language Fundamentals – Preschool (CELF-P)										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	serious[e,f]	none	25	26	-	SMD **0.96 lower** (1.54 lower to 0.38 lower)	⊕⊕◯◯ Low
0 studies for light, moderate, heavy & very heavy										
>5 yrs: Peabody Picture Vocabulary Test										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	53	53	-	**SMD 0.13 lower** (0.51 lower lower to 0.25 higher)	⊕◯◯◯ Very low
0 studies for light, moderate, heavy & very heavy										
>5 yrs: NEPSY Language sub-tests										
Confirmed unquantifiable										
3	serious[a]	serious[b]	not serious	serious[e]	none	222	238	-	SMD **0.61 lower** (1.00 lower to 0.21 lower)	⊕◯◯◯ Very low
0 studies for light, moderate, heavy & very heavy										
>5yrs: Evaluation of Language Fundamentals – 5 (CELF-5) (CELF-5 Core Language Index ≤ 1 SD below the mean or 2 or more core subtests ≤ 1 SD below the mean)										
Confirmed unquantifiable										

1	serious[a]	not serious	not serious	very serious[d,e,f]	none	31	29	**OR 1.04** (0.36 to 3.02)	-	⊕◯◯◯ Very Low

>5yrs: GFTA-3 Speech Sound

Confirmed unquantifiable

1	serious[a]	not serious	not serious	very serious[d,e,f]	none	31	29	-	**SMD 0.34 lower** (0.85 lower to 0.17 higher)	⊕◯◯◯ Very Low

>5yrs: Children's Communication Checklist-Second Edition – Parent Report

Confirmed unquantifiable

1	serious[a]	not serious	not serious	serious[e,f]	none	31	29	-	**SMD 0.92 lower** (1.45 lower to 0.38 lower)	⊕⊕◯◯ Low

DIAGNOSED STUDIES

>5 yrs: Evaluation of Language Fundamentals – 4 (CELF-4)

FASD

1	serious[a]	not serious	not serious	serious[e,f]	none	38	29	-	**SMD 3.03 lower** (3.75 lower to 2.32 lower)	⊕⊕◯◯ Low

>5 yrs: Peabody Picture Vocabulary Test - Revised (PPVT-R)

FASD

3	serious[a]	not serious	not serious	serious[e,f]	none	69	60	-	**SMD 1.13 lower** (1.52 lower to 0.75 lower)	⊕⊕◯◯ Low

>5 yrs & 3-16 yrs: NEPSY Language sub-tests

FASD

2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	53	110	-	**SMD 1.5 lower** (3.56 lower to 0.55 higher)	⊕◯◯◯ Very Low

>5 yrs: Higher scores favoured (mean/SD)

FASD

2	serious[a]	not serious	not serious	serious[e,f]	none	108	95	-	**SMD 0.70 lower** (1.06 lower to 0.35 lower)	⊕⊕◯◯ Low

FAS

1	serious[a]	not serious	serious[c]	serious[e,f]	none	34	34	-	**SMD 6.8 lower** (8.07 lower to 5.53 lower)	⊕◯◯◯ Very Low

pFAS

3	serious[a]	serious[b]	not serious	serious[e,f]	none	51	122	-	**SMD 0.95 lower** (1.68 lower to 0.21 lower)	⊕◯◯◯ Very Low

ARND/Others

1	serious[a]	not serious	not serious	serious[e,f]	none	6	5	-	**SMD 5.26 lower** (8.25 lower to 2.27 lower)	⊕⊕◯◯ Low

>5 yrs: Rustioni Test of Language Comprehension (Errors)

pFAS

2	serious[a]	serious[b]	not serious	serious[e,f]	none	45	117	-	**SMD 0.76 higher** (0.13 higher to 1.39 higher)	⊕◯◯◯ Very Low

>5 yrs: Narrative – Total Number of Different Words

FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	69	69	-	**SMD 0.49 lower** (0.83 lower to 0.15 lower)	⊕⊕◯◯ Low

>5 yrs: Connors Comprehensive Behaviour Rating Scale – Parent Report										
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	17	24	-	**SMD 2.22 higher** (1.42 higher to 3.02 higher)	⊕⊕◯◯ Low

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.
Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I^2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CIs for overall estimate crossed the line of no effect; e)) Wide CIs for overall estimate; f) optimal information size criteria not met.

Meta-analyses for language

EXPOSURE STUDIES

Language Measures (<3 years)
Light PAE & Ages and Stages (1 study)

Moderate PAE & Ages and Stages (1 study)

Bayley Scale of Infant Development – Language (<3yrs)
Moderate PAE and BSID (2 studies)

Confirmed PAE-Level Unquantifiable and BSID (1 study)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Donald et al 2016 (6 months; BSID-III)	104.13	15.24	28	101.7	14.49	45	100.0%	0.16 [-0.31, 0.64]		–
Total (95% CI)			28			45	100.0%	0.16 [-0.31, 0.64]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.67 (P = 0.50)

Risk of bias legend
(A) Overall RoB

Language Measures (3 – 5 years)

Confirmed PAE-Level Unquantifiable and Clinical Evaluation of Language Fundamentals – Preschool (1 study)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
McGee et al 2009 (3-5yrs; CELF-P Composite)	92.76	12.84	25	106.27	14.75	26	100.0%	-0.96 [-1.54, -0.38]		–
Total (95% CI)			25			26	100.0%	-0.96 [-1.54, -0.38]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.23 (P = 0.001)

Risk of bias legend
(A) Overall RoB

Note: McGee et al 2009 also reports CELF-P Subdomains

Language: Peabody Picture Vocabulary Test (>5yrs)

Confirmed PAE – Level Unquantifiable and PPVT (1 study)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Vaurio et al 2011 (6-16yrs; PPVT-R)	96.38	18.06	53	98.77	18.36	53	100.0%	-0.13 [-0.51, 0.25]		–
Total (95% CI)			53			53	100.0%	-0.13 [-0.51, 0.25]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.67 (P = 0.50)

Risk of bias legend
(A) Overall RoB

Language: NEPSY Measures (>5yrs)

Confirmed PAE – Level Unquantifiable and NEPSY Language Measures (3 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Doyle et al 2018 (10-16yrs; NEPSY-II; WG)	7.3	3	142	8.3	3.04	160	41.9%	-0.33 [-0.56, -0.10]		–
Glass et al 2015 (8-16yrs; NEPSY-II; PP)	7.3	3.68	49	10.2	2.31	47	31.3%	-0.93 [-1.35, -0.51]		–
Gómez et al 2022 (7-15yrs; NEPSY-PP)	8	3	31	10	3	31	26.8%	-0.66 [-1.17, -0.15]		–
Total (95% CI)			222			238	100.0%	-0.61 [-1.00, -0.21]		

Heterogeneity: Tau² = 0.08; Chi² = 6.52, df = 2 (P = 0.04); I² = 69%
Test for overall effect: Z = 3.01 (P = 0.003)

Risk of bias legend
(A) Overall RoB

Note: WG – word generation and PP – Phonological Processing. Gómez et al 2022 also reports NEPSY comprehension of instructions.

Confirmed PAE – Level Unquantifiable and CELF-5 Language Impairment (1 study)

Study or Subgroup	Confirmed Unquantifiable Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Poth et al 2022 (12-17yrs; CELF-5)	11	31	10	29	100.0%	1.04 [0.36, 3.02]		–
Total (95% CI)		31		29	100.0%	1.04 [0.36, 3.02]		
Total events	11		10					

Heterogeneity: Not applicable
Test for overall effect: Z = 0.08 (P = 0.94)

Risk of bias legend
(A) Overall RoB

Confirmed PAE – Level Unquantifiable and GFTA-3 Speech Sound (1 study)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Poth et al 2022 (12-17yrs; GFTA-3 Speech Sound)	102	3.97	31	103	0.78	29	100.0%	-0.34 [-0.85, 0.17]		🔴
Total (95% CI)			31			29	100.0%	-0.34 [-0.85, 0.17]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 1.30 (P = 0.19)										

Confirmed Unquantifiable   Control

Risk of bias legend
(A) Overall RoB

Confirmed PAE – Level Unquantifiable and Children's Communication Checklist-2 General Language – Parent (1 study)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Poth et al 2022 (12-17yrs; CCC-2 General Language)	79	22.62	31	98.7	19.67	29	100.0%	-0.92 [-1.45, -0.38]		🔴
Total (95% CI)			31			29	100.0%	-0.92 [-1.45, -0.38]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 3.36 (P = 0.0008)										

Confirmed Unquantifiable   Control

Risk of bias legend
(A) Overall RoB

Note: Poth et al 2022 also reports CCC-2 Social Interaction Difference Index and Student Functional Assessment of Verbal Reasoning and Executive Strategies. CELF receptive and expressive.

DIAGNOSED STUDIES

Language Measures (>5yrs)

FASD and Clinical Evaluation of Language Fundamentals – 4 (CELF-4) (1 study)

Study or Subgroup	FASD			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Crawford et al 2020 (8-12yrs; CELF-4)	-2.23	0.89	38	0.36	0.78	29	100.0%	-3.03 [-3.75, -2.32]		🔴
Total (95% CI)			38			29	100.0%	-3.03 [-3.75, -2.32]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 8.29 (P < 0.00001)										

FASD   Control

Risk of bias legend
(A) Overall RoB

Language: Peabody Picture Vocabulary Test (>4yrs)

Peabody Picture Vocabulary Test (PPVT-R) (3 studies)

Study or Subgroup	FASD			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Fryer et al 2012 (9-21yrs; PPVT-R)	84.05	15.53	21	105.1	17.44	7	17.1%	-1.28 [-2.21, -0.35]		🔴
Rasmussen et al 2009b (4-8yrs, PPVT-R)	99.46	9.13	25	108.5	10.26	28	45.7%	-0.91 [-1.48, -0.35]		🔴
Way et al 2012 (5-14.5yrs; PPVT-R)	85.7	20.4	23	106.8	9.2	25	37.2%	-1.33 [-1.96, -0.70]		🔴
Total (95% CI)			69			60	100.0%	-1.13 [-1.52, -0.75]		
Heterogeneity: Tau² = 0.00; Chi² = 1.04, df = 2 (P = 0.59); I² = 0%										
Test for overall effect: Z = 5.77 (P < 0.00001)										

FASD   Control

Risk of bias legend
(A) Overall RoB

Note: Way et al 2012 also reports PPVT-R age equivalent

Language: NEPSY Measures (>3yrs)

NEPSY Language Measures (2 studies)

Study or Subgroup	FASD			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Popova et al 2019 (6-10yrs; NEPSY-II; WG-Letters)	7.53	6.19	21	10	4.98	80	50.7%	-0.47 [-0.95, 0.02]		🔴
Rasmussen et al 2013 (3-16yrs; NEPSY-II; CoI)	7.66	0.9	32	10.85	1.5	30	49.3%	-2.57 [-3.25, -1.88]		🔴
Total (95% CI)			53			110	100.0%	-1.50 [-3.56, 0.55]		
Heterogeneity: Tau² = 2.11; Chi² = 24.15, df = 1 (P < 0.00001); I² = 96%										
Test for overall effect: Z = 1.43 (P = 0.15)										

FASD   Control

Risk of bias legend
(A) Overall RoB

Note: WG-Letter – Word Generation (Letters) and CoI – Comprehension of Instructions. Popova et al 2019 also reports NEPSY WG-Semantic.

Language: Higher Scores Favoured (>5yrs)

FASD and Higher Scores Favoured (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2006 (6-7yrs; Rustioni)	3.2	2.3	11	4.9	1.8	67	30.0%	-0.90 [-1.55, -0.24]		●
Quattlebaum & O'Connor 2013 (6-12yrs; ToLC)	8.13	2.89	97	9.93	2.85	28	70.0%	-0.62 [-1.05, -0.19]		●
Total (95% CI)			108			95	100.0%	-0.70 [-1.06, -0.35]		

Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 1 (P = 0.49); I² = 0%
Test for overall effect: Z = 3.86 (P = 0.0001)

Axis: -4 -2 0 2 4 (FASD Control)

Risk of bias legend
(A) Overall RoB

FAS and Higher Scores Favoured (mean/SD) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Adnams et al 2001 (6-8yrs; GMDS)	74.34	2.04	34	87.63	1.82	34	100.0%	-6.80 [-8.07, -5.53]		●
Total (95% CI)			34			34	100.0%	-6.80 [-8.07, -5.53]		

Heterogeneity: Not applicable
Test for overall effect: Z = 10.50 (P < 0.00001)

Axis: -10 -5 0 5 10 (FAS Control)

Risk of bias legend
(A) Overall RoB

pFAS and Higher Scores Favoured (mean/SD) (3 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008a (6-7yrs; Rustioni; FAS/pFAS)	3.35	2.1	23	4.42	1.87	57	45.0%	-0.55 [-1.04, -0.05]		?
Astley et al 2009b (8-10yrs; TOLD-1:3; FAS/pFAS)	7.5	2.4	6	16	2.5	5	10.5%	-3.18 [-5.22, -1.14]		●
Kodituwakku et al 2006b(6-7yrs;Rustioni;FAS/pFAS)	3.36	2.15	22	4.9	1.74	60	44.5%	-0.82 [-1.33, -0.32]		?
Total (95% CI)			51			122	100.0%	-0.95 [-1.68, -0.21]		

Heterogeneity: Tau² = 0.25; Chi² = 6.18, df = 2 (P = 0.05); I² = 68%
Test for overall effect: Z = 2.53 (P = 0.01)

Axis: -10 -5 0 5 10 (pFAS Contorl)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009 also reports 3x other language subdomains (TLC-1, TLC-2, and TOWK). Kodituwakku et al 2006b had one participant diagnosed with ARND/Other.

ARND/Others and Higher Scores Favoured (mean/SD) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-10yrs; TOLD-1:3; SE/AE)	5.5	1	6	16	2.5	5	100.0%	-5.26 [-8.25, -2.27]		●
Total (95% CI)			6			5	100.0%	-5.26 [-8.25, -2.27]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.45 (P = 0.0006)

Axis: -10 -5 0 5 10 (ARND/Others Control)

Risk of bias legend
(A) Overall RoB

Other Language Measures:

pFAS and Rustioni Test of Language Comprehension (Errors) (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008a (6-7yrs; Rustioni; FAS/pFAS)	7.57	3.1	23	6.37	2.46	57	50.9%	0.45 [-0.04, 0.94]		?
Kodituwakku et al 2006b(6-7yrs;Rustioni;FAS/pFAS)	7.95	2.32	22	5.27	2.48	60	49.1%	1.09 [0.57, 1.61]		?
Total (95% CI)			45			117	100.0%	0.76 [0.13, 1.39]		

Heterogeneity: Tau² = 0.14; Chi² = 3.11, df = 1 (P = 0.08); I² = 68%
Test for overall effect: Z = 2.38 (P = 0.02)

Axis: -4 -2 0 2 4 (Control pFAS)

Risk of bias legend
(A) Overall RoB

FASD and Oral Narrative (total different words) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Thorne et al 2017 (7-12yrs; Narrative)	94.6	26.4	69	107.4	25.26	69	100.0%	-0.49 [-0.83, -0.15]		?
Total (95% CI)			69			69	100.0%	-0.49 [-0.83, -0.15]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.85 (P = 0.004)

Risk of bias legend
(A) Overall RoB

Note: Thorne et al 2017 also reports 9 other oral narrative subdomains.

FASD and Connors Comprehensive Behaviour Rating Scale – Parent (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Way et al 2012 (5-14yrs; CCBRS)	88.2	21.3	17	51.1	11.8	24	100.0%	2.22 [1.42, 3.02]		●
Total (95% CI)			17			24	100.0%	2.22 [1.42, 3.02]		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.43 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Summary of available outcomes for **motor**

Motor			
Study type	**Outcome**	**Data**	**# studies**
Exposure Studies	**<12 months Total Motor Measures**: BSID and BNBAS	mean/SD	**6 studies:** 3 moderate, 2 very heavy, 2 confirmed unquantifiable
	<12 months Total Motor: BSID	OR/Frequency	**1 study:** 1 moderate PAE
	1-4yrs Total Motor: BSID	mean/SD	**2 studies:** 2 moderate, 1 very heavy
	>5yrs Total Motor: MABC Impairment Score	OR/Frequency	**1 study:** 1 light, 1 moderate, 1 heavy
	<1yrs Gross Motor: BSID	OR/Frequency	**1 study:** 1 confirmed/unquantifiable
	1-4yrs Gross Motor: BSID	mean/SD	**1 study:** 1 light, 1 moderate, 1 heavy
	>5yrs Gross Motor: Motor Age Test	mean/SD	**1 study:** 1 confirmed/unquantifiable
	<1yrs Fine Motor: BSID	OR/Frequency	**1 study:** 1 confirmed/unquantifiable
	1-4yrs Fine Motor: Hand Game	mean/SD	**1 study:** 1 heavy
	>5yrs Fine Motor: Motor Age Test	mean/SD	**1 study:** 1 confirmed/unquantifiable
	Fine Motor – >5yrs: GPT completion time	mean/SD	**1 study:** 1 confirmed/unquantifiable
	>5yrs Total Motor – >5yrs, incl: Grooved Pegboard Test (GPT) dominant completion time	z-score	**1 study:** 1 confirmed unquantifiable
	Fine Motor – >5yrs, incl: GPT non-dominant	z-score	**1 study:** 1 confirmed unquantifiable
	>5 Visual Motor Integration: Beery VMI	mean/SD	**2 studies:** 2 confirmed/unquantifiable
Diagnosed Studies	**Total Motor**: GMDS, BOTMP, COMPS and BOT-2	mean/SD	**4 studies:** 3 FASD, 1 FAS
	Total Motor: M-Fun Draw-a-kid	mean/SD	**1 study:** 1 FASD and 1 ARND/other

	Total Motor: % <5th centile M-ABC impairment	Frequency/OR	**1 study:** 1 FASD
	Gross Motor: % delay <2SD BOT-2, % delay <1SD BOT-2	Frequency/OR	**1 study:** 1 FASD
	Fine Motor: BOT-2	mean/SD	**1 study:** 1 FASD, 1 ARND/Others
	Fine Motor: % delay <2SD BOT-2	Frequency/OR	**1 study:** 1 FASD, 1 ARND/Others
	Fine Motor: GPT completion time	mean/SD	**1 study:** 1 FASD
	Fine Motor: GPT-Dominant	z-score	**3 studies:** 1 FASD, 2 FAS, 2 pFAS (incl FAS/pFAS), 1 ARND/Other
	Fine Motor: GPT-Non-Dominant	z-score	**3 studies:** 1 FASD, 2 FAS, 1 pFAS (incl FAS/pFAS), 1 ARND/Other
	Visual Motor Integration: Beery VMI (standard score)	mean/SD	**8 studies:** 4 FASD, 2 FAS, 2 pFAS, 3 ARND/Others
	Visual Motor Integration: Beery VMI (raw score)	mean/SD	**2 studies:** FASD
	Visual Motor Integration: Beery VMI (percentile)	mean/SD	**1 study:** FASD
	Visual Motor Integration: < 5th percentile Beery VMI	Frequency/OR	**1 study:** 1 FASD, 1 ARND/Others

Note. all diagnosed studies > 5 years.

GRADE ratings for motor

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	Certainty
EXPOSURE STUDIES										
< 12 Months Total Motor Measures (BSID)										
Moderate										
3	serious[a]	serious[b]	serious[c]	serious[d,e]	none	245	562	-	**SMD 0.26 lower** (0.6 lower to 0.08 higher)	⊕◯◯◯ Very low
Very Heavy										
2	serious[a]	not serious	not serious	serious[e,f]	none	46	332	-	**SMD 0.83 lower** (1.33 lower to 0.32 lower)	⊕⊕◯◯ Low
Confirmed Unquantifiable										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	40	57	-	**SMD 0.63 lower** (1.53 lower to 0.28 higher)	⊕◯◯◯ Very low
0 studies for light and heavy										
<12 months Total Motor Measures (BSID) (Psychomotor Development Index <85)										
Moderate PAE										
1	serious[a]	not serious	not serious	serious[f]	none	89/243	75/323	**OR 1.91** (1.32 to 2.76)	-	⊕⊕◯◯ Low
1-4 yrs Total Motor Measures (BSID)										
Moderate										
2	serious[a]	serious[b]	not serious	serious[d,e]	none	75	403	-	**SMD 0.46 lower** (1.18 lower to 0.26 higher)	⊕◯◯◯ Very low

Very Heavy										
1	serious[a]	not serious	serious[c]	serious[e,f]	none	24	277	-	**SMD 1.1 lower** (1.53 lower to 0.67 lower)	⊕◯◯◯ Very low
0 studies for light and heavy										
>5yrs Total Motor Measures (<5th percentile on the M-ABC: Total Impairment Score)										
Light										
1	not serious	not serious	not serious	serious[d,f]	none	325	267	**aOR 0.79** (0.35 to 1.78)	-	⊕⊕⊕◯ Moderate
Moderate										
1	not serious	not serious	not serious	serious[d,f]	none	82	325	**aOR 0.18** (0.03 to 1.08)	-	⊕⊕⊕◯ Moderate
Heavy										
1	not serious	not serious	not serious	very serious[d,e,f]	none	11	325	**aOR 2.05** (0.12 to 34.85)	-	⊕⊕◯◯ Low
0 studies for very heavy										
<1yrs Gross Motor (BSID-III) (Cut-offs unclear)										
Confirmed unquantifiable										
1	serious[a]	not serious	serious[c]	serious[e,f]	none	105	52	**OR 0.16** (0.06 to 0.44)	-	⊕◯◯◯ Very Low
1-4 yrs Gross Motor (BSID) (adjusted mean/95% CI)										
Light										
1	serious[a]	not serious	not serious	serious[d]	none	291	514	-	**SMD 0.14 lower** (0.28 lower to 0.01 higher)	⊕⊕◯◯ Low
Moderate										
1	serious[a]	not serious	not serious	serious[d,f]	none	55	514	-	**SMD 0.24 lower** (0.51 lower to 0.04 higher)	⊕⊕◯◯ Low
Heavy										
1	serious[a]	not serious	not serious	serious[d]	none	184	514	-	**SMD 0.02 lower** (0.19 lower to 0.15 higher)	⊕⊕◯◯ Low
0 studies for very heavy										
>5 yrs Gross Motor (Motor Age Test)										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	serious[e,f]	none	21	21	-	**SMD 1.18 higher** (0.52 higher to 1.84 higher)	⊕⊕◯◯ Low
<1yr Fine Motor (BSID-III) (Cut-offs unclear)										
Confirmed Unquantifiable										
1	serious[a]	not serious	serious[c]	serious[e,f]	none	52	104	**OR 0.16** (0.06 to 0.43)	-	⊕◯◯◯ Very Low
1-4 yrs Fine Motor (Hand Game)										
Heavy										

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	n	Relative	Absolute / SMD	Certainty
1	serious[a]	not serious	serious[c]	serious[d,e]	none	101	158	-	**SMD 0.13 lower** (0.38 lower to 0.12 higher)	⊕◯◯◯ Very Low

0 studies for light, moderate or very heavy

>5 yrs Fine Motor (Motor Age Test, GPT completion time mean, GPT completion time z-score dominant and non-dominant respectively)

Confirmed unquantifiable

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	n	Relative	Absolute / SMD	Certainty
1	serious[a]	not serious	not serious	serious[e,f]	none	21	21	-	**SMD 0.97 lower** (1.61 lower to 0.33 lower)	⊕⊕◯◯ Low
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	55	55	-	**SMD 0.33 higher** (0.04 lower to 0.71 higher)	⊕◯◯◯ Very Low
1	serious[a]	not serious	not serious	serious[e,f]	none	38	60	-	**SMD 1.1 higher** (0.67 higher to 1.54 higher)	⊕⊕◯◯ Low
1	serious[a]	not serious	not serious	serious[e,f]	none	38	60	-	**SMD 0.92 higher** (0.49 higher to 1.35 higher)	⊕⊕◯◯ Low

0 studies for light, moderate, heavy or very heavy

>5yrs Visual Motor Integration (Beery)

Confirmed unquantifiable (mean/SD)

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	n	Relative	Absolute / SMD	Certainty
2	serious[a]	serious[b]	not serious	serious[e,f]	none	93	115	-	**SMD 0.57 lower** (1.15 lower to 0)	⊕◯◯◯ Very low

0 studies for light, moderate, or very heavy

DIAGNOSED STUDIES

Total Motor >5yrs (GMDS, BOTMP, COMPS, BOT-2)

FASD

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	n	Relative	Absolute / SMD	Certainty
3	serious[a]	serious[b]	not serious	serious[e,f]	none	76	108	-	**SMD 0.97 lower** (1.49 lower to 0.44 lower)	⊕◯◯◯ Very low

FAS

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	n	Relative	Absolute / SMD	Certainty
1	serious[a]	not serious	serious[c]	serious[e,f]	none	34	34	-	**SMD 2.01 lower** (2.60 lower to 1.42 lower)	⊕◯◯◯ Very low

Total Motor M-Fun Draw-a-kid (m/SD)

FASD

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	n	Relative	Absolute / SMD	Certainty
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	21	43	-	**SMD 0.29 lower** (0.81 lower to 0.24 higher)	⊕◯◯◯ Very low

ARND/Others

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	n	Relative	Absolute / SMD	Certainty
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	39	43	-	**SMD 0.14 lower** (0.58 lower to 0.29 higher)	⊕◯◯◯ Very low

Total Motor (<5th percentile on the M-ABC total impairment score)

FASD

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n	n	Relative	Absolute	Certainty
1	serious[a]	not serious	not serious	serious[e,f]	none	14/30	2/39	**OR 16.19** (3.29 to 79.65)	**415 more per 1000** (from 100 more to 760 more)	⊕⊕◯◯ Low

Gross Motor (<2SD on the BOT-2)

FASD

1	seriousᵃ	not serious	not serious	very seriousᵈ,ᵉ,ᶠ	none	2/21 (9.5%)	1/43 (2.3%)	**OR 4.42** (0.38 to 51.79)	**72 more per 1000** (from 14 fewer to 529 more)	⊕◯◯◯ Very Low

Gross Motor (<1SD on the BOT-2)

FASD

1	seriousᵃ	not serious	not serious	very seriousᵈ,ᵉ,ᶠ	none	5/21 (23.8%)	8/43 (18.6%)	**OR 1.37** (0.39 to 4.84)		⊕◯◯◯ Very Low

Fine Motor (BOT-2)

FASD

1	seriousᵃ	not serious	not serious	seriousᵉ,ᶠ	none	21	43	-	**SMD 0.62 lower** (1.15 lower to 0.08 lower)	⊕⊕◯◯ Low

ARND/Other

1	seriousᵃ	not serious	not serious	very seriousᵈ,ᵉ,ᶠ	none	39	43	-	**SMD 0.15 lower** (0.58 lower to 0.29 higher)	⊕◯◯◯ Very Low

Fine Motor (<3ʳᵈ percentile on the BOT-2)

FASD

1	seriousᵃ	not serious	not serious	very seriousᵈ,ᵉ,ᶠ	none	1/21 (4.8%)	0/43 (0%)	**OR 6.37** (0.25 to 163.10)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very Low

ARND/Other

1					none	0/39 (0%)	0/43 (0%)	**Not estimable**	-	NA

Fine Motor (GPT completion time)

FASD

1	seriousᵃ	not serious	not serious	very seriousᵈ,ᵉ,ᶠ	none	13	20	-	**SMD 0.48 higher** (0.23 lower to 1.18 higher)	⊕◯◯◯ Very Low

Fine Motor (GPT dominant hand completion time z-score)

FASD

1	seriousᵃ	not serious	not serious	very seriousᵈ,ᵉ,ᶠ	none	24	32	-	**SMD 0.02 higher** (0.51 lower to 0.55 higher)	⊕◯◯◯ Very Low

FAS

2	seriousᵃ	seriousᵇ	not serious	very seriousᵈ,ᵉ,ᶠ	none	51	78	-	**SMD 0.69 higher** (0.05 lower to 1.43 higher)	⊕◯◯◯ Very low

pFAS (1x pFAS/FAS)

2	seriousᵃ	not serious	not serious	very seriousᵈ,ᵉ,ᶠ	none	29	58	-	**SMD 0.53 higher** (0.19 lower to 1.25 higher)	⊕⊕◯◯ Low

ARND/Others

1	seriousᵃ	not serious	not serious	seriousᵉ,ᶠ	none	10	26	-	**SMD 1.96 higher** (1.09 higher to 2.84 higher)	⊕⊕◯◯ Low

Fine Motor (GPT non-dominant hand completion time z-score)

FASD

1	seriousᵃ	not serious	not serious	seriousᵉ,ᶠ	none	24	32	-	**SMD 0.55 higher** (0.01 higher to 1.09 higher)	⊕⊕◯◯ Low

FAS

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n1	n2	Relative (95% CI)	Absolute effect	Certainty
2	serious[a]	not serious	not serious	serious[e,f]	none	51	78	-	**SMD 0.73 higher** (0.35 higher to 1.1 higher)	⊕⊕◯◯ Low
pFAS (included FAS)										
1	serious[a]	not serious	not serious	serious[e,f]	none	15	26	-	**SMD 4.72 higher** (3.47 higher to 5.95 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e,f]	none	10	26	-	**SMD 2.13 higher** (1.23 higher to 3.02 higher)	⊕⊕◯◯ Low
Visual Motor Integration (Beery VMI) (standard score)										
FASD										
4	serious[a]	not serious	not serious	serious[e]	none	145	1091	-	**SMD 0.46 lower** (0.73 lower to 0.19 lower)	⊕⊕◯◯ Low
FAS										
2	serious[a]	not serious	not serious	serious[e,f]	none	102	98	-	**SMD 0.64 lower** (0.92 lower to 0.35 lower)	⊕⊕◯◯ Low
pFAS (2x FAS/pFAS)										
2	serious[a]	serious[b]	not serious	serious[e,f]	none	43	51	-	**SMD 1.38 lower** (2.55 lower to 0.21 lower)	⊕◯◯◯ Very low
ARND/Other										
3	serious[a]	not serious	not serious	serious[e,f]	none	121	102	-	**SMD 0.47 lower** (0.78 lower to 0.16 lower)	⊕⊕◯◯ Low
Visual Motor Integration (Beery VMI) (raw score)										
FASD										
2	serious[a]	not serious	not serious	serious[e,f]	none	36	46	-	**SMD 0.97 lower** (1.44 lower to 0.51 lower)	⊕⊕◯◯ Low
Visual Motor Integration (Beery VMI) (percentile)										
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	36	98	-	**SMD 0.54 lower** (0.93 lower to 0.16 lower)	⊕⊕◯◯ Low
Visual Motor Integration (<5th percentile on the Beery VMI)										
FASD										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	14/21 (66.7%)	18/43 (41.9%)	**OR 2.78** (0.93 to 8.27)	248 more per 1000 (from 18 fewer to 438 more)	⊕◯◯◯ Very low
ARND/Other										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	17/39 (43.6%)	18/43 (41.9%)	**OR 1.07** (0.45 to 2.58)	17 more per 1000 (from 174 fewer to 231 more)	⊕◯◯◯ Very low

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.

Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I^2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CIs for overall estimate crossed the line of no effect; e) Wide CIs for overall estimate; f) optimal information size criteria not met.

Meta-analyses for motor

EXPOSURE STUDIES

Total Motor Measures (<12 months) (mean/SD)

Moderate PAE and Total Motor Scores (<12 months) (mean/SD) (3 studies)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bakhireva et al 2018 (5-8 months; BSID-III)	97	11.2	39	96.4	11.9	54	28.9%	0.05 [-0.36, 0.46]		?
Bandoli et al 2019 (6 months; BSID-II)	82.9	9.9	23	89.9	10.4	277	27.9%	-0.67 [-1.10, -0.24]		●
Coles et al 2019 (6 months; BSID-II)	88.07	12.29	183	90.36	10.16	231	43.3%	-0.20 [-0.40, -0.01]		●
Total (95% CI)			245			562	100.0%	-0.26 [-0.60, 0.08]		

Heterogeneity: Tau² = 0.06; Chi² = 5.97, df = 2 (P = 0.05); I² = 66%
Test for overall effect: Z = 1.52 (P = 0.13)

Risk of bias legend
(A) Overall RoB

Very Heavy PAE and Total Motor Scores (<12 months) (mean/SD) (2 studies)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bandoli et al 2019 (6 months; BSID-II)	78.6	12.2	24	89.9	10.4	277	53.5%	-1.07 [-1.49, -0.64]		●
Coles et al 1987 (3 days; BNBAS)	4.4	1.06	22	4.96	0.98	55	46.5%	-0.55 [-1.06, -0.05]		●
Total (95% CI)			46			332	100.0%	-0.83 [-1.33, -0.32]		

Heterogeneity: Tau² = 0.08; Chi² = 2.36, df = 1 (P = 0.12); I² = 58%
Test for overall effect: Z = 3.22 (P = 0.001)

Risk of bias legend
(A) Overall RoB

Note: Coles et al 1987 also reports 'Stopped PAE', used 'Continued PAE'. Bandoli et al 2019 had 5 trajectories, used trajectory C for moderate (60.76g/week) and trajectory E (309.68g/week) for very heavy.

Confirmed PAE Level Unquantifiable and Total Motor Scores (<12 months) (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Donald et al 2016 (6 months; BSID-III)	108.19	13.18	28	111.48	14.49	45	58.1%	-0.23 [-0.71, 0.24]		●
Golden et al 1982 (12 months; BSID-II)	90	20	12	110	12	12	41.9%	-1.17 [-2.05, -0.29]		●
Total (95% CI)			40			57	100.0%	-0.63 [-1.53, 0.28]		

Heterogeneity: Tau² = 0.31; Chi² = 3.40, df = 1 (P = 0.07); I² = 71%
Test for overall effect: Z = 1.35 (P = 0.18)

Risk of bias legend
(A) Overall RoB

Note: Donald et al 2016 also reports Dubowitz Optimality Scores.

Total Motor Measures (<12 months) (Frequency/OR)

Moderate PAE and Total Motor Scores (<12 months) (Frequency/OR) (1 study)

Study or Subgroup	Moderate PAE Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Bandoli et al 2022 (6-12 months; BSID)	89	243	75	323	100.0%	1.91 [1.32, 2.76]		●
Total (95% CI)		243		323	100.0%	1.91 [1.32, 2.76]		
Total events	89		75					

Heterogeneity: Not applicable
Test for overall effect: Z = 3.46 (P = 0.0005)

Risk of bias legend
(A) Overall RoB

Total Motor Measures (1-4 years)

Moderate PAE and Total Motor Scores (1-4 years) (2 studies)

Study or Subgroup	Moderate PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Bandoli et al 2019 (12 months; BSID-II)	90.1	13.7	23	99.6	11	277	48.0%	-0.84 [-1.28, -0.41]		🔴
Halliday et al 2017 (24 months; BSID-III)	109.2	17.4	52	110.8	13.1	126	52.0%	-0.11 [-0.43, 0.21]		🔴
Total (95% CI)			**75**			**403**	**100.0%**	**-0.46 [-1.18, 0.26]**		

Heterogeneity: Tau² = 0.23; Chi² = 7.14, df = 1 (P = 0.008); I² = 86%
Test for overall effect: Z = 1.26 (P = 0.21)

Risk of bias legend
(A) Overall RoB

Very Heavy PAE and Total Motor Scores (1-4 years) (1 study)

Study or Subgroup	Very Heavy PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Bandoli et al 2019 (12 months; BSID-II)	86.5	19.6	24	99.6	11	277	100.0%	-1.10 [-1.53, -0.67]		🔴
Total (95% CI)			**24**			**277**	**100.0%**	**-1.10 [-1.53, -0.67]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.05 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Bandoli et al 2019 had 5 trajectories, used trajectory C for moderate (60.76g/week) and trajectory E (309.68g/week) for very heavy.

Total Motor Measures (>5 years) (Adjusted Odds Ratio)

Light PAE and M-ABC Total Impairment Score (>5 years) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Bay et al 2012 (5yrs; MABC Total Impairment)	-0.237	0.4151	100.0%	0.79 [0.35, 1.78]		🟢
Total (95% CI)			**100.0%**	**0.79 [0.35, 1.78]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.57 (P = 0.57)

Risk of bias legend
(A) Overall RoB

Moderate PAE and M-ABC Total Impairment Score (>5 years) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Bay et al 2012 (5yrs; MABC Total Impairment)	-1.7148	0.9142	100.0%	0.18 [0.03, 1.08]		🟢
Total (95% CI)			**100.0%**	**0.18 [0.03, 1.08]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.88 (P = 0.06)

Risk of bias legend
(A) Overall RoB

Heavy PAE and MABC Total Impairment Score (>5 years) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Bay et al 2012 (5yrs; MABC Total Impairment)	0.7178	1.4455	100.0%	2.05 [0.12, 34.85]		🟢
Total (95% CI)			**100.0%**	**2.05 [0.12, 34.85]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.50 (P = 0.62)

Risk of bias legend
(A) Overall RoB

Gross Motor Measures (<1 years) (OR)
Confirmed Unquantifiable PAE and BSID-III Gross Motor (<1 years) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Hendricks et al 2020 (6 months; BSID-III)	-1.8172	0.5083	100.0%	0.16 [0.06, 0.44]		?
Total (95% CI)			100.0%	**0.16 [0.06, 0.44]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.58 (P = 0.0004)

Risk of bias legend
(A) Overall RoB

Gross Motor Measures (1-4 years) (adjusted mean/95% CI)
Light PAE and Gross Motor Measures (1-4 years) (1 study)

Study or Subgroup	Light PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Hutchinson et al 2019 (0.5-2yrs; BSID-III)	8.98	2.7735	291	9.36	2.7696	514	100.0%	-0.14 [-0.28, 0.01]		?
Total (95% CI)			291			514	100.0%	**-0.14 [-0.28, 0.01]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.87 (P = 0.06)

Risk of bias legend
(A) Overall RoB

Moderate PAE and Gross Motor Measures (1-4 years) (1 study)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Hutchinson et al 2019 (0.5-2yrs; BSID-III)	8.71	2.6633	55	9.36	2.7696	514	100.0%	-0.24 [-0.51, 0.04]		?
Total (95% CI)			55			514	100.0%	**-0.24 [-0.51, 0.04]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.66 (P = 0.10)

Risk of bias legend
(A) Overall RoB

Heavy PAE and Gross Motor Measures (1-4 years) (1 study)

Study or Subgroup	Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Hutchinson et al 2019 (0.5-2yrs; BSID-III)	9.31	2.75	184	9.36	2.7696	514	100.0%	-0.02 [-0.19, 0.15]		?
Total (95% CI)			184			514	100.0%	**-0.02 [-0.19, 0.15]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.21 (P = 0.83)

Risk of bias legend
(A) Overall RoB

Gross Motor Measures (>5 years)
Confirmed PAE-Level Unquantifiable and Gross Motor Scores (>5 years) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kyllerman et al 1985 (5-6yrs; Motor Age Test)	103	10	21	87	16	21	100.0%	1.18 [0.52, 1.84]		?
Total (95% CI)			21			21	100.0%	**1.18 [0.52, 1.84]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.49 (P = 0.0005)

Risk of bias legend
(A) Overall RoB

Note: Kyllerman et al 1985 also reports other coordination measures

Fine Motor Measures (<1 years)

Confirmed Unquantifiable and Fine Motor Measures (<1 years) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Hendricks et al 2020 (6 months; BSID-III)	-1.8326	0.5004	100.0%	0.16 [0.06, 0.43]		?
Total (95% CI)			100.0%	**0.16 [0.06, 0.43]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.66 (P = 0.0002)

Confirmed Unquantifiable Control

Risk of bias legend
(A) Overall RoB

Fine Motor Measures (1-4 years)

Heavy PAE and Fine Motor Measures (1-4 years) (1 study)

Study or Subgroup	Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 2021 (4yrs; Hand Game)	12.8	3.63	101	13.23	3.13	158	100.0%	-0.13 [-0.38, 0.12]		−
Total (95% CI)			101			158	100.0%	**-0.13 [-0.38, 0.12]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.01 (P = 0.31)

Heavy PAE Control

Risk of bias legend
(A) Overall RoB

Fine Motor Measures (>5 years)

Confirmed PAE-Level Unquantifiable and Motor Age Test (>5 years) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kyllerman et al 1985 (5-6yrs; Motor Age Test)	91	14	21	103	10	21	100.0%	-0.97 [-1.61, -0.33]		?
Total (95% CI)			21			21	100.0%	**-0.97 [-1.61, -0.33]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.95 (P = 0.003)

Confirmed Unquantifiable Control

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and Grooved Pegboard Test (>5 years) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Vaurio et al 2011 (6-16yrs; GPT)	101.45	10.96	55	97.7	11.45	55	100.0%	0.33 [-0.04, 0.71]		−
Total (95% CI)			55			55	100.0%	**0.33 [-0.04, 0.71]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.73 (P = 0.08)

Control Confirmed Unquantifiable

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and Grooved Pegboard Test Dominant Hand (>5 years) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2010 (7-21yrs; GPT)	0.62	1.14	38	-0.38	0.71	60	100.0%	1.10 [0.67, 1.54]		−
Total (95% CI)			38			60	100.0%	**1.10 [0.67, 1.54]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.96 (P < 0.00001)

Control Confirmed Unquantifiable

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and Grooved Pegboard Test Non-Dominant Hand (>5 years) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2010 (7-21yrs; GPT)	0.93	1.8	38	-0.22	0.69	60	100.0%	0.92 [0.49, 1.35]		−
Total (95% CI)			38			60	100.0%	**0.92 [0.49, 1.35]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.22 (P < 0.0001)

Control Confirmed Unquantifiable

Risk of bias legend
(A) Overall RoB

Visual Motor Integration (> 5yrs)

Confirmed PAE-Level Unquantifiable and VMI Score (>5 years) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2010 (7-21yrs; Beery VMI)	79.37	11.97	38	91	13.81	60	48.5%	-0.88 [-1.30, -0.45]		
Vaurio et al 2011 (6-16yrs; Beery VMI)	85.85	12.9	55	89.6	12.93	55	51.5%	-0.29 [-0.66, 0.09]		
Total (95% CI)			**93**			**115**	**100.0%**	**-0.57 [-1.15, 0.00]**		

Heterogeneity: Tau² = 0.13; Chi² = 4.16, df = 1 (P = 0.04); I² = 76%
Test for overall effect: Z = 1.95 (P = 0.05)

Risk of bias legend
(A) Overall RoB

DIAGNOSED STUDIES

Total Motor Measures: Higher is Better

FASD and Total Motor Measures (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Jirikowic et al 2008a (5-8yrs; BOTMP)	49.1	14	25	57.7	9.4	26	32.5%	-0.71 [-1.28, -0.15]		
Kooistra et al 2009 (8-9yrs; COMPS)	0.3	1.4	30	2.1	1	39	33.6%	-1.50 [-2.04, -0.95]		
Lucas et al 2016a (7-9yrs; BOT-2 Motor)	43	8	21	48.3	7.5	43	33.9%	-0.68 [-1.22, -0.15]		
Total (95% CI)			**76**			**108**	**100.0%**	**-0.97 [-1.49, -0.44]**		

Heterogeneity: Tau² = 0.14; Chi² = 5.52, df = 2 (P = 0.06); I² = 64%
Test for overall effect: Z = 3.60 (P = 0.0003)

Risk of bias legend
(A) Overall RoB

Note: Kooistra et al 2009 also reports M-ABC Ball Skills (m/SD). Jirikowic et al 2008a also reports BOTMP sensori-motor.

FAS and Total Motor Measures (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Adnams et al 2001 (6-8yrs; GMDS Motor)	102.13	1.45	34	104.93	1.3	34	100.0%	-2.01 [-2.60, -1.42]		
Total (95% CI)			**34**			**34**	**100.0%**	**-2.01 [-2.60, -1.42]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 6.69 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Adnams et al 2001 also reports GMDS eye-hand score (m/SD). Lucas et al 2016a also reports BOT-2 coordination and balance measures.

Total Motor: M-FUN Draw-a-kid

FASD and Total Motor: M-FUN Draw-a-kid (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Doney et al 2017a (7-10yrs; M-FUN)	12.2	3.1	21	13	2.6	43	100.0%	-0.29 [-0.81, 0.24]		
Total (95% CI)			**21**			**43**	**100.0%**	**-0.29 [-0.81, 0.24]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.07 (P = 0.29)

Risk of bias legend
(A) Overall RoB

ARND/Others and Total Motor: M-FUN Draw-a-kid (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Doney et al 2017a (7-10yrs; M-FUN; non-syndromal)	12.6	2.9	39	13	2.6	43	100.0%	-0.14 [-0.58, 0.29]		
Total (95% CI)			**39**			**43**	**100.0%**	**-0.14 [-0.58, 0.29]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.65 (P = 0.51)

Risk of bias legend
(A) Overall RoB

Note: Doney et al 2017a was included due to its relevant measure but could not be included in the total motor: higher is better analysis due to cohort overlap with Lucas et al 2016a.

Total Motor <5th percentile (M-ABC)

FASD and Frequency of Total Motor (M-ABC) <5th Percentile (1 study)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Kooistra et al 2009 (8-9yrs; M-ABC Impairment)	14	30	2	39	100.0%	16.19 [3.29, 79.65]		−
Total (95% CI)		30		39	100.0%	16.19 [3.29, 79.65]		
Total events	14		2					
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.42 (P = 0.0006)								

Control FASD

Risk of bias legend
(A) Overall RoB

Note: Kooistra et al 2009 also reports M-ABC Impairment Score centile (m/SD)

Gross Motor <2SD (BOT-2)

FASD and Frequency of Gross Motor <2SD (BOT-2) (1 study)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Lucas et al 2016b (7-9yrs; BOT-2)	2	21	1	43	100.0%	4.42 [0.38, 51.79]		−
Total (95% CI)		21		43	100.0%	4.42 [0.38, 51.79]		
Total events	2		1					
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.18 (P = 0.24)								

Control FASD

Risk of bias legend
(A) Overall RoB

Gross Motor <1SD (BOT-2)

FASD and Frequency of Gross Motor <1SD (BOT-2) (1 study)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Lucas et al 2016b (7-9yrs; BOT-2)	5	21	8	43	100.0%	1.37 [0.39, 4.84]		−
Total (95% CI)		21		43	100.0%	1.37 [0.39, 4.84]		
Total events	5		8					
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.48 (P = 0.63)								

Control FASD

Risk of bias legend
(A) Overall RoB

Fine Motor (BOT-2)

FASD and Fine Motor Score (BOT-2) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Doney et al 2017b (7-9yrs; BOTS-2)	45.2	7.7	21	49.8	7.2	43	100.0%	-0.62 [-1.15, -0.08]		−
Total (95% CI)			21			43	100.0%	-0.62 [-1.15, -0.08]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 2.27 (P = 0.02)										

FASD Control

Risk of bias legend
(A) Overall RoB

ARND/Others and Fine Motor Score (BOT-2) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Doney et al 2017b (7-9yrs; BOTS-2; non-syndromal)	48.8	6.2	39	49.8	7.2	43	100.0%	-0.15 [-0.58, 0.29]		−
Total (95% CI)			39			43	100.0%	-0.15 [-0.58, 0.29]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.66 (P = 0.51)										

ARND/Others Control

Risk of bias legend
(A) Overall RoB

Fine Motor <2SD (BOT-2)

FASD and Frequency of Fine Motor <2SD (BOT-2) (1 study)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Doney et al 2017b (7-9yrs; BOTS-2)	1	21	0	43	100.0%	6.37 [0.25, 163.10]		⊖
Total (95% CI)		21		43	100.0%	6.37 [0.25, 163.10]		
Total events	1		0					
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.12 (P = 0.26)								

Risk of bias legend
(A) Overall RoB

ARND/Others and Frequency of Fine Motor <2SD (BOT-2) (1 study)

Study or Subgroup	ARND/Others Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Doney et al 2017b (7-9yrs; BOTS-2; non-syndromal)	0	39	0	43		Not estimable		⊖
Total (95% CI)		39		43		Not estimable		
Total events	0		0					
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								

Risk of bias legend
(A) Overall RoB

Note: Doney et al 2017b also reported BOT-2 subdomains.

Fine Motor (GPT completion time)

FASD and Fine Motor (Grooved Pegboard Test Completion Time) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Pinner et al 2020 (12-21yrs; GPT)	70.18	10.29	13	65.06	10.65	20	100.0%	0.48 [-0.23, 1.18]		⊖
Total (95% CI)			13			20	100.0%	0.48 [-0.23, 1.18]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 1.31 (P = 0.19)										

Risk of bias legend
(A) Overall RoB

Fine Motor (GPT dominant hand completion time)

FASD and Fine Motor (Grooved Pegboard Test – DH Completion Time) (z-score) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008b (7-17yrs; GPT)	0.38	12	24	0.15	10.7	32	100.0%	0.02 [-0.51, 0.55]		?
Total (95% CI)			24			32	100.0%	0.02 [-0.51, 0.55]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.07 (P = 0.94)										

Risk of bias legend
(A) Overall RoB

FAS and Fine Motor (Grooved Pegboard Test – DH Completion Time) (z-score) (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008b (7-17yrs; GPT)	0.43	1.11	10	0.15	1.07	32	43.1%	0.25 [-0.46, 0.97]		?
Mattson et al 2010 (7-21yrs; GPT)	0.56	1.12	41	-0.42	0.78	46	56.9%	1.02 [0.57, 1.47]		⊖
Total (95% CI)			51			78	100.0%	0.69 [-0.05, 1.43]		
Heterogeneity: Tau² = 0.20; Chi² = 3.15, df = 1 (P = 0.08); I² = 68%										
Test for overall effect: Z = 1.82 (P = 0.07)										

Risk of bias legend
(A) Overall RoB

pFAS and Fine Motor (Grooved Pegboard Test – DH Completion Time) (z-score) (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008b (7-17yrs; GPT)	0.35	1.3	14	0.15	1.07	32	51.2%	0.17 [-0.46, 0.80]		?
Candelaria-Cook et al 2021 (8-12yrs; GPT;FAS/pFAS)	0.69	1.3555	15	-0.17	0.5609	26	48.8%	0.91 [0.24, 1.58]		–
Total (95% CI)			29			58	100.0%	0.53 [-0.19, 1.25]		

Heterogeneity: Tau² = 0.16; Chi² = 2.48, df = 1 (P = 0.12); I² = 60%
Test for overall effect: Z = 1.44 (P = 0.15)

Risk of bias legend
(A) Overall RoB

ARND/Others and Fine Motor (Grooved Pegboard Test – DH Completion Time) (z-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Candelaria-Cook et al 2021 (8-12yrs; GPT; ARND)	3.02	2.9409	10	-0.17	0.5609	26	100.0%	1.96 [1.09, 2.84]		–
Total (95% CI)			10			26	100.0%	1.96 [1.09, 2.84]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.41 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

Fine Motor (GPT non-dominant hand completion time z-score)

FASD and Fine Motor (Grooved Pegboard Test – non-DH Completion Time) (z-score) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008b (7-17yrs; GPT)	0.52	0.77	24	0.07	0.84	32	100.0%	0.55 [0.01, 1.09]		?
Total (95% CI)			24			32	100.0%	0.55 [0.01, 1.09]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.99 (P = 0.05)

Risk of bias legend
(A) Overall RoB

FAS and Fine Motor (Grooved Pegboard Test – non-DH Completion Time) (z-score) (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008b (7-17yrs; GPT)	0.54	0.64	10	0.07	0.84	32	26.9%	0.58 [-0.14, 1.30]		?
Mattson et al 2010 (7-21yrs; GPT)	0.58	1.38	41	-0.28	0.74	46	73.1%	0.78 [0.35, 1.22]		–
Total (95% CI)			51			78	100.0%	0.73 [0.35, 1.10]		

Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 1 (P = 0.63); I² = 0%
Test for overall effect: Z = 3.81 (P = 0.0001)

Risk of bias legend
(A) Overall RoB

pFAS and Fine Motor (Grooved Pegboard Test – non-DH Completion Time) (z-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Candelaria-Cook et al 2021 (8-12yrs; GPT;FAS/pFAS)	1.06	0.46	15	-0.31	0.09	26	100.0%	4.72 [3.47, 5.96]		–
Total (95% CI)			15			26	100.0%	4.72 [3.47, 5.96]		

Heterogeneity: Not applicable
Test for overall effect: Z = 7.41 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and Fine Motor (Grooved Pegboard Test – non-DH Completion Time) (z-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Candelaria-Cook et al 2021 (8-12yrs; GPT; ARND)	2.85	2.7196	10	-0.31	0.4589	26	100.0%	2.13 [1.23, 3.02]		–
Total (95% CI)			10			26	100.0%	2.13 [1.23, 3.02]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.65 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Visual Motor Integration (Beery) (Standard Scores)

FASD and Beery VMI (Standard Score) (4 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Doney et al 2016 (7-9yrs; Beery VMI)	84.2	8.3	21	89.6	10.4	43	16.5%	-0.55 [-1.08, -0.02]	🔴
May et al 2020a (6-7yrs; Beery VMI)	91.8	13.2	38	97.9	7.1	273	26.6%	-0.75 [-1.10, -0.41]	🔴
May et al 2020b (6-7yrs; Beery VMI)	93.6	7.6	49	95.4	10.6	444	30.1%	-0.17 [-0.47, 0.12]	🔴
May et al 2020c (6-7yrs; Beery VMI)	93.9	8.6	37	97.2	7.4	331	26.8%	-0.44 [-0.78, -0.10]	🔴
Total (95% CI)			**145**			**1091**	**100.0%**	**-0.46 [-0.73, -0.19]**	

Heterogeneity: Tau² = 0.04; Chi² = 6.46, df = 3 (P = 0.09); I² = 54%
Test for overall effect: Z = 3.37 (P = 0.0007)

Risk of bias legend
(A) Overall RoB

FAS and Beery VMI (Standard Score) (2 studies)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kalberg et al 2013 (6-7yrs; Beery VMI)	68	12.4	61	79.3	19.3	52	55.9%	-0.70 [-1.09, -0.32]	🔴
Mattson et al 2010 (7-21yrs; Beery VMI)	83.27	14.5141	41	91.39	14.57	46	44.1%	-0.55 [-0.98, -0.12]	🔴
Total (95% CI)			**102**			**98**	**100.0%**	**-0.64 [-0.92, -0.35]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 4.38 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

pFAS and Beery VMI (Standard Score) (2 studies)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; Beery VMI; FAS/pFAS)	76.2	12.7	18	102.7	12.9	16	46.1%	-2.02 [-2.87, -1.18]	🔴
Coles et al 1997 (7-8yrs; Beery VMI; FAS/pFAS)	87.84	13.9	25	97.82	10.31	35	53.9%	-0.83 [-1.36, -0.29]	🔴
Total (95% CI)			**43**			**51**	**100.0%**	**-1.38 [-2.55, -0.21]**	

Heterogeneity: Tau² = 0.59; Chi² = 5.49, df = 1 (P = 0.02); I² = 82%
Test for overall effect: Z = 2.31 (P = 0.02)

Risk of bias legend
(A) Overall RoB

ARND/Others and Beery VMI (Standard Score) (3 studies)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; Beery VMI; SE/AE)	90.9	11.8	20	102.7	12.9	16	17.6%	-0.94 [-1.63, -0.24]	🔴
Coles et al 1997 (7-8yrs; Beery VMI; non-syndromal)	92.79	11.37	62	97.82	10.4	43	44.2%	-0.45 [-0.85, -0.06]	🔴
Doney et al 2016 (7-9yrs; Beery VMI)	87	8.3	39	89.6	10.4	43	38.2%	-0.27 [-0.71, 0.16]	🔴
Total (95% CI)			**121**			**102**	**100.0%**	**-0.47 [-0.78, -0.16]**	

Heterogeneity: Tau² = 0.02; Chi² = 2.53, df = 2 (P = 0.28); I² = 21%
Test for overall effect: Z = 2.97 (P = 0.003)

Risk of bias legend
(A) Overall RoB

Note: Doney et al 2016 also reports Beery VMI motor coordination and error type (m/SD)

Visual Motor Integration (Beery) (Raw Scores)

FASD and Beery VMI (raw) (2 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Colby et al 2012 (7-13yrs; Beery VMI)	21.26	3.97	19	24.72	3.61	27	56.5%	-0.90 [-1.52, -0.29]	🔴
Sowell et al 2008 (7-15yrs; Beery VMI)	19.82	3.73	17	24	3.97	19	43.5%	-1.06 [-1.76, -0.36]	🔴
Total (95% CI)			**36**			**46**	**100.0%**	**-0.97 [-1.44, -0.51]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.11, df = 1 (P = 0.75); I² = 0%
Test for overall effect: Z = 4.10 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

Visual Motor Integration (Beery) (Percentile)

FASD and Beery VMI (raw) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2014 (6-7yrs; Beery VMI)	34.1	15.7	36	42.3	14.7	98	100.0%	-0.54 [-0.93, -0.16]	■	⊖
Total (95% CI)			36			98	100.0%	**-0.54 [-0.93, -0.16]**	◆	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.75 (P = 0.006)

(scale: -4 -2 0 2 4, FASD Control)

Risk of bias legend
(A) Overall RoB

Visual Motor Integration <5th percentile (Beery)

FASD and Beery VMI <5th percentile (1 study)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Doney et al 2016 (7-9yrs; Beery VMI)	14	21	18	43	100.0%	2.78 [0.93, 8.27]	■	⊖
Total (95% CI)		21		43	100.0%	**2.78 [0.93, 8.27]**	◆	
Total events	14		18					

Heterogeneity: Not applicable
Test for overall effect: Z = 1.84 (P = 0.07)

(scale: 0.01 0.1 1 10 100, Control FASD)

Risk of bias legend
(A) Overall RoB

ARND/Others and Beery VMI <5th percentile (1 study)

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Doney et al 2016 (7-9yrs; Beery VMI)	17	39	18	43	100.0%	1.07 [0.45, 2.58]	■	⊖
Total (95% CI)		39		43	100.0%	**1.07 [0.45, 2.58]**	◆	
Total events	17		18					

Heterogeneity: Not applicable
Test for overall effect: Z = 0.16 (P = 0.87)

(scale: 0.1 0.2 0.5 1 2 5 10, Control ARND/Others)

Risk of bias legend
(A) Overall RoB

Summary of available outcomes for memory

Memory			
Study type	**Measures**	**Data**	**# studies**
Exposure Studies	**Verbal 'Short Delay'**: RAVLT, NEPSY Word list interference	mean/SD	**3 studies**: 1 light, 1 moderate, 1 confirmed unquantifiable, 2 Any PAE
	Verbal 'Short Delay': CVLT-C	z-score	**1 study**: 1 confirmed/unquantifiable
	Verbal 'Long Delay': CVLT-C, RAVLT	mean/SD	**4 studies**: 1 light, 1 moderate, 1 confirmed unquantifiable, 2 Any PAE
	Verbal 'Long Delay': CVLT-C	z-score	**1 studies**: 1 confirmed unquantifiable
	Visual/Verbal 'Short Delay': K-ABC	mean/SD	**1 study**: 1 very heavy
	Visual/Verbal 'Long Delay'	N/A	
	Non-Verbal 'Short Delay': RCFT	mean/SD	**1 study**: 1 confirmed unquantifiable
	Non-Verbal Long Delay': RCFT	mean/SD	**1 study**: 1 confirmed unquantifiable
Diagnosed Studies	**Verbal– 'Short Delay'**: WRAML-Verbal Memory Index, Story memory, CMS-Stories, CVLT-C, VSRT-mean	mean/SD	**7 studies**: 4 FASD, 1 FAS, 1 pFAS, 2 ARND/Others
	Verbal– 'Short Delay': CVLT-C	T-score	**1 study**: 1 pFAS, 1 ARND/Others
	Verbal– 'Long Delay': CVLT-C, VSRT, CMS-stories	mean/SD	**6 studies**: 3 FASD, 1 FAS, 1 FAS/pFAS, 2 ARND/Others
	Verbal– 'Long Delay': CVLT-C	OR/Frequency	**1 study**: 1 FASD
	Verbal 'Long Delay': CVLT-C	z-score	**1 studies**: 1 FASD

	Visual/Verbal – 'Short Delay': K-ABC, Word Stem Completion Target, NEPSY-II memory for names, Memory of 16 objects	mean/SD	**5 studies:** 5 FASD, 1 ARND/Others
	Visual/Verbal– 'Short Delay': NEPSY-II memory for names	OR/Frequency	**1 study:** 1 FASD
	Visual/Verbal– 'Long Delay': NEPSY-II memory for names	OR/Frequency	**1 study:** 1 FASD
	Visual/Verbal– 'Long Delay': Memory of 16 objects, NEPSY-II Memory for Names	mean/SD	**2 study:** 2 FASD
	Non-Verbal– 'Short Delay': WRAML-Visual memory index, NVSRT, TOMAL	mean/SD	**3 studies:** 1 FASD, 1 FAS, 1 ARND/Other
	Non-Verbal– 'Short Delay': RCFT	T-score	**3 studies:** 2 FASD, 1 pFAS, 1 ARND/Others
	Non-Verbal– 'Short Delay': CANTAB Pattern Recognition	OR/Frequency	**1 study:** 1 FASD
	Non-Verbal– 'Long Delay': NVRST, TOMAL	mean/SD	**2 studies:** 1 FAS, 1 ARND/Others
	Non-Verbal– 'Long Delay': RCFT	T-score	**3 studies:** 2 FASD, 1 pFAS, 1 ARND/Others
	Non-Verbal– 'Long Delay': BFLT	OR/Frequency	**1 study:** 1 FASD
	Self-Report: Everyday Memory Questionnaire	mean/SD	**1 studies**: 1 FASD

GRADE ratings for **memory**

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	Certainty
Certainty assessment						**№ of patients**		**Effect**		**Certainty**
EXPOSURE STUDIES										
Verbal 'short delay' (RAVLT, NEPSY Word list interference)										
Light										
1	serious[a]	not serious	not serious	serious[d]	none	93	6669	-	**SMD 0.00** (0.2 lower to 0.2 higher)	⊕⊕◯◯ Low
Moderate										
1	serious[a]	not serious	not serious	not serious	none	755	6669	-	**SMD 0.10** (0.03 higher to 0.18 higher)	⊕⊕⊕◯ Moderate
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	serious[e,f]	none	49	47	-	**SMD 1.12 lower** (1.55 lower to 0.69 lower)	⊕⊕◯◯ Low
Any level										
2	serious[a]	not serious	not serious	not serious	none	2546	7229	-	**SMD 0.14** (0.09 higher to 0.18 higher)	⊕⊕⊕◯ Moderate
0 studies for heavy or very heavy										
Verbal 'short delay' z-score (CVLT-C)										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	serious[e,f]	none	81	81	-	**SMD 0.8 lower** (1.12 lower to 0.48 lower)	⊕⊕◯◯ Low
0 studies for light, moderate, heavy & very heavy										
Verbal 'long delay' (CVLT-C, RAVLT)										
Light										

1	serious[a]	not serious	not serious	not serious	none	755	6669	-	**SMD 0.10** (0.03 higher to 0.18 higher)	⊕⊕⊕◯ Moderate

Moderate

1	serious[a]	not serious	not serious	not serious	none	755	6669	-	**SMD 0.16** (0.08 higher to 0.23 higher)	⊕⊕⊕◯ Moderate

Confirmed unquantifiable

1	serious[a]	not serious	not serious	serious[e,f]	none	81	81	-	**SMD 1.75 lower** (2.12 lower to 1.39 lower)	⊕◯◯◯ Very Low

Any level

2	serious[a]	not serious	not serious	not serious	none	2546	7529	-	**SMD 0.16 higher** (0.11 higher to 0.20 higher)	⊕⊕⊕◯ Moderate

0 studies for heavy or very heavy

Verbal 'long delay' z-score (CVLT-C)

Confirmed unquantifiable

1	serious[a]	not serious	not serious	serious[e,f]	none	81	81	-	**SMD 0.96 lower** (1.29 lower to 0.64 lower)	⊕⊕◯◯ Low

0 studies for light, moderate, heavy & very heavy

Visual/Verbal 'short delay' (K-ABC)

Heavy

1	serious[a]	not serious	not serious	serious[e,f]	none	25	21	-	**SMD 0.61 lower** (1.21 lower to 0.02 lower)	⊕⊕◯◯ Low

0 studies for light, moderate, very heavy & unquantified

Non-verbal 'short delay' (RCFT)

Confirmed unquantifiable

1	serious[a]	not serious	not serious	serious[e,f]	none	28	28	-	**SMD 0.67 lower** (1.21 lower to 0.13 lower)	⊕⊕◯◯ Low

0 studies for light, moderate, heavy & very heavy

Non-verbal 'long delay' (RCFT)

Confirmed unquantifiable

1	serious[a]	not serious	not serious	serious[e,f]	none	28	28	-	**SMD 0.86 lower** (1.41 lower to 0.31 lower)	⊕⊕◯◯ Low

0 studies for light, moderate, heavy & very heavy

DIAGNOSED STUDIES

Verbal 'short delay' (WRAML-story memory, CMS-stories, Story Memory

FASD

3	serious[a]	serious[b]	not serious	serious[e,f]	none	100	90	-	**SMD 1.10 lower** (2.13 lower to 0.07 lower)	⊕◯◯◯ Very Low

Verbal 'short delay' (CVLT-C Story Memory)

FASD

1	serious[a]	not serious	not serious	serious[e,f]	none	19	18	-	**SMD 0.95 lower** (1.63 lower to 0.26 lower)	⊕⊕◯◯ Low

Verbal 'short delay' (WRAML-Verbal Memory Index, Story Memory, CMS-Stories, CVLT-C, VSRT-mean)

FASD										
4	serious[a]	serious[b]	not serious	serious[e,f]	none	124	121	-	**SMD 1.24 lower** (2.11 lower to 0.38 lower)	⊕◯◯◯ Very Low
FAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	45	49	-	**SMD 0.78 lower** (1.2 lower to 0.36 lower)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	36	60	-	**SMD 0.92 lower** (1.36 lower to 0.49 lower)	⊕⊕◯◯ Low
ARND/Other										
2	serious[a]	serious[b]	not serious	serious[e,f]	none	73	77	-	**SMD 0.61 lower** (1.54 lower to 0.32 lower)	⊕◯◯◯ Very Low
Verbal 'short delay' (CVLT-C) T-score										
pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	20	16	-	**SMD 2.06 lower** (2.89 lower to 1.24 lower)	⊕⊕◯◯ Low
ARND/Other										
1	serious[a]	not serious	not serious	serious[e,f]	none	24	16	-	**SMD 2.54 lower** (3.4 lower to 1.68 lower)	⊕⊕◯◯ Low
Verbal 'long delay' (CVLT-C, VSRT, CMS-stories)										
FASD										
3	serious[a]	not serious	not serious	serious[e,f]	none	90	94	-	**SMD 0.89 lower** (1.19 lower to 0.58 lower)	⊕⊕◯◯ Low
FAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	45	59	-	**SMD 0.79 lower** (1.19 lower to 0.39 lower)	⊕⊕◯◯ Low
pFAS (1x FAS/pFAS)										
1	serious[a]	not serious	not serious	serious[e,f]	none	36	60	-	**SMD 0.78 lower** (1.21 lower to 0.35 lower)	⊕⊕◯◯ Low
ARND/Other										
2	serious[a]	serious[b]	not serious	serious[e,f]	none	73	77	-	**SMD 0.83 lower** (2.59 lower to 0.94 lower)	⊕◯◯◯ Very Low
Verbal 'long delay' (CVLT-C) Frequency (Cut-offs unclear)										
FASD										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	24/35 (68.6%)	23/35 (65.7%)	**OR 1.14** (0.42 to 3.09)	**29 more per 1,000** (from 211 fewer to 198 more)	⊕◯◯◯ Very Low
Verbal 'long delay' (CVLT-C) z-score										
FASD										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	21	7	-	**SMD 0.64 lower** (1.52 lower to 0.23 higher)	⊕◯◯◯ Very Low
Visual/Verbal 'short delay' (K-ABC, Word Stem Completion Target, NEPSY-II memory for names, Memory of 16 objects)										

FASD										
5	serious[a]	serious[b]	not serious	serious[e,]	none	228	275	-	**SMD 0.44 lower** (0.87 lower to 0.01 lower)	⊕◯◯◯ Very Low
ARND/Other										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	62	35	-	**SMD 0.09 lower** (0.51 lower to 0.32 higher)	⊕◯◯◯ Very Low
Visual/Verbal 'short delay' (NEPSY-II memory for names) (Frequency of children <1SD below normative mean)										
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	21/32 (65.6%)	8/30 (26.7%)	**OR 5.25** (1.77 to 15.61)	**390 more per 1,000** (from 125 more to 584 more)	⊕⊕◯◯ Low
Visual/Verbal 'long delay' (NEPSY-II memory for names) (Frequency of children <1SD below normative mean)										
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	25/32 (78.1%)	12/30 (40.0%)	**OR 5.36** (1.76 to 16.28)	**381 more per 1,000** (from 140 more to 516 more)	⊕⊕◯◯ Low
Visual/Verbal 'long delay' (16 objects, NEPSY-II Memory for Names)										
FASD										
2	serious[a]	not serious	not serious	serious[e,f]	none	79	84	-	**SMD 0.79 lower** (1.11 lower to 0.47 lower)	⊕⊕◯◯ Low
Non-verbal 'short delay' (various measures)										
FASD (WRAML-VMI)										
1	serious[a]	not serious	not serious	serious[e,f]	none	20	20	-	**SMD 7.25 lower** (9.04 lower to 5.47 lower)	⊕⊕◯◯ Low
FAS (NVRST)										
1	serious[a]	not serious	not serious	serious[e,f]	none	47	58	-	**SMD 0.58 lower** (0.97 lower to 0.18 lower)	⊕⊕◯◯ Low
ARND/Other (TOMAL)										
1	serious[a]	not serious	not serious	serious[e,f]	none	19	21	-	**SMD 1.00 lower** (1.66 lower to 0.34 lower)	⊕⊕◯◯ Low
Non-verbal 'short delay' (RCFT) (T-score)										
FASD										
2	serious[a]	not serious	not serious	serious[e,f]	none	67	106	-	**SMD 0.78 lower** (1.10 lower to 0.45 lower)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	20	16	-	**SMD 1.60 lower** (2.37 lower to 0.84 lower)	⊕⊕◯◯ Low
ARND/Other										
1	serious[a]	not serious	not serious	serious[e,f]	none	22	16	-	**SMD 1.72 lower** (2.49 lower to 0.96 lower)	⊕⊕◯◯ Low
Non-verbal 'short delay' (CANTAB) Frequency (Cut-offs unclear)										
FASD										

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Int	Ctrl	Relative	Absolute	Certainty
1	serious[a]	not serious	not serious	serious[d,f]	none	18/24 (75.0%)	22/26 (84.6%)	OR 0.55 (0.13 to 2.23)	**95 fewer per 1,000** (from 429 fewer to 78 more)	⊕⊕◯◯ Low

Non-verbal 'long delay' (NVRST & TOMAL)

FAS

| 1 | serious[a] | not serious | not serious | serious[e,f] | none | 47 | 58 | - | **SMD 0.50 lower** (0.89 lower to 0.11 lower) | ⊕⊕◯◯ Low |

ARND/Other

| 1 | serious[a] | not serious | not serious | serious[e,f] | none | 19 | 21 | - | **SMD 1.04 lower** (1.70 lower to 0.37 lower) | ⊕⊕◯◯ Low |

Non-verbal 'long delay' (RCFT) (T-score)

FASD

| 2 | serious[a] | not serious | not serious | serious[e,f] | none | 67 | 106 | - | **SMD 0.77 lower** (1.09 lower to 0.45 lower) | ⊕⊕◯◯ Low |

pFAS

| 1 | serious[a] | not serious | not serious | serious[e,f] | none | 20 | 16 | - | **SMD 2.28 lower** (3.14 lower to 1.42 lower) | ⊕⊕◯◯ Low |

ARND/Other

| 1 | serious[a] | not serious | not serious | serious[e,f] | none | 21 | 16 | - | **SMD 2.20 lower** (3.04 lower to 1.36 lower) | ⊕⊕◯◯ Low |

Non-verbal 'long delay' (BFLT) Frequency (Cut-offs unclear)

FASD

| 1 | serious[a] | not serious | not serious | serious[d,f] | none | 26/35 (74.3%) | 28/35 (80.0%) | OR 0.72 (0.24 to 2.22) | **58 fewer per 1,000** (from 310 fewer to 99 more) | ⊕⊕◯◯ Low |

Self-report (Everyday memory questionnaire – Spatial Memory)

FASD

| 1 | serious[a] | not serious | not serious | serious[f] | none | 41 | 64 | - | **SMD 1.71 higher** (1.25 higher to 2.17 higher) | ⊕⊕◯◯ Low |

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.
Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CIs for overall estimate crossed the line of no effect; e) Wide 95% CIs for overal effect; f) optimal information size criteria not met.

Meta-analyses for memory

EXPOSURE STUDIES

Verbal 'Short delay': RAVLT, NEPSY Word list interference (mean/SD)
Light PAE and Verbal 'Short Delay' (mean/SD) (1 study)

Note: Lees et al 2020 also reports RAVLT learning.

Moderate PAE and Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; RAVLT)	10	2.9	755	9.7	3	6669	100.0%	0.10 [0.03, 0.18]	🔴
Total (95% CI)			755			6669	100.0%	**0.10 [0.03, 0.18]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.61 (P = 0.009)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports RAVLT learning.

Confirmed PAE-Level Unquantifiable and Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	Confirmed unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Glass et al 2015 (8-16yrs; NEPSY)	8	2.57	49	10.9	2.56	47	100.0%	-1.12 [-1.55, -0.69]	🔴
Total (95% CI)			49			47	100.0%	**-1.12 [-1.55, -0.69]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 5.09 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Any PAE Level and Verbal 'Short Delay' (mean/SD) (2 studies)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Furtado et al 2016 (11-12yrs; RAVLT)	7.11	1.45	28	6.71	1.94	28	0.7%	0.23 [-0.30, 0.76]	🔴
Lees et al 2020 (9-11yrs; RAVLT)	10	2.9	2518	9.6	3	7201	99.3%	0.13 [0.09, 0.18]	🔴
Total (95% CI)			2546			7229	100.0%	**0.14 [0.09, 0.18]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 1 (P = 0.72); I² = 0%
Test for overall effect: Z = 5.86 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Furtado et al 2016 also reports RCFT figure copy, RAVLT total score, recognition, proactive interference, and retroactive interference. Lees et al 2020 also reports RAVLT learning.

Verbal 'Short Delay': CVLT-C (z-score)

Confirmed PAE-Level Unquantifiable and Verbal 'Short Delay' (z-score) (1 study)

Study or Subgroup	Confirmed unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Gross et al 2018 (10-16yrs; CVLT-C)	-0.329	0.937	81	0.363	0.783	81	100.0%	-0.80 [-1.12, -0.48]	🔴
Total (95% CI)			81			81	100.0%	**-0.80 [-1.12, -0.48]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 4.88 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Gross et al 2018 also reports CVLT-C total learning A (T-score) and recognition discriminability (z-score).

Verbal 'Long Delay': CVLT-C/RAVLT (mean/SD)

Light PAE and Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	Light PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; RAVLT)	10	2.9	755	9.7	3	6669	100.0%	0.10 [0.03, 0.18]	🔴
Total (95% CI)			755			6669	100.0%	**0.10 [0.03, 0.18]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.61 (P = 0.009)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports RAVLT learning.

Moderate PAE and Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	Moderate PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Lees et al 2020 (9-11yrs; RAVLT)	9.6	3.1	755	9.1	3.2	6669	100.0%	0.16 [0.08, 0.23]		–
Total (95% CI)			755			6669	100.0%	0.16 [0.08, 0.23]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.08 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports RAVLT learning.

Confirmed PAE-Level Unquantifiable PAE and Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	Confirmed unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Gross et al 2018 (10-16yrs; CVLT-C)	10	1.33	81	12.3	1.28	81	100.0%	-1.75 [-2.12, -1.39]		–
Total (95% CI)			81			81	100.0%	-1.75 [-2.12, -1.39]		

Heterogeneity: Not applicable
Test for overall effect: Z = 9.45 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Gross et al 2018 also reports CVLT-C total learning A (T-score) and recognition discriminability (z-score).

Any PAE and Verbal 'Long Delay' (mean/SD) (2 studies)

Study or Subgroup	Any PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Furtado et al 2016 (11-12yrs; RAVLT)	13.5	1.55	28	13.11	1.75	28	0.7%	0.23 [-0.29, 0.76]		–
Lees et al 2020 (9-11yrs; RAVLT)	9.6	3.1	2518	9.1	3.2	7501	99.3%	0.16 [0.11, 0.20]		–
Total (95% CI)			2546			7529	100.0%	0.16 [0.11, 0.20]		

Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 6.88 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Furtado et al 2016 also reports RCFT figure copy, RAVLT total score, recognition, proactive interference, and retroactive interference. Lees et al 2020 also reports RAVLT learning.

Verbal 'Long Delay': CVLT-C (z-score)

Confirmed PAE-Level Unquantifiable and Verbal 'Long Delay' (z-score) (1 study)

Study or Subgroup	Confirmed unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Gross et al 2018 (10-16yrs; CVLT-C)	-0.237	0.922	81	0.527	0.629	81	100.0%	-0.96 [-1.29, -0.64]		–
Total (95% CI)			81			81	100.0%	-0.96 [-1.29, -0.64]		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.80 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Gross et al 2018 also reports CVLT-C total learning A (T-score) and recognition discriminability (z-score).

Visual/Verbal 'Short Delay': K-ABC (mean/SD)

Very Heavy PAE and Visual/Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	Very Heavy PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Coles et al 1991 (5-8yrs; K-ABC)	83.96	12.48	25	92.62	15.43	21	100.0%	-0.61 [-1.21, -0.02]		–
Total (95% CI)			25			21	100.0%	-0.61 [-1.21, -0.02]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.02 (P = 0.04)

Risk of bias legend
(A) Overall RoB

Note: Coles et al 1991 reports Stopped PAE (320.88g/w) and Continued PAE (330.96g/w), used Continued (T1-T3) exposure.

Non-Verbal 'Short Delay': RCFT (mean/SD)

Confirmed PAE-Level Unquantifiable PAE and Non-Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	Confirmed unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Furtado et al 2016 (11-12yrs; RCFT)	16.66	5.95	28	20.7	5.95	28	100.0%	-0.67 [-1.21, -0.13]		–
Total (95% CI)			28			28	100.0%	-0.67 [-1.21, -0.13]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.43 (P = 0.01)

Risk of bias legend
(A) Overall RoB

Note: Furtado et al 2016 also reports RCFT figure copy, RAVLT total score, recognition, proactive interference, and retroactive interference.

Non-Verbal 'Long Delay': RCFT (mean/SD)

Confirmed PAE-Level Unquantifiable PAE and Non-Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	Confirmed unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Furtado et al 2016 (11-12yrs; RCFT)	15.68	5.15	28	20.2	5.17	28	100.0%	-0.86 [-1.41, -0.31]		–
Total (95% CI)			28			28	100.0%	-0.86 [-1.41, -0.31]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.08 (P = 0.002)

Risk of bias legend
(A) Overall RoB

Note: Furtado et al 2016 also reports RCFT figure copy, RAVLT total score, recognition, proactive interference, and retroactive interference.

DIAGNOSED STUDIES

Verbal 'Short Delay': WRAML-story memory/CMS-stories/Story Memory (mean/SD)

FASD and Verbal 'short delay' (mean/SD) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kaemingk et al 2000 (6-16yrs; WRAML-SM)	5.55	2.52	20	10.1	2.4	20	31.7%	-1.81 [-2.56, -1.06]		–
Kalberg et al 2013 (8-8yrs; Story Memory)	65.9	18.6	61	70.9	21.8	52	36.3%	-0.25 [-0.62, 0.12]		–
Willoughby et al 2008 (9-15yrs; CMS-stories)	34.73	20.9	19	60.22	15.17	18	32.0%	-1.36 [-2.08, -0.64]		–
Total (95% CI)			100			90	100.0%	-1.10 [-2.13, -0.07]		

Heterogeneity: Tau² = 0.73; Chi² = 17.42, df = 2 (P = 0.0002); I² = 89%
Test for overall effect: Z = 2.09 (P = 0.04)

Risk of bias legend
(A) Overall RoB

Note: Kaemingk et al 2000 also reports Localisation task - quadrant localisation, WRAML visual learning and verbal learning. Willoughby et al 2008 also reports CMS measures (cohort exclusion: Agnihotri et al 2019), CVLT-C cued recall, ROCF delayed spatial recall.

Verbal 'Short Delay': CVLT-C Story Memory (mean/SD)

FASD and Verbal 'Short Delay': CVLT-C Story Memory (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Willoughby et al 2008 (9-15yrs; CVLT-C)	9.44	4.15	19	12.61	1.98	18	100.0%	-0.95 [-1.63, -0.26]		–
Total (95% CI)			19			18	100.0%	-0.95 [-1.63, -0.26]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.71 (P = 0.007)

Risk of bias legend
(A) Overall RoB

Note: Willoughby et al 2008 also reports CMS measures (cohort exclusion: Agnihotri et al 2019), CVLT-C cued recall, ROCF delayed spatial recall.

Verbal 'Short Delay': WRAML-Verbal Memory Index/Story Memory/CMS-Stories/CVLT-C/VSRT (mean/SD)

FASD and Verbal 'Short Delay' (mean/SD) (4 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kaemingk et al 2003 (6-16yrs; WRAML-VMI)	66.7	11.6276	20	88.95	9.302	20	23.3%	-2.07 [-2.85, -1.29]		?
Kalberg et al 2013 (6-8yrs; Story Memory)	65.9	18.6	61	70.9	21.8	52	27.4%	-0.25 [-0.62, 0.12]		−
Willoughby et al 2008 (9-15yrs; CMS-stories)	34.73	20.9	19	60.22	15.17	18	24.0%	-1.36 [-2.08, -0.64]		−
Wozniak et al 2013 (10-17 yrs; CVLT-C-total)	43	11.5	24	57	7.6	31	25.3%	-1.45 [-2.06, -0.85]		−
Total (95% CI)			**124**			**121**	**100.0%**	**-1.24 [-2.11, -0.38]**		

Heterogeneity: Tau² = 0.67; Chi² = 25.24, df = 3 (P < 0.0001); I² = 88%
Test for overall effect: Z = 2.83 (P = 0.005)

Risk of bias legend
(A) Overall RoB

Note: Kaemingk et al 2003 also reports WRAML General Memory Index. Willoughby et al 2008 also reports CMS measures (cohort exclusion: Agnihotri et al 2019), other CVLT-C measures, and ROCF delayed spatial recall. Wozniak et al 2013 also reports CVLT-C trial 1 and long-delay recall (z-scores).

FAS and Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 2010 (22-23yrs; VSRT-mean)	7.13	2.05	45	8.49	1.36	49	100.0%	-0.78 [-1.20, -0.36]		−
Total (95% CI)			**45**			**49**	**100.0%**	**-0.78 [-1.20, -0.36]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.65 (P = 0.0003)

Risk of bias legend
(A) Overall RoB

pFAS and Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lewis et al 2015 (10yrs; CVLT-C; FAS/pFAS)	7.1	3.1	36	9.7	2.6	60	100.0%	-0.92 [-1.36, -0.49]		−
Total (95% CI)			**36**			**60**	**100.0%**	**-0.92 [-1.36, -0.49]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.16 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

Note: Lewis et al 2015 also reports CVLT-C immediate and total learning, and recognition discrimination.

ARND/Other and Verbal 'Short Delay' (mean/SD) (2 studies)

Study or Subgroup	ARND/Other Mean	ARND/Other SD	ARND/Other Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Dudek et al 2014 (11-14 yrs; CMS-stories; ARND)	9.3	3.2	18	12.6	2.4	17	44.5%	-1.14 [-1.86, -0.41]		−
Lewis et al 2015 (10yrs; CVLT-C; non-syndromal)	9.2	2.9	55	9.7	2.6	60	55.5%	-0.18 [-0.55, 0.19]		−
Total (95% CI)			**73**			**77**	**100.0%**	**-0.61 [-1.54, 0.32]**		

Heterogeneity: Tau² = 0.37; Chi² = 5.35, df = 1 (P = 0.02); I² = 81%
Test for overall effect: Z = 1.28 (P = 0.20)

Risk of bias legend
(A) Overall RoB

Note: Dudek et al 2014 also reports TOMAL word selective immediate and delayed, CMS picture and faces, and RCFT delayed (z-score). Lewis et al 2015 also reports CVLT-C immediate and total learning, and recognition discrimination.

Verbal 'Short Delay': CVLT-C (T-score)

pFAS and Verbal 'Short Delay': CVLT-C (T-score) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8.5-16yrs; CVLT-C-total)	38.6	13.1	20	61.2	6.5	16	100.0%	-2.06 [-2.89, -1.24]		−
Total (95% CI)			**20**			**16**	**100.0%**	**-2.06 [-2.89, -1.24]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.88 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009 also reports CVLT-C List A Trial 1 free recall (T-score).

ARND/Other and Verbal 'Short Delay': CVLT-C (T-score) (1 study)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b(8.5-16yrs; CVLT-C-total; SE/AE)	38.8	9.8	24	61.2	6.5	16	100.0%	-2.54 [-3.40, -1.68]	■	🔴
Total (95% CI)			24			16	100.0%	**-2.54 [-3.40, -1.68]**	◆	

Heterogeneity: Not applicable
Test for overall effect: Z = 5.77 (P < 0.00001)

-4 -2 0 2 4
ARND/Other   Control

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009 also reports CVLT-C List A Trial 1 free recall (T-score).

Verbal 'Long Delay': CVLT-C/VSRT/CMS-stories (mean/SD)

FASD and Verbal 'Long Delay': CVLT-C/VSRT/CMS-stories (mean/SD) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Crocker et al 2011 (7-14yrs; CVLT-C)	8.36	4.12	22	11.41	2.2	22	23.8%	-0.91 [-1.53, -0.28]	■	🔴
Gautam et al 2014 (6-17yrs; CVLT-C)	8.86	3.11	49	11.4	2.54	54	56.0%	-0.89 [-1.30, -0.49]	■	🔴
Willoughby et al 2008 (9-15yrs; CVLT-C)	9.53	4.05	19	12.28	1.87	18	20.2%	-0.85 [-1.52, -0.17]	■	🔴
Total (95% CI)			90			94	100.0%	**-0.89 [-1.19, -0.58]**	◆	

Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 2 (P = 0.99); I² = 0%
Test for overall effect: Z = 5.71 (P < 0.00001)

-4 -2 0 2 4
FASD   Control

Risk of bias legend
(A) Overall RoB

Note: Crocker et al 2011 also reports CVLT-C retention and CVLT-C recognition discriminability (mean/SD). Crocker et al 2011 has confirmed unquantifiable PAE for all participants, with 59% FAS. Willoughby et al 2008 also reports CMS measures (cohort exclusion: Agnihotri et al 2019), CVLT-C cued recall, ROCF delayed spatial recall.

FAS and Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 2010 (22-23yrs; VSRT-delayed)	6.27	2.98	45	8.47	2.6	59	100.0%	-0.79 [-1.19, -0.39]	■	🔴
Total (95% CI)			45			59	100.0%	**-0.79 [-1.19, -0.39]**	◆	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.83 (P = 0.0001)

-4 -2 0 2 4
FAS   Control

Risk of bias legend
(A) Overall RoB

Note: Coles et al 2010 VSRT learning slope, recall 8th, NVSRT learning slope etc.

pFAS and Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lewis et al 2015 (10yrs; CVLT-C; FAS/pFAS)	7.4	3.1	36	9.6	2.6	60	100.0%	-0.78 [-1.21, -0.35]	■	🔴
Total (95% CI)			36			60	100.0%	**-0.78 [-1.21, -0.35]**	◆	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.57 (P = 0.0004)

-4 -2 0 2 4
pFAS   Control

Risk of bias legend
(A) Overall RoB

Note: Lewis et al 2015 also reports CVLT-C immediate and total learning, and recognition discrimination.

ARND/Other and Verbal 'Long Delay' (mean/SD) (2 studies)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Dudek et al 2014 (11-14 yrs; CMS-stories; ARND)	8.2	1.9	18	12.5	2.8	17	48.0%	-1.77 [-2.56, -0.97]	■	🔴
Lewis et al 2015 (10yrs; CVLT-C; non-syndromal)	9.7	2.6	55	9.6	2.6	60	52.0%	0.04 [-0.33, 0.40]	■	🔴
Total (95% CI)			73			77	100.0%	**-0.83 [-2.59, 0.94]**	◆	

Heterogeneity: Tau² = 1.53; Chi² = 16.32, df = 1 (P < 0.0001); I² = 94%
Test for overall effect: Z = 0.92 (P = 0.36)

-4 -2 0 2 4
ARND/Other   Control

Risk of bias legend
(A) Overall RoB

Note: Dudek et al 2014 also reports TOMAL word selective immediate and delayed, CMS picture and faces, and RCFT delayed (z-score).
Lewis et al 2015 also reports CVLT-C immediate and total learning, and recognition discrimination.

Verbal 'Long Delay': CVLT-C (OR/Frequency)

FASD and Verbal 'Long Delay' (OR/Frequency) (1 study)

Study or Subgroup	FASD Events	FASD Total	Control Events	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Mattson & Roebuck 2002 (8.5-17yrs; CVLT-C)	24	35	23	35	100.0%	1.14 [0.42, 3.09]	■	●
Total (95% CI)		35		35	100.0%	**1.14 [0.42, 3.09]**	◆	
Total events	24		23					

Heterogeneity: Not applicable
Test for overall effect: Z = 0.25 (P = 0.80)

Risk of bias legend
(A) Overall RoB

Note: Mattson & Roebuck 2002 also reports CVLT-C total learning and delayed recall, BFLT total learning and delayed recall (unadj) and WRAML sound symbol learning (% correct).

Verbal 'Long Delay': CVLT-C (z-score)

FASD and Verbal 'Long Delay' (z-score) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Fryer et al 2012 (9-21yrs; CVLT-C)	-0.7	1.62	21	0.29	0.95	7	100.0%	-0.64 [-1.52, 0.23]	■	●
Total (95% CI)			21			7	100.0%	**-0.64 [-1.52, 0.23]**	◆	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.44 (P = 0.15)

Risk of bias legend
(A) Overall RoB

Note: Fryer et al 2012 also reports CVLT-C List A Learning. Fryer et al 2012 has confirmed unquantifiable PAE for all participants, with 57% FAS.

Visual/Verbal 'Short Delay': K-ABC/Word Stem Completion Target/NEPSY-II/Memory of 16 objects)

FASD and Visual/Verbal 'Short Delay' (mean/SD) (5 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 1997 (7-8.5yrs; KABC-SPC)	83.64	11.09	22	90.97	13.18	35	19.0%	-0.58 [-1.13, -0.04]	■	●
Mattson & Riley 1999 (8.5-18yrs; Word Stem-CT)	59	24.27	21	64.1	19.72	21	17.7%	-0.23 [-0.83, 0.38]	■	●
McLachlan et al 2020 (8-19yrs; NEPSY-II-MfN)	7.2	3.3	65	9.9	29	69	23.2%	-0.13 [-0.47, 0.21]	■	?
Treit et al 2016 (5-19yrs; NEPSY-II: MfN)	6.1	3.6	105	9.3	2.9	135	24.5%	-0.99 [-1.26, -0.72]	■	●
Uecker & Nadel 1996 (~10yrs; Memory of 16 Objects)	7.07	1.91	15	7.27	1.67	15	15.6%	-0.11 [-0.82, 0.61]	■	●
Total (95% CI)			228			275	100.0%	**-0.44 [-0.87, -0.01]**	◆	

Heterogeneity: Tau² = 0.18; Chi² = 18.59, df = 4 (P = 0.0009); I² = 78%
Test for overall effect: Z = 1.99 (P = 0.05)

Note: NEPSY-II MFN is Memory for Names, K-ABC SPC is Sequential Processing Composite, Word Stem-CT is completion target. Mattson & Riley 1999 also reports Word Stem Completion subdomains, free and recognition free recall subdomains.

ARND/Other and Visual/Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	ARND/Other Mean	ARND/Other SD	ARND/Other Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 1997 (7-8.5yrs;KABC-SPC;non-syndromal)	89.68	14.07	62	90.97	13.18	35	100.0%	-0.09 [-0.51, 0.32]	■	●
Total (95% CI)			62			35	100.0%	**-0.09 [-0.51, 0.32]**	◆	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.44 (P = 0.66)

Risk of bias legend
(A) Overall RoB

Visual/Verbal 'Short Delay': NEPSY-II (Frequency/OR)

FASD and Visual/Verbal 'Short Delay' (Frequency/OR) (1 study)

Study or Subgroup	FASD Events	FASD Total	Control Events	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Rasmussen et al 2013 (6-16yrs; NEPSY-II-MfN)	21	32	8	30	100.0%	5.25 [1.77, 15.61]	■	●
Total (95% CI)		32		30	100.0%	**5.25 [1.77, 15.61]**	◆	
Total events	21		8					

Heterogeneity: Not applicable
Test for overall effect: Z = 2.98 (P = 0.003)

Risk of bias legend
(A) Overall RoB

Note: NEPSY-II MfN is Memory for Names.

Visual/Verbal 'Long Delay': NEPSY-II (Frequency/OR)

FASD and Visual/Verbal 'Long delay' (Frequency/OR) (1 study)

Study or Subgroup	FASD Events	FASD Total	Control Events	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Rasmussen et al 2013 (6-16yrs; NEPSY-II-MfN)	25	32	12	30	100.0%	5.36 [1.76, 16.28]		🔴
Total (95% CI)		32		30	100.0%	**5.36 [1.76, 16.28]**		
Total events	25		12					
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.96 (P = 0.003)								

0.01 0.1 1 10 100
Control FASD

Risk of bias legend
(A) Overall RoB

Note: NEPSY-II MfN is Memory for Names.

Visual/Verbal 'Long Delay': NEPSY-II/Memory of 16 objects (mean/SD)

FASD and Visual/Verbal 'Long Delay' (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McLachlan et al 2020 (8-19yrs; NEPSY-II-MfN)	7.3	3.3	64	9.6	2.5	69	81.8%	-0.79 [-1.14, -0.43]		🟡 ?
Uecker & Nadel 1996 (~10yrs; Memory of 16 Objects)	6.87	1.88	15	8.33	1.59	15	18.2%	-0.82 [-1.57, -0.07]		🔴
Total (95% CI)			79			84	100.0%	**-0.79 [-1.11, -0.47]**		
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.94); I² = 0%										
Test for overall effect: Z = 4.85 (P < 0.00001)										

-4 -2 0 2 4
FASD Control

Risk of bias legend
(A) Overall RoB

Note: Uecker & Nadel 1996 also reports Memory of 16 objects – spatial and distortion.

Non-Verbal 'Short delay': WRAML/NVRST/TOMAL/ROCF/RCFT (mean/SD)

FASD and Non-Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kaemingk et al 2003 (6-16yrs; WRAML-VMI)	79.47	3.22	20	100.55	2.42	20	100.0%	-7.25 [-9.04, -5.47]		🟡 ?
Total (95% CI)			20			20	100.0%	**-7.25 [-9.04, -5.47]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 7.96 (P < 0.00001)										

-4 -2 0 2 4
FASD Control

Risk of bias legend
(A) Overall RoB

Note: Kaemingk et al 2003 also reports WRAML General Memory Index.

FAS and Non-Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 2010 (22-23yrs; NVRST-mean)	5.18	1.58	47	5.97	1.15	58	100.0%	-0.58 [-0.97, -0.18]		🔴
Total (95% CI)			47			58	100.0%	**-0.58 [-0.97, -0.18]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 2.88 (P = 0.004)										

-4 -2 0 2 4
FAS Control

Risk of bias legend
(A) Overall RoB

Note: Coles et al 2010 VSRT learning slope, recall 8th. NVSRT learning slope and other subdomains.

ARND/Other and Non-Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	ARND/Other Mean	ARND/Other SD	ARND/Other Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Wheeler et al 2012 (10-14yrs; TOMAL; ARND)	7.79	2.92	19	10.76	2.9	21	100.0%	-1.00 [-1.66, -0.34]		🔴
Total (95% CI)			19			21	100.0%	**-1.00 [-1.66, -0.34]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 2.96 (P = 0.003)										

-4 -2 0 2 4
ARND/Other Control

Risk of bias legend
(A) Overall RoB

Note: Wheeler et al 2012 also reports CMS measures (cohort exclusion – Willoughby et al 2008).

Non-Verbal 'Short Delay': RCFT (mean/SD)

FASD and Non-verbal 'short delay' (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Pei et al 2011 (6-12yrs; ROCF)	34.69	8.62	34	42.4	13.64	35	43.9%	-0.67 [-1.15, -0.18]
Treit et al 2017 (5-32yrs; RCFT)	36	14	33	47	12	71	56.1%	-0.86 [-1.29, -0.43]
Total (95% CI)			67			106	100.0%	-0.78 [-1.10, -0.45]

Heterogeneity: Tau² = 0.00; Chi² = 0.35, df = 1 (P = 0.55); I² = 0%
Test for overall effect: Z = 4.73 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Pei et al 2011 also reports ROCF copy raw (mean/SD). Treit et al 2017 also reports RCFT recognition.

pFAS and Non-Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Astley et al 2009b (8.5-16yrs; RCFT; FAS/pFAS)	30.1	10.3	20	49.8	13.9	16	100.0%	-1.60 [-2.37, -0.84]
Total (95% CI)			20			16	100.0%	-1.60 [-2.37, -0.84]

Heterogeneity: Not applicable
Test for overall effect: Z = 4.10 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009 also reports CVLT-C List A Trial 1 free recall (T-score).

ARND/Other and Non-Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Astley et al 2009b (8.5-16yrs; RCFT; SE/AE)	28.7	10.4	22	49.8	13.9	16	100.0%	-1.72 [-2.49, -0.96]
Total (95% CI)			22			16	100.0%	-1.72 [-2.49, -0.96]

Heterogeneity: Not applicable
Test for overall effect: Z = 4.43 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009 also reports CVLT-C List A Trial 1 free recall (T-score).

Non-Verbal 'Short Delay': CANTAB (mean/SD)

FASD and Non-Verbal 'Short Delay' (mean/SD) (1 study)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI
Rasmussen et al 2013 (6-16yrs; CANTAB-PRM)	18	24	22	26	100.0%	0.55 [0.13, 2.23]
Total (95% CI)		24		26	100.0%	0.55 [0.13, 2.23]
Total events	18		22			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.84 (P = 0.40)

Risk of bias legend
(A) Overall RoB

Non-Verbal 'Long Delay': NVRST/TOMAL (mean/SD)

FAS and Non-Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Coles et al 2010 (22-23yrs; NVRST)	5.15	2.27	47	6.12	1.61	58	100.0%	-0.50 [-0.89, -0.11]
Total (95% CI)			47			58	100.0%	-0.50 [-0.89, -0.11]

Heterogeneity: Not applicable
Test for overall effect: Z = 2.50 (P = 0.01)

Risk of bias legend
(A) Overall RoB

Note: Coles et al 2010 VSRT learning slope, recall 8th. NVSRT learning slope other subdomains.

ARND/Other and Non-Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Wheeler et al 2012 (10-14yrs; TOMAL; ARND)	8.84	1.57	19	10.62	1.77	21	100.0%	-1.04 [-1.70, -0.37]	⊖
Total (95% CI)			19			21	100.0%	-1.04 [-1.70, -0.37]	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.06 (P = 0.002)

Risk of bias legend
(A) Overall RoB

Non-Verbal 'Long Delay': RCFT (mean/SD)

FASD and Non-Verbal 'Long Delay' (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Pei et al 2011 (6-12yrs; ROCF)	33.51	8.66	34	40.74	13.38	35	44.1%	-0.63 [-1.12, -0.15]	⊖
Treit et al 2017 (5-32yrs; RCFT)	36	15	33	47	11	71	55.9%	-0.88 [-1.31, -0.45]	⊖
Total (95% CI)			67			106	100.0%	-0.77 [-1.09, -0.45]	

Heterogeneity: Tau² = 0.00; Chi² = 0.57, df = 1 (P = 0.45); I² = 0%
Test for overall effect: Z = 4.70 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Pei et al 2011 also reports ROCF copy raw (mean/SD).

pFAS and Non-Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8.5-16yrs; RCFT; FAS/pFAS)	28.9	9.4	20	53.2	11.6	16	100.0%	-2.28 [-3.14, -1.42]	⊖
Total (95% CI)			20			16	100.0%	-2.28 [-3.14, -1.42]	

Heterogeneity: Not applicable
Test for overall effect: Z = 5.18 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009 also reports CVLT-C List A Trial 1 free recall (T-score).

ARND/Other and Non-Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8.5-16yrs; RCFT; SE/AE)	29.5	9.7	21	53.2	11.6	16	100.0%	-2.20 [-3.04, -1.36]	⊖
Total (95% CI)			21			16	100.0%	-2.20 [-3.04, -1.36]	

Heterogeneity: Not applicable
Test for overall effect: Z = 5.13 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009b also reports CVLT-C List A Trial 1 free recall (T-score).

Non-Verbal 'Long Delay': BFLT (mean/SD)

FASD and Non-Verbal 'Long Delay' (mean/SD) (1 study)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Mattson & Roebuck 2002 (8.5-17yrs; BFLT)	26	35	28	35	100.0%	0.72 [0.24, 2.22]	⊖
Total (95% CI)		35		35	100.0%	0.72 [0.24, 2.22]	
Total events	26		28				

Heterogeneity: Not applicable
Test for overall effect: Z = 0.57 (P = 0.57)

Risk of bias legend
(A) Overall RoB

Note: Mattson & Roebuck 2002 also reports CVLT-C total learning and delayed recall, BFLT total learning and delayed recall (unadj) and WRAML verbal and visual learning (frequency).

Self-report: Everyday memory questionnaire (mean/SD)

FASD and Self-report (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Agnihotri et al 2019 (9-17yrs; EMQ-SR)	4.32	2.34	41	1.62	0.73	64	100.0%	1.71 [1.25, 2.17]	■	●
Total (95% CI)			41			64	100.0%	**1.71 [1.25, 2.17]**	◆	

Heterogeneity: Not applicable
Test for overall effect: Z = 7.33 (P < 0.00001)

-4 -2 0 2 4
FASD   Control

Risk of bias legend
(A) Overall RoB

Note: Agnihotri et al 2019 also reports other EMQ subdomains. Adjusted mean (SD) used in meta-analysis.

Summary of available outcomes for attention

Attention			
Study type	**Measures**	**Data**	**# studies**
Exposure Studies	**NEPSY**: Visual Attention	mean/SD	**1 study:** 1 heavy PAE
	TOVA: commission errors (ss), commission errors (block 1), omission errors (ss) and omission errors (block 1)	mean/SD	**2 studies:** 2 confirmed unquantifiable (different measures)
	Selective/ Sustained Attention: Leiter Sustained Attention (ss)	mean/SD	**1 study:** 1 heavy
	Selective/ Sustained Attention: TEACh-5 Selective/Sustained	OR/Frequency	**1 study:** 1 light, 1 moderate, 1 heavy
	Selective/ Sustained Attention: TEACh-5 Selective	OR/Frequency	**1 study:** 1 light, 1 moderate, 1 heavy
	Selective/ Sustained Attention: TEACh-5 Sustained	OR/Frequency	**1 study:** 1 light, 1 moderate, 1 heavy
	Other Attention Measures: NES3, D2 test of attention	mean/SD	**2 studies:** 1 confirmed unquantifiable, 1 any PAE (different measures)
	Ext: Attention – Caregiver Report: CBCL	T-score	**6 studies:** 1 very heavy, 4 confirmed unquantifiable, 1 Any
	Ext: Attention – Caregiver Report: CBCL	OR/Frequency	**2 studies:** 1 light, 1 moderate, 2 heavy PAE
	Ext: Attention – Teacher Report	N/A	
	Ext: Attention – Self Report: YSR	OR/Frequency	**1 study:** 1 moderate, 1 heavy
Diagnosed Studies	**NEPSY-II Measures**: NEPSY Auditory Attention	mean/SD	**6 studies:** 6 FASD
	NEPSY-II Measures: NEPSY Response Set	mean/SD	**6 studies:** 6 FASD
	Other Attention Measures: VIGIL/W visual total errors and auditory total errors, CPT-II omission errors	mean/SD	**2 studies:** 1 FASD, 1 ARND/Others (different measures)
	Other Attention Measures: IVA CPT	Frequency	**1 study:** 1 pFAS, 1 ARND/Other
	Other Selective/ Sustained Attention Measures: Selective/Sustained Correct Response – TEACh-Map Mission, NES3 Animal Following (no. correct)	mean/SD	**2 studies:** 2 FASD
	Ext: Attention – Caregiver Report: CBCL-C, CBRS	T-score	**10 studies:** 6 FASD, 2 FAS, 2 pFAS, 4 ARND/Others
	Ext: Attention – Caregiver Report: CBCL-C	OR/Frequency	**1 study:** 1 FASD

	Ext: Attention – Caregiver Report: DBD	mean/SD	**2 studies:** 2 pFAS
	Ext: Attention – Teacher Report: TRF	T-score	**5 studies:** 3 FASD, 2 FAS, 2 pFAS, 2 ARND/Others
	Ext: Attention – Teacher Report: DBD	mean/SD	**2 studies:** 2 pFAS
	Ext: Attention – Self Report: YSR	T-score	**1 study:** 1 pFAS, 1 ARND/Others

GRADE ratings for attention

Certainty assessment						№ of patients		Effect		**Certainty**
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	
EXPOSURE STUDIES										
NEPSY-II: Visual attention										
Heavy										
1	serious[a]	not serious	serious[c]	serious[d,f]	none	108	165	-	**SMD 0.2 lower** (0.44 lower to 0.05 higher)	⊕○○○ Very Low
TOVA omission errors (ss), commission errors (ss), omission errors block 1, and commission errors block 1										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	serious[e,f]	none	30	30	-	**SMD 0.68 lower** (1.20 lower to 0.16 lower)	⊕⊕○○ Low
1	serious[a]	not serious	not serious	serious[e,f]	none	30	30	-	**SMD 0.57 lower** (1.09 lower to 0.06 lower)	⊕⊕○○ Low
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	55	55	-	**SMD 0.18 lower** (0.55 lower to 0.20 higher	⊕○○○ Very Low
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	54	54	-	**SMD 0.11 higher** (0.27 lower to 0.48 higher)	⊕○○○ Very Low
Leiter sustained attention										
Heavy										
1	serious[a]	not serious	serious[c]	serious[d,f]	none	109	168	-	**SMD 0.22 lower** (0.46 lower to 0.02 higher)	⊕⊕○○ Low
TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean)										
Light										
1	not serious	not serious	not serious	serious[d,f]	none	675	758	**aOR 1.17** (0.75 to 1.81		⊕⊕⊕○ Moderate
Moderate										
1	not serious	not serious	not serious	serious[d,f]	none	175	758	**aOR 1.37** (0.63 to 2.97)		⊕⊕⊕○ Moderate
Heavy										
1	not serious	not serious	not serious	serious[e,f]	none	20	758	**aOR 3.21**		⊕⊕⊕○ Moderate

								(1.08 to 9.53)		
TEACH selective (<1SD below the mean)										
Light										
1	not serious	not serious	not serious	serious[d,f]	none	675	758	**aOR 0.97** (0.61 to 1.54)		⊕⊕⊕◯ Moderate
Moderate										
1	not serious	not serious	not serious	serious[d,f]	none	175	758	**aOR 0.94** (0.45 to 1.95)		⊕⊕⊕◯ Moderate
Heavy										
1	not serious	not serious	not serious	very serious[d,e,f]	none	20	758	**aOR 3.22** (0.94 to 11.05)		⊕⊕◯◯ Low
TEACH sustained (<1SD below the mean)										
Light										
1	not serious	not serious	not serious	serious[d,f]	none	675	758	**aOR 1.17** (0.75 to 1.81)		⊕⊕⊕◯ Moderate
Moderate										
1	not serious	not serious	not serious	very serious[d,e,f]	none	175	758	**aOR 2.05** (0.95 to 4.41)		⊕⊕◯◯ Low
Heavy										
1	not serious	not serious	not serious	serious[e,f]	none	20	758	**aOR 4.19** (1.17 to 14.96)		⊕⊕⊕◯ Moderate
NES3 – Animal Following (number correct)										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	serious[e,f]	none	38	60	-	**SMD 0.95 lower** (1.38 lower to 0.52 lower)	⊕⊕◯◯ Low
D2 Test of Attention										
Any PAE										
1	serious[a]	not serious	serious[c]	serious[d,f]	none	28	28	-	**SMD 0.39 higher** (0.14 lower to 0.92 higher)	⊕◯◯◯ Very Low
CBCL Attention Caregiver Report (T-score)										
Very heavy										
1	serious[a]	not serious	not serious	serious[e,f]	none	20	19	-	**SMD 1.22 higher** (0.53 higher to 1.91 higher)	⊕⊕◯◯ Low
Confirmed unquantifiable										
4	serious[a]	serious[b]	not serious	serious[e]	none	179	276	-	**SMD 1.95 higher** (0.61 higher to 3.29 higher)	⊕◯◯◯ Very Low
Any PAE										
1	serious[a]	not serious	not serious	not serious	none	2518	7201	-	**SMD 0.10 higher** (0.05	⊕⊕⊕◯ Moderate

									higher to 0.15 higher)	
CBCL Attention Caregiver Report (OR) (Cut-offs unclear)										
Light										
1	not serious	not serious	not serious	serious[d,e]	none	208	690	**OR 1.68** (0.77, 3.68)		⊕⊕⊕◯ Moderate
Moderate										
1	serious	not serious	not serious	serious[d]	none	194	3609	**OR 0.6** (0.3, 1.2)	-	⊕⊕⊕◯ Moderate
Heavy										
2	serious[a]	not serious	not serious	serious[d]	none	164	4299	**OR 2.04** (0.73, 5.71)	-	⊕⊕◯◯ Low
0 studies for very heavy PAE										
YSR Attention Self-Report (OR) (Cut-offs unclear)										
Moderate										
1	serious[a]	not serious	not serious	serious[d]	none	194	3609	**OR 0.7** (0.3, 1.6)	-	⊕⊕◯◯ Low
Heavy										
1	serious[a]	not serious	not serious	serious[d]	**none**	107	3609	**OR 1.1** (0.4, 3.0)	-	⊕⊕◯◯ Low
0 studies for light or very heavy PAE										
DIAGNOSED STUDIES										
NEPSY Auditory Attention										
FASD										
6	serious[a]	serious[b]	not serious	serious[e]	none	330	444	-	**SMD 0.81 lower** (1.07 lower to 0.55 lower)	⊕◯◯◯ Very Low
NEPSY Response Set										
FASD										
6	serious[a]	serious[b]	not serious	serious[e]	none	328	448	-	**SMD 0.64 lower** (0.90 lower to 0.37 lower)	⊕◯◯◯ Very Low
Other Attention Measures (VIGIL/W: Visual Total Errors, Auditory Total Errors)										
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	46	53	-	**SMD 0.50 higher** (0.10 higher to 0.90 higher)	⊕⊕◯◯ Low
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	46	53	-	**SMD 0.02 lower** (0.37 lower to 0.42 higher)	⊕◯◯◯ Very Low
Other Attention Measures (CPT-II Omission Errors)										
ARND/Others										
1	serious[a]	not serious	not serious	serious[e,f]	none	22	21	-	**SMD 1.29 higher** (0.63 higher to 1.95 higher)	⊕⊕◯◯ Low
Other Attention Measures: IVA CPT Full Response Quotient (<2SD below population mean)										
pFAS										

No. of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Intervention	Control	Relative effect (OR)	Absolute effect (SMD)	Certainty
1	serious[a]	not serious	not serious	serious[e,f]	none	15/20	2/16	**OR 21.0** (3.49 to 126.3)	-	⊕⊕◯◯ Low

ARND/Others

| 1 | serious[a] | not serious | not serious | serious[e,f] | none | 13/24 | 2/16 | **OR 8.27** (1.53 to 44.62) | - | ⊕⊕◯◯ Low |

Other Selective/Sustained Attention Measures (TEACh-Map Mission, NES Animal Following (no. correct))

FASD

| 2 | serious[a] | serious[b] | not serious | very serious[d,e,f] | none | 55 | 60 | - | **SMD 0.19 higher** (1.17 lower to 1.55 higher) | ⊕◯◯◯ Very Low |

Ext: Attention – Caregiver Report: CBCL-C, CBRS (T-score)

FASD

| 6 | serious[a] | serious[b] | not serious | serious[e] | none | 189 | 1132 | - | **SMD 1.01 higher** (0.54 higher to 1.48 higher) | ⊕◯◯◯ Very Low |

FAS

| 2 | serious[a] | not serious | not serious | serious[e] | none | 30 | 796 | - | **SMD 0.62 higher** (0.17 higher to 1.07 higher) | ⊕⊕◯◯ Low |

pFAS

| 2 | serious[a] | serious[b] | not serious | serious[d,e] | none | 73 | 777 | - | **SMD 1.17 higher** (0.62 lower to 2.95 higher) | ⊕◯◯◯ Very Low |

ARND/Others

| 4 | serious[a] | serious[b] | not serious | serious[e] | none | 152 | 833 | - | **SMD 1.46 higher** (0.61 higher to 2.31 higher) | ⊕◯◯◯ Very Low |

Ext: Attention – Caregiver Report: CBCL-C (Attention Problems T-score >65 or ADHD T-score >65)

FASD

| 1 | serious[a] | not serious | not serious | serious[e,f] | none | 173/223 | 14/78 | **OR 15.82** (8.19 to 30.55) | - | ⊕⊕◯◯ Low |

Ext: Attention – Caregiver Report: DBD

pFAS

| 2 | serious[a] | serious[b] | not serious | very serious[d,e,f] | none | 45 | 117 | - | **SMD 1.06 higher** (0.23 lower to 2.36 higher) | ⊕◯◯◯ Very Low |

Ext: Attention – Teacher Report: TRF (T-score)

FASD

| 3 | serious[a] | not serious | not serious | not serious | none | 124 | 1048 | - | **SMD 0.78 higher** (0.59 higher to 0.97 higher) | ⊕⊕⊕◯ Moderate |

FAS

| 2 | serious[a] | not serious | not serious | not serious | none | 74 | 967 | - | **SMD 0.62 higher** (0.36 | ⊕⊕⊕◯ Moderate |

72

									higher to 0.89 higher)	
pFAS										
2	serious[a]	not serious	not serious	not serious	none	132	967	-	**SMD 0.38 higher** (0.11 higher to 0.66 higher)	⊕⊕⊕◯ Moderate
ARND/Others										
2	serious[a]	not serious	not serious	not serious	none	83	967	-	**SMD 0.91 higher** (0.68 higher to 1.14 higher)	⊕⊕⊕◯ Moderate
Ext: Attention – Teacher Report: DBD										
pFAS										
2	serious[a]	not serious	not serious	serious[e]	none	45	117	-	**SMD 0.84 higher** (0.48 higher to 1.19 higher)	⊕⊕◯◯ Low
Ext: Attention – Self Report: YSR										
pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	47	58	-	**SMD 1.98 higher** (1.51 higher to 2.45 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e,f]	none	34	58	-	**SMD 4.87 higher** (4.04 higher to 5.71 higher)	⊕⊕◯◯ Low

Notes: CI: confidence interval; SMD: standardized mean difference; OR: odds ratio.
Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I^2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CIs for overall estimate crossed the line of no effect; e) Wide CIs for overall estimate; f) optimal information size criteria not met

Meta-analyses for attention

EXPOSURE STUDIES

NEPSY Visual Attention (mean/SD)
Heavy PAE and NEPSY Visual Attention (mean/SD) (1 study)

Risk of bias legend
(A) Overall RoB

TOVA Omission Errors (standard score) (mean/SD)

Confirmed Unquantifiable PAE and TOVA Omission Errors (ss) (mean/SD) (1 study)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Lee et al 2004 (9-17yrs; TOVA)	66.1	30.77	30	86.5	28.29	30	100.0%	-0.68 [-1.20, -0.16]		●
Total (95% CI)			30			30	100.0%	-0.68 [-1.20, -0.16]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.56 (P = 0.01)

Confirmed Unquantifiable Control

Risk of bias legend
(A) Overall RoB

TOVA Commission Errors (standard score) (mean/SD)

Confirmed Unquantifiable PAE and TOVA Commission Errors (ss) (mean/SD) (1 study)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Lee et al 2004 (9-17yrs; TOVA)	81.9	21.76	30	95.1	23.53	30	100.0%	-0.57 [-1.09, -0.06]		●
Total (95% CI)			30			30	100.0%	-0.57 [-1.09, -0.06]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.18 (P = 0.03)

Control Confirmed Unquantifiable

Risk of bias legend
(A) Overall RoB

TOVA Omission Errors Block 1 (mean/SD)

Confirmed Unquantifiable PAE and TOVA Omission Errors Block 1 (mean/SD) (1 study)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Vaurio et al 2011 (6-16yrs; TOVA)	84.61	31.46	55	90.05	30.19	55	100.0%	-0.18 [-0.55, 0.20]		●
Total (95% CI)			55			55	100.0%	-0.18 [-0.55, 0.20]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.92 (P = 0.36)

Control Confirmed Unquantifiable

Risk of bias legend
(A) Overall RoB

Note: Vaurio et al 2011 also reports Block 2-4.

TOVA Commission Errors Block 1 (mean/SD)

Confirmed Unquantifiable PAE and TOVA Commission Errors Block 1 (mean/SD) (1 study)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Vaurio et al 2011 (6-16yrs; TOVA)	92.8	23.8	54	89.79	31.41	54	100.0%	0.11 [-0.27, 0.48]		●
Total (95% CI)			54			54	100.0%	0.11 [-0.27, 0.48]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.56 (P = 0.58)

Control Confirmed Unquantifiable

Risk of bias legend
(A) Overall RoB

Note: Vaurio et al 2011 also reports Block 2-4.

Selective/Sustained Attention: Leiter Sustained Attention (mean/SD)

Heavy PAE and Leiter Sustained Attention (ss) (mean/SD) (1 study)

Study or Subgroup	Heavy PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Coles et al 2021 (3.5-4.5yrs; Leiter-ss)	10.14	2.43	109	10.68	2.47	168	100.0%	-0.22 [-0.46, 0.02]		●
Total (95% CI)			109			168	100.0%	-0.22 [-0.46, 0.02]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.78 (P = 0.08)

Heavy PAE Control

Risk of bias legend
(A) Overall RoB

Note: Coles et al 2021 also reports Leiter Sustained Attention total correct (ss) (mean/SD).

Selective/Sustained Attention: TEACh-5 Selective/Sustained Attention (OR/Frequency)

Light PAE and TEACh-5 Selective/Sustained Attention (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Underbjerg et al 2012 (~5yrs; TEACh-5)	0.1528	0.2248	100.0%	1.17 [0.75, 1.81]		+
Total (95% CI)			100.0%	**1.17 [0.75, 1.81]**		
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.68 (P = 0.50)						

Risk of bias legend
(A) Overall RoB

Moderate PAE and TEACh-5 Selective/Sustained Attention (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Underbjerg et al 2012 (~5yrs; TEACh-5)	0.3133	0.3956	100.0%	1.37 [0.63, 2.97]		+
Total (95% CI)			100.0%	**1.37 [0.63, 2.97]**		
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.79 (P = 0.43)						

Risk of bias legend
(A) Overall RoB

Heavy PAE and TEACh-5 Selective/Sustained Attention (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Underbjerg et al 2012 (~5yrs; TEACh-5)	1.1657	0.5555	100.0%	3.21 [1.08, 9.53]		+
Total (95% CI)			100.0%	**3.21 [1.08, 9.53]**		
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.10 (P = 0.04)						

Risk of bias legend
(A) Overall RoB

Selective Attention: TEACh-5 Selective Attention (OR)

Light PAE and TEACh-5 Selective Attention (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Underbjerg et al 2012 (~5yrs; TEACh-5)	-0.0305	0.2358	100.0%	0.97 [0.61, 1.54]		+
Total (95% CI)			100.0%	**0.97 [0.61, 1.54]**		
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.13 (P = 0.90)						

Risk of bias legend
(A) Overall RoB

Moderate PAE and TEACh-5 Selective Attention (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Underbjerg et al 2012 (~5yrs; TEACh-5)	-0.0619	0.3723	100.0%	0.94 [0.45, 1.95]		+
Total (95% CI)			100.0%	**0.94 [0.45, 1.95]**		
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.17 (P = 0.87)						

Risk of bias legend
(A) Overall RoB

Heavy PAE and TEACh-5 Selective Attention (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Underbjerg et al 2012 (~5yrs; TEACh-5)	1.1694	0.6291	100.0%	3.22 [0.94, 11.05]		+
Total (95% CI)			100.0%	3.22 [0.94, 11.05]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.86 (P = 0.06)

Scale: 0.01 0.1 1 10 100 — Control / Heavy PAE

Risk of bias legend
(A) Overall RoB

Sustained Attention: TEACh-5 Selective Attention (OR)

Light PAE and TeaCh-5 Sustained Attention (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Underbjerg et al 2012 (~5yrs; TEACh-5)	0.1528	0.2248	100.0%	1.17 [0.75, 1.81]		+
Total (95% CI)			100.0%	1.17 [0.75, 1.81]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.68 (P = 0.50)

Scale: 0.01 0.1 1 10 100 — Control / Light PAE

Risk of bias legend
(A) Overall RoB

Moderate PAE and TeaCh-5 Sustained Attention (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Underbjerg et al 2012 (~5yrs; TEACh-5)	0.7178	0.3908	100.0%	2.05 [0.95, 4.41]		+
Total (95% CI)			100.0%	2.05 [0.95, 4.41]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.84 (P = 0.07)

Scale: 0.01 0.1 1 10 100 — Control / Moderate PAE

Risk of bias legend
(A) Overall RoB

Heavy PAE and TeaCh-5 Sustained Attention (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Underbjerg et al 2012 (~5yrs; TEACh-5)	1.4327	0.6493	100.0%	4.19 [1.17, 14.96]		+
Total (95% CI)			100.0%	4.19 [1.17, 14.96]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.21 (P = 0.03)

Scale: 0.01 0.1 1 10 100 — Control / Heavy PAE

Risk of bias legend
(A) Overall RoB

Note: Underbjerg et al 2012 also reports these measures as mean difference.

Other Attention Measures: NES3 Animal Following (mean/SD)

Confirmed Unquantifiable PAE and NES3 Animal Sorting (mean/SD) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2010 (7-21yrs; NES3-AF)	32.26	7.98	38	37.43	2.7	60	100.0%	-0.95 [-1.38, -0.52]		−
Total (95% CI)			38			60	100.0%	-0.95 [-1.38, -0.52]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.35 (P < 0.0001)

Scale: -4 -2 0 2 4 — Confirmed Unquantifiable / Control

Risk of bias legend
(A) Overall RoB

Note: NES-AF for Animal Following. Mattson 2010 also reports other NES measures.

Other Attention Measures: D2 Test of Attention – Net Result (mean/SD)

Any PAE and D2 Test of Attention – Net Result (mean/SD) (1 study)

Study or Subgroup	Any PAE Mean	Any PAE SD	Any PAE Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Furtado et al 2016 (11-12yrs; D2 attention)	299.32	70.09	28	275.21	49.72	28	100.0%	0.39 [-0.14, 0.92]		🔴
Total (95% CI)			28			28	100.0%	0.39 [-0.14, 0.92]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.45 (P = 0.15)

Risk of bias legend
(A) Overall RoB

Note: Furtado et al 2016 also reports D2 Test of Attention rough results and total errors.

Externalising Behaviour: CBCL Attention – Caregiver Report (T-score)

Very Heavy PAE and CBCL Attention - Caregiver (T-score) (1 study)

Study or Subgroup	Very Heavy PAE Mean	Very Heavy PAE SD	Very Heavy PAE Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Brown et al 1991 (4-6yrs; CBCL-C)	66.28	10.78	20	56.32	2.85	19	100.0%	1.22 [0.53, 1.91]		🔴
Total (95% CI)			20			19	100.0%	1.22 [0.53, 1.91]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.47 (P = 0.0005)

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and CBCL Attention - Caregiver (T-score) (4 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	Confirmed Unquantifiable SD	Confirmed Unquantifiable Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Gautam et al 2015 (7-16yrs; CBCL-C)	61	71	9	54	5	58	24.4%	0.27 [-0.43, 0.98]		🔴
Lee et al 2004 (9-17yrs; CBCL-C)	72.7	9.12	30	53.4	5.31	30	24.5%	2.55 [1.86, 3.25]		🔴
Vaurio et al 2011 (6-16yrs; CBCL-C)	71.64	10.55	55	56.87	9.49	55	25.5%	1.46 [1.04, 1.88]		🔴
Ware et al 2013 (6-18yrs; CBCL-C)	73.09	9.44	85	51.33	2.68	133	25.5%	3.47 [3.04, 3.90]		🔴
Total (95% CI)			179			276	100.0%	1.95 [0.61, 3.29]		

Heterogeneity: Tau² = 1.78; Chi² = 75.54, df = 3 (P < 0.00001); I² = 96%
Test for overall effect: Z = 2.86 (P = 0.004)

Risk of bias legend
(A) Overall RoB

Any PAE and CBCL Attention - Caregiver (T-score) (1 study)

Study or Subgroup	Any PAE Mean	Any PAE SD	Any PAE Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; CBCL-C)	54.2	6.3	2518	53.6	5.9	7201	100.0%	0.10 [0.05, 0.15]		🔴
Total (95% CI)			2518			7201	100.0%	0.10 [0.05, 0.15]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.31 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

Externalising Behaviour: CBCL Attention – Caregiver Report (OR)

Light PAE and CBCL Attention – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2009 (2, 5, 8yrs; CBCL-C)	0.5182	0.3997	100.0%	1.68 [0.77, 3.68]		🟢
Total (95% CI)			100.0%	1.68 [0.77, 3.68]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.30 (P = 0.19)

Risk of bias legend
(A) Overall RoB

Moderate PAE and CBCL Attention - Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Callaghan et al 2007 (~14yrs; CBCL-C)	-0.5093	0.3529	100.0%	0.60 [0.30, 1.20]		?
Total (95% CI)			100.0%	0.60 [0.30, 1.20]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.44 (P = 0.15)

Control Moderate PAE

Risk of bias legend
(A) Overall RoB

Note: O'Callaghan et al 2007 reports OR to one decimal place. Added OR and lower CI to revman, with upper CI auto-generated by revman.

Heavy PAE and CBCL Attention (OR) (2 studies)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2009 (2, 5, 8yrs; CBCL-C)	0.8286	0.7231	52.6%	2.29 [0.56, 9.45]		+
O'Callaghan et al 2007 (~14yrs; CBCL-C)	0.5872	0.762	47.4%	1.80 [0.40, 8.01]		?
Total (95% CI)			100.0%	2.04 [0.73, 5.71]		

Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = 0.82); I² = 0%
Test for overall effect: Z = 1.36 (P = 0.17)

Control Heavy PAE

Risk of bias legend
(A) Overall RoB

Note: O'Callaghan et al 2007 reports OR to one decimal place. Added OR and lower CI to revman, with upper CI auto-generated by revman.

Externalising Behaviour: Attention – Teacher Report
N/A

Externalising Behaviour: YSR Attention – Self Report (OR/Frequency)

Moderate PAE and YSR Attention – Self Report (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Callaghan et al 2007 (~14yrs; YSR)	-0.3567	0.4323	100.0%	0.70 [0.30, 1.63]		?
Total (95% CI)			100.0%	0.70 [0.30, 1.63]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)

Control Moderate PAE

Risk of bias legend
(A) Overall RoB

Note: O'Callaghan et al 2007 reports OR to one decimal place. Added OR and lower CI to revman, with upper CI auto-generated by revman.

Heavy PAE and YSR Attention – Self Report (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Callaghan et al 2007 (~14yrs; YSR)	0.0953	0.5161	100.0%	1.10 [0.40, 3.02]		?
Total (95% CI)			100.0%	1.10 [0.40, 3.02]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.18 (P = 0.85)

Control Heavy PAE

Risk of bias legend
(A) Overall RoB

Note: O'Callaghan et al 2007 reports OR to one decimal place. Added OR and lower CI to revman, with upper CI auto-generated by revman.

DIAGNOSED STUDIES

NEPSY-II Auditory Attention (mean/SD)

FASD and NEPSY Auditory Attention (mean/SD) (6 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McLachlan et al 2020 (7-19yrs; NEPSY-II)	7.6	4	65	11.1	2.4	69	17.9%	-1.06 [-1.43, -0.70]		?
Paolozza et al 2014a (5-17yrs; NEPSY-II)	7.5	3.3941	72	10.8	2.846	90	19.0%	-1.06 [-1.39, -0.73]		─
Popova et al 2019 (7-9yrs; NEPSY-II)	9.45	7.9	21	10.26	5.56	80	14.1%	-0.13 [-0.61, 0.35]		─
Rasmussen et al 2013 (6-16yrs; NEPSY-II)	8.12	1.56	32	8.94	1.47	30	13.4%	-0.53 [-1.04, -0.03]		─
Treit et al 2016 (5-19yrs; NEPSY-II)	7.1	4.1	103	10.3	3.1	135	21.3%	-0.89 [-1.16, -0.63]		─
Ware et al 2021 (6-18yrs; NEPSY-II)	8	4	37	11	2	40	14.3%	-0.95 [-1.42, -0.48]		─
Total (95% CI)			330			444	100.0%	-0.81 [-1.07, -0.55]		

Heterogeneity: Tau² = 0.06; Chi² = 13.19, df = 5 (P = 0.02); I² = 62%
Test for overall effect: Z = 6.15 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

NEPSY-II Response Set (mean/SD)

FASD and NEPSY Response Set (mean/SD) (6 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McLachlan et al 2020 (7-19yrs; NEPSY-II)	10	3	65	11.7	2.6	79	18.7%	-0.61 [-0.94, -0.27]		?
Paolozza et al 2014a (5-17yrs; NEPSY-II)	9.6	3.3941	72	11.4	2.846	90	19.3%	-0.58 [-0.89, -0.26]		─
Popova et al 2019 (7-9yrs; NEPSY-II)	7.22	7.5	21	11.13	5.88	80	14.0%	-0.62 [-1.11, -0.13]		─
Rasmussen et al 2013 (6-16yrs; NEPSY-II)	8.28	1.15	32	10.42	1.58	30	11.9%	-1.54 [-2.11, -0.97]		─
Treit et al 2016 (5-19yrs; NEPSY-II)	8.9	3.9	101	10.1	3.5	129	21.1%	-0.32 [-0.59, -0.06]		─
Ware et al 2021 (6-18yr; NEPSY-II)	11	2	37	12	2	40	15.0%	-0.49 [-0.95, -0.04]		─
Total (95% CI)			328			448	100.0%	-0.64 [-0.90, -0.37]		

Heterogeneity: Tau² = 0.07; Chi² = 14.56, df = 5 (P = 0.01); I² = 66%
Test for overall effect: Z = 4.70 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Other Attention Measures: VIGIL/W Measures (mean/SD)

FASD and VIGIL/W: Visual Total Errors (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 2002 (13-17yrs; VIGIL/W)	15.21	13.37	46	9.57	8.98	53	100.0%	0.50 [0.10, 0.90]		─
Total (95% CI)			46			53	100.0%	0.50 [0.10, 0.90]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.43 (P = 0.01)

Risk of bias legend
(A) Overall RoB

FASD and VIGIL/W: Auditory Total Errors (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 2002 (13-17yrs; VIGIL/W)	12.93	12.71	46	12.66	11.52	53	100.0%	0.02 [-0.37, 0.42]		─
Total (95% CI)			46			53	100.0%	0.02 [-0.37, 0.42]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.11 (P = 0.91)

Risk of bias legend
(A) Overall RoB

Note: Coles et al 2002 also reports VIGIL/W Visual and Auditory Commission and Omission Errors, and False Alarm/ and Total Errors.

Other Attention Measures: CPT-II Omission Errors (mean/SD)
ARND/Others and CPT-II Errors of Omission (mean/SD) (1 study)

Study or Subgroup	ARND/Others			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
O'Conaill et al 2015 (10-14yrs; CPT-II; ARND)	59.3	13.9	22	45.4	5.2	21	100.0%	1.29 [0.63, 1.95]		●
Total (95% CI)			22			21	100.0%	1.29 [0.63, 1.95]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.81 (P = 0.0001)

Risk of bias legend
(A) Overall RoB

Note: O'Conaill et al 2015 also reports CPT-II cognitive/inattention.

Other Attention Measures: Frequency <2SD on IVA CPT Full Response Quotient (%)
pFAS and IVA CPT Full Response Quotient (%) (1 study)

Study or Subgroup	pFAS		Control		Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
	Events	Total	Events	Total				
Astley et al 2009b (8-16yrs; IVA CPT; FAS/pFAS)	15	20	2	16	100.0%	21.00 [3.49, 126.32]		●
Total (95% CI)		20		16	100.0%	21.00 [3.49, 126.32]		
Total events	15		2					

Heterogeneity: Not applicable
Test for overall effect: Z = 3.33 (P = 0.0009)

Risk of bias legend
(A) Overall RoB

ARND/Others and IVA CPT Full Response Quotient (%) (1 study)

Study or Subgroup	ARND/Others		Control		Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
	Events	Total	Events	Total				
Astley et al 2009b (8-16yrs; IVA CPT; SE/AE)	13	24	2	16	100.0%	8.27 [1.53, 44.62]		●
Total (95% CI)		24		16	100.0%	8.27 [1.53, 44.62]		
Total events	13		2					

Heterogeneity: Not applicable
Test for overall effect: Z = 2.46 (P = 0.01)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009 also reports ND/AE. Astley et al 2009 also reports these measures as mean/SD.

Other Selective/Sustained Attention Measures:
TEACh Map Mission + NES3 Animal Following (number correct) (mean/SD)
FASD and TEACh Map Mission/NES3 Animal Following (mean/SD) (2 studies)

Study or Subgroup	FASD			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Lane et al 2014 (7-12yrs; TEA-Ch Map Mission)	11.79	3.09	14	8.86	3.06	14	47.1%	0.93 [0.14, 1.71]		●
Mattson et al 2010 (7-21yrs; NES3-AF)	35.46	7.25	41	37.89	2.15	46	52.9%	-0.46 [-0.89, -0.04]		●
Total (95% CI)			55			60	100.0%	0.19 [-1.17, 1.55]		

Heterogeneity: Tau² = 0.86; Chi² = 9.25, df = 1 (P = 0.002); I² = 89%
Test for overall effect: Z = 0.28 (P = 0.78)

Risk of bias legend
(A) Overall RoB

Note: NES3-AF for animal following. Mattson et al 2010 also reports other NES3 subdomains. Lane et al 2014 also reports other TEA-Ch subdomains: Sky Search, Creature Counting, and Opposite Worlds.

Externalising Behaviour: CBCL/CBRS Attention – Caregiver Report (T-score)

FASD and CBCL/CBRS Attention - Caregiver (T-score) (6 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lane et al 2014 (7-12yrs; CPRS)	77.9	9.97	13	45.5	2.88	12	6.8%	4.19 [2.70, 5.68]		🔴
Mattson & Riley 2000 (4-16yrs; CBCL-C)	73.3	9.8	33	57.5	11.19	33	16.9%	1.48 [0.94, 2.03]		🔴
May et al 2020a (6-7yrs; CBCL-C)	59.5	10.5	38	53.8	6.4	273	19.6%	0.81 [0.46, 1.16]		🔴
May et al 2020b (6-7yrs; CBCL-C)	59.3	9.2	49	55.2	7.6	444	20.2%	0.53 [0.23, 0.82]		🔴
May et al 2020c (6-7yrs; CBCL-C)	59.9	10.4	37	54.4	6.4	331	19.6%	0.80 [0.45, 1.14]		🔴
Popova et al 2019 (7-9yrs; CBCL-C)	56.64	17.72	19	52.69	9.13	39	16.9%	0.31 [-0.24, 0.86]		🔴
Total (95% CI)			189			1132	100.0%	1.01 [0.54, 1.48]		

Heterogeneity: Tau² = 0.26; Chi² = 32.11, df = 5 (P < 0.00001); I² = 84%
Test for overall effect: Z = 4.22 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Attention - Caregiver (T-score) (2 studies)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	61.4	10.1	5	56.8	8.1	761	26.4%	0.57 [-0.31, 1.45]		🔴
Coles et al 1997 (7-8yrs; CBCL-C)	61.47	9.96	25	55.97	7.21	35	73.6%	0.64 [0.12, 1.17]		🔴
Total (95% CI)			30			796	100.0%	0.62 [0.17, 1.07]		

Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.89); I² = 0%
Test for overall effect: Z = 2.70 (P = 0.007)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Attention - Caregiver (T-score) (2 studies)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; CBCL-C; FAS/pFAS)	70.8	11.2	29	51.2	1.9	16	48.1%	2.11 [1.35, 2.88]		🔴
Chambers et al 2019 (6-7yrs; CBCL-C)	59.2	9.9	44	56.8	8.1	761	51.9%	0.29 [-0.01, 0.60]		🔴
Total (95% CI)			73			777	100.0%	1.17 [-0.62, 2.95]		

Heterogeneity: Tau² = 1.57; Chi² = 18.92, df = 1 (P < 0.0001); I² = 95%
Test for overall effect: Z = 1.28 (P = 0.20)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Attention (T-score) (4 studies)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; CBCL-C; SE)	71.5	10.3	24	51.2	1.9	16	22.3%	2.46 [1.61, 3.31]		🔴
Chambers et al 2019 (6-7yrs; CBCL-C; ARND)	65.7	10.2	44	56.8	8.1	761	27.7%	1.08 [0.77, 1.39]		🔴
Coles et al 1997 (7-8yrs; CBCL; non-syndromal)	58.37	7.82	62	55.97	7.21	35	26.9%	0.31 [-0.10, 0.73]		🔴
O'Conaill et al 2015 (10-14yrs; CPRS; ARND)	71.7	12.4	22	49.4	5.2	21	23.1%	2.28 [1.50, 3.07]		🔴
Total (95% CI)			152			833	100.0%	1.46 [0.61, 2.31]		

Heterogeneity: Tau² = 0.65; Chi² = 32.09, df = 3 (P < 0.00001); I² = 91%
Test for overall effect: Z = 3.37 (P = 0.0008)

Risk of bias legend
(A) Overall RoB

Externalising Behaviour: CBCL Attention – Caregiver Report (OR/Frequency)

FASD and Frequency of Clinical CBCL Attention Score - Caregiver (1 study)

Study or Subgroup	FASD Events	FASD Total	Control Events	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Mattson et al 2023 (4-17yrs; CBCL-C)	173	223	14	78	100.0%	15.82 [8.19, 30.55]		🔴
Total (95% CI)		223		78	100.0%	15.82 [8.19, 30.55]		
Total events	173		14					

Heterogeneity: Not applicable
Test for overall effect: Z = 8.22 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Externalising Behaviour: DBD Attention – Caregiver Report (mean/SD)

pFAS and DBD Attention (mean/SD) (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008a (6-7yrs; DBD-C; FAS/pFAS)	1.17	1.87	23	0.52	1.44	57	50.5%	0.41 [-0.08, 0.90]		?
Kodituwakku et al 2006b (6-7yrs; DBD-C; FAS/pFAS)	4.32	3.46	22	0.65	1.31	60	49.5%	1.73 [1.17, 2.29]		?
Total (95% CI)			45			117	100.0%	1.06 [-0.23, 2.36]		

Heterogeneity: Tau² = 0.80; Chi² = 12.19, df = 1 (P = 0.0005); I² = 92%
Test for overall effect: Z = 1.61 (P = 0.11)

Risk of bias legend
(A) Overall RoB

Note: Kodituwakku et al 2006b includes one participant with an ARND diagnosis.

Externalising Behaviour: CBCL/CBRS Attention – Teacher Report (T-score)

FASD and CBCL Attention – Teacher (T-score) (6 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; TRF-T)	59.8	9.6	38	54	6.1	273	29.8%	0.87 [0.53, 1.22]		−
May et al 2020b (6-7yrs; TRF-T)	58.1	8.9	49	53.6	6.5	444	40.2%	0.66 [0.37, 0.96]		−
May et al 2020c (6-7yrs; TRF-T)	57.6	9.2	37	53	4.8	331	30.0%	0.85 [0.51, 1.20]		−
Total (95% CI)			124			1048	100.0%	0.78 [0.59, 0.97]		

Heterogeneity: Tau² = 0.00; Chi² = 1.03, df = 2 (P = 0.60); I² = 0%
Test for overall effect: Z = 8.11 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Attention – Teacher (T-score) (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	59.6	6.9	5	53.6	6.1	761	9.0%	0.98 [0.10, 1.86]		−
May et al 2016 (6-7yrs; TRF-T)	17.2	14.1	69	10.3	10.8	206	91.0%	0.59 [0.31, 0.86]		−
Total (95% CI)			74			967	100.0%	0.62 [0.36, 0.89]		

Heterogeneity: Tau² = 0.00; Chi² = 0.70, df = 1 (P = 0.40); I² = 0%
Test for overall effect: Z = 4.62 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Attention – Teacher (T-score) (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	55	7	44	53.6	6.1	761	45.4%	0.23 [-0.08, 0.53]		−
May et al 2016 (6-7yrs; TRF-T)	16.3	13.6	88	10.3	10.8	206	54.6%	0.51 [0.26, 0.76]		−
Total (95% CI)			132			967	100.0%	0.38 [0.11, 0.66]		

Heterogeneity: Tau² = 0.02; Chi² = 1.98, df = 1 (P = 0.16); I² = 49%
Test for overall effect: Z = 2.70 (P = 0.007)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Attention (T-score) (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	58.9	7.4	44	53.6	6.1	761	57.0%	0.86 [0.55, 1.16]		−
May et al 2016 (6-7yrs; TRF-T; ARND)	21	11.7	39	10.3	10.8	206	43.0%	0.97 [0.62, 1.33]		−
Total (95% CI)			83			967	100.0%	0.91 [0.68, 1.14]		

Heterogeneity: Tau² = 0.00; Chi² = 0.24, df = 1 (P = 0.62); I² = 0%
Test for overall effect: Z = 7.68 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Externalising Behaviour: DBD Attention – Teacher Report (mean/SD)

pFAS and DBD Attention – Teacher (mean/SD) (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008a (6-7yrs; DBD-T; FAS/pFAS)	2.17	3.02	23	0.6	1.83	57	51.6%	0.70 [0.20, 1.19]		?
Kodituwakku et al 2006b (6-7yrs; DBD-T; FAS/pFAS)	2.18	2.97	22	0.45	0.98	60	48.4%	0.99 [0.47, 1.50]		?
Total (95% CI)			45			117	100.0%	0.84 [0.48, 1.19]		

Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 4.60 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Kodituwakku et al 2006b includes one participant with an ARND diagnosis.

Externalising Behaviour: YSR Attention – Self Report (T-score)

pFAS and YSR Attention – Self Report (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR)	6.76	0.68	47	5.46	0.63	58	100.0%	1.98 [1.51, 2.45]		–
Total (95% CI)			47			58	100.0%	1.98 [1.51, 2.45]		

Heterogeneity: Not applicable
Test for overall effect: Z = 8.22 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and YSR Attention – Self Report (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR)	9.21	0.95	34	5.46	0.63	58	100.0%	4.87 [4.04, 5.71]		–
Total (95% CI)			34			58	100.0%	4.87 [4.04, 5.71]		

Heterogeneity: Not applicable
Test for overall effect: Z = 11.44 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Summary of available outcomes for **executive functioning**

Executive Function			
Study type	**Outcome**	**Data**	**# studies**
Exposure Studies	**NEPSY**: Speeded Naming	mean/SD	**4 studies**: 1 heavy, 3 confirmed unquantifiable
	NEPSY: Inhibition Errors (ss)	mean/SD	**1 studies**: 1 confirmed unquantifiable
	NEPSY: Inhibition Errors (raw)	mean/SD	**1 study**: 1 confirmed unquantifiable
	Wisconsin Card Sorting Test (WCST): Composite	mean/SD	**2 studies**: 2 confirmed unquantifiable
	WCST: Total Errors (raw)	mean/SD	**1 studies**: 1 Any PAE
	NIH Toolbox: Dimensional Change Card Sort	mean/SD	**1 study**: 1 light, 1 moderate, 1 any PAE
	Verbal Fluency: D-KEFS (total correct letter)	mean/SD	**3 studies**: 3 confirmed unquantifiable
	Letter Fluency: F-A-S test (words/mins)	mean/SD	**1 study**: 1 confirmed unquantifiable
	Verbal Fluency: D-KEFS (Verbal Fluency Switching)	mean/SD	**3 studies**: 3 confirmed unquantifiable
	Category Fluency: McCarthy, D-KEFS	mean/SD	**2 studies**: 2 confirmed unquantifiable
	Other D-KEFS: Tower Test (total)	mean/SD	**2 studies**: 2 confirmed unquantifiable

	Other D-KEFS: Multiple other subdomains (colour inference, trail making, tower test).	mean/SD	3 studies, all different measures
	BRIEF Global Executive Composite – Caregiver Report	mean difference/ mean/SD	**2 studies:** 1 light, moderate, heavy, 1 confirmed unquantifiable
	BRIEF Behaviour Regulation Index – Caregiver Reports	mean difference/ mean/SD	**2 studies:** 1 light, moderate, heavy, 1 confirmed unquantifiable
	BRIEF Behaviour Regulation Index – Teacher Report	mean difference	**1 study:** light, moderate, heavy
	BRIEF Metacognition Index – Caregiver Report	mean difference/ mean/SD	**2 studies:** 1 light, moderate, heavy, 1 confirmed unquantifiable
	BRIEF Metacognition Index – Teacher Report	mean difference	**1 study:** light, moderate, heavy
	BRIEF 8 Subdomains - Caregiver	mean/SD	**2 studies:** 2 confirmed unquantifiable
Diagnosed Studies	**NEPSY**: Speeded Naming	mean/SD	**5 studies:** 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Other
	NEPSY: INN	mean/SD	**9 studies:** 8 FASD, 1 FAS, 1 pFAS, 2 ARND/Other
	NEPSY: INI	mean/SD	**10 studies:** 9 FASD, 1 FAS, 1 pFAS, 2 ARND/Other
	NEPSY: INS	mean/SD	**9 studies:** 8 FASD, 1 FAS, 1 pFAS, 2 ARND/Other
	NEPSY: INN vs INI	mean/SD	**5 studies:** 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Other
	NEPSY: Animal Sorting	mean/SD	**6 studies:** 6 FASD
	WCST: Multiple sub-domains	mean/SD	**4 studies:** 2 FASD, 2 pFAS, 2 ARND/Other (all different measures)
	Letter Fluency: D-KEFS, NEPSY-II (total correct)	mean/SD	**4 studies:** 3 FAS, 1 pFAS, 1 ARND/Others
	Letter Fluency: D-KEFS (speed)	mean/SD	**1 study:** 1 FAS, 1 ARND/Others
	Letter Fluency: F-A-S test (words/mins)	mean/SD	**1 study:** 1 FASD
	Verbal Fluency: D-KEFS (Verbal Fluency Switching)	mean/SD	**3 studies:** 1 FASD, 2 FAS, 1 ARND/Others
	Category Fluency: D-KEFS, NEPSY-II (total correct)	mean/SD	**3 studies:** 1 FASD, 2 FAS
	Category Fluency: F-A-S test (words/min)	mean/SD	**1 study:** 1 FASD
	Other D-KEFS Measures: Any age, incl: D-KEFS Tower Test (total)	mean/SD	**2 studies:** 2 FASD
	Other D-KEFS Measures: Any age, incl: Multiple other subdomains (colour inference, trail making, tower test)	mean/SD	**5 studies:** 2 FAS, 1 pFAS, 1 ARND/Others (all different measures/units)
	Other Measures: Trail Making Test Trial B, Test of Executive Function	mean/SD	**3 studies:** 3 FASD
	BRIEF Global Executive Composite – Caregiver Report	T-score	**5 studies:** 3 FASD, 2 pFAS, 2 ARND/Others
	BRIEF Behaviour Regulation Index – Caregiver Report	T-score	**5 studies:** 3 FASD, 2 pFAS, 2 ARND/Others
	BRIEF Behaviour Regulation Index – Teacher Report	T-score	**1 study:** 1 FASD
	BRIEF Metacognition Index – Caregiver Report	T-score	**5 studies:** 3 FASD, 2 pFAS, 2 ARND/Others
	BRIEF Metacognition Index – Teacher Report	T-score	**1 study:** 1 FASD

	BRIEF Other Subdomains – Caregiver: Inhibit, Shift, Monitor, Plan/Organise, Working Memory	T-score	**3 studies:** 2 FASD (inhibit + shift), 1 FASD (all others), 1 ARND/Others

GRADE ratings for executive functioning

Certainty assessment						№ of patients		Effect		Certainty
№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	
EXPOSURE STUDIES										
NEPSY Speeded Naming										
Heavy										
1	serious[a]	not serious	serious[c]	serious[e,f]	none	82	132	-	**SMD 0.64 lower** (0.92 lower to 0.35 lower)	⊕◯◯◯ Very Low
Confirmed unquantifiable										
3	serious[a]	serious[b]	not serious	serious[e]	none	222	238	-	**SMD 0.57 lower** (0.96 lower to 0.17 lower)	⊕◯◯◯ Very Low
NEPSY Inhibition errors (ss)										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	serious[f]	none	142	160	-	**SMD 0.68 lower** (0.91 lower to 0.44 lower)	⊕⊕◯◯ Low
NEPSY Inhibition errors (raw)										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	25	16	-	**SMD 0.25 higher** (0.38 lower to 0.88 higher)	⊕◯◯◯ Very Low
Wisconsin Card Sorting Test (WCST): Composite										
Confirmed unquantifiable										
2	serious[a]	not serious	not serious	serious[e,f]	none	100	113	-	**SMD 0.56 lower** (0.95 lower to 0.17 lower)	⊕⊕◯◯ Low
Wisconsin Card Sorting Test (WCST): Total Errors (raw)										
Any PAE										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	28	28	-	**SMD 0.36 higher** (0.17 lower to 0.89 higher)	⊕◯◯◯ Very Low
NIH Toolbox: Dimensional Change Card Sort										
Light PAE										
1	serious[a]	not serious	not serious	serious[d]	none	93	6669	-	**SMD 0.18 higher** (0.03 lower to 0.38 higher)	⊕⊕◯◯ Low
Moderate PAE										
1	serious[a]	not serious	not serious	not serious	none	755	6669	-	**SMD 0.16 higher** (0.08 higher to 0.23 higher)	⊕⊕⊕◯ Moderate
Any PAE										

1	serious[a]	not serious	not serious	not serious	none	2518	7501	-	**SMD 0.13 higher** (0.08 higher to 0.17 higher)	⊕⊕⊕◯ Moderate

Verbal Fluency: D-KEFS (total correct letter)

Confirmed unquantifiable

3	serious[a]	not serious	not serious	not serious	none	388	314	-	**SMD 0.90 lower** (1.07 lower to 0.73 lower)	⊕⊕⊕◯ Moderate

Verbal Fluency: D-KEFS (Verbal Fluency Switching)

Confirmed unquantifiable

3	serious[a]	not serious	not serious	not serious	none	389	378	-	**SMD 1.07 lower** (1.33 lower to 0.82 lower)	⊕⊕⊕◯ Moderate

Category Fluency: McCarthy, D-KEFS

Confirmed unquantifiable

2	serious[a]	serious[b]	not serious	serious[e,f]	none	84	273	-	**SMD 0.61 lower** (1.54 lower to 0.32 lower)	⊕◯◯◯ Very Low

D-KEFS: Tower Test (total achievement)

Confirmed unquantifiable

2	serious[a]	not serious	not serious	not serious	none	231	205	-	**SMD 0.78 lower** (0.98 lower to 0.58 lower)	⊕⊕⊕◯ Moderate

BRIEF Global Executive Composite – Caregiver Report

Light

1	not serious	not serious	not serious	serious[d]	none	675	758	-	**SMD 0.06 higher** (0.04 lower to 0.17 higher)	⊕⊕⊕◯ Moderate

Moderate

1	not serious	not serious	not serious	serious[d]	none	175	758	-	**SMD 0.00 lower** (0.17 lower to 0.16 higher)	⊕⊕⊕◯ Moderate

Heavy

1	not serious	not serious	not serious	serious[d,e]	none	20	758	-	**SMD 0.05 higher** (0.39 lower to 0.5 higher)	⊕⊕⊕◯ Moderate

Confirmed Unquantifiable

1	serious[a]	not serious	not serious	serious[e,f]	none	28	15	-	**SMD 4.63 higher** (3.43 higher to 5.84 higher)	⊕⊕◯◯ Low

0 studies for very heavy or any pae

BRIEF Behaviour Regulation Index – Caregiver Reports

Light

1	not serious	not serious	not serious	serious[d]	none	675	758	-	**SMD 0.07 higher** (0.04 lower to 0.17 higher)	⊕⊕⊕◯ Moderate

Moderate

1	not serious	not serious	not serious	serious[d]	none	175	758	-	**SMD 0.01 lower** (0.18 lower to 0.15 higher)	⊕⊕⊕◯ Moderate

Heavy

1	not serious	not serious	not serious	serious[d,e]	none	20	758	-	**SMD 0.20 higher** (0.24 lower to 0.64 higher)	⊕⊕⊕◯ Moderate

Confirmed Unquantifiable										
1	serious[a]	not serious	not serious	serious[e,f]	none	28	15	-	**SMD 3.00 higher** (2.09 higher to 3.92 higher)	⊕⊕◯◯ Low
0 studies for very heavy, unquantified or any pae										
BRIEF Behaviour Regulation Index – Teacher Report										
Light										
1	not serious	not serious	not serious	serious[d]	none	675	758	-	**SMD 0.01 lower** (0.11 lower to 0.09 higher)	⊕⊕⊕◯ Moderate
Moderate										
1	not serious	not serious	not serious	serious[d]	none	175	758	-	**SMD 0.08 lower** (0.25 lower to 0.08 higher)	⊕⊕⊕◯ Moderate
Heavy										
1	not serious	not serious	not serious	serious[d,e]	none	20	758	-	**SMD 0.19 lower** (0.63 lower to 0.26 higher)	⊕⊕⊕◯ Moderate
0 studies for very heavy or any pae										
BRIEF Metacognition Index – Caregiver Report										
Light										
1	not serious	not serious	not serious	serious[d]	none	675	758	-	**SMD 0.09** (0.01 lower to 0.20 higher)	⊕⊕⊕◯ Moderate
Moderate										
1	not serious	not serious	not serious	serious[d,e]	none	175	758	-	**SMD 0.01 higher** (0.16 lower to 0.17 higher)	⊕⊕⊕◯ Moderate
Heavy										
1	not serious	not serious	not serious	serious[d,e]	none	20	758	-	**SMD 0.38 higher** (0.07 lower to 0.82 higher)	⊕⊕⊕◯ Moderate
Confirmed Unquantifiable										
1	serious[a]	not serious	not serious	serious[e,f]	none	28	15	-	**SMD 5.19 higher** (3.88 higher to 6.50 higher)	⊕⊕◯◯ Low
0 studies for very heavy or any pae										
BRIEF Metacognition Index – Teacher Report										
Light										
1	not serious	not serious	not serious	serious[d]	none	675	758	-	**SMD 0.02 higher** (0.08 lower to 0.12 higher)	⊕⊕⊕◯ Moderate
Moderate										
1	not serious	not serious	not serious	serious[d]	none	175	758	-	**SMD 0.02 lower** (0.18 lower to 0.15 higher)	⊕⊕⊕◯ Moderate
Heavy										
1	not serious	not serious	not serious	serious[d,e]	none	20	758	-	**SMD 0.21 lower** (0.66 lower to 0.23 higher)	⊕⊕⊕◯ Moderate
0 studies for very heavy, unquantified or any pae										
BRIEF Subdomains – Caregiver Report: Inhibit										
Confirmed Unquantifiable										

2	serious[a]	serious[b]	not serious	serious[e]	none	101	302	-	**SMD 2.94 higher** (1.39 higher to 4.49 higher)	⊕◯◯◯ Very Low

BRIEF Subdomains – Caregiver Report: Shift

Confirmed Unquantifiable

2	serious[a]	not serious	not serious	serious[e]	none	101	302	-	**SMD 2.84 higher** (2.49 higher to 3.19 higher)	⊕⊕◯◯ Low

BRIEF Subdomains – Caregiver Report: Emotional Control

Confirmed Unquantifiable

2	serious[a]	not serious	not serious	serious[e]	none	101	302	-	**SMD 2.30 higher** (1.97 higher to 2.62 higher)	⊕◯◯◯ Very Low

BRIEF Subdomains – Caregiver Report: Initiate

Confirmed Unquantifiable

2	serious[a]	not serious	not serious	serious[e]	none	101	302	-	**SMD 3.46 higher** (2.64 higher to 4.28 higher)	⊕⊕◯◯ Low

BRIEF Subdomains – Caregiver Report: Working Memory

Confirmed Unquantifiable

2	serious[a]	serious[b]	not serious	serious[e]	none	101	302	-	**SMD 4.71 higher** (2.02 higher to 7.41 higher)	⊕◯◯◯ Very Low

BRIEF Subdomains – Caregiver Report: Plan/Organise

Confirmed Unquantifiable

2	serious[a]	not serious	not serious	serious[e]	none	101	302	-	**SMD 4.14 higher** (3.70 higher to 4.58 higher)	⊕⊕◯◯ Low

BRIEF Subdomains – Caregiver Report: Monitor

Confirmed Unquantifiable

2	serious[a]	not serious	not serious	serious[e]	none	101	302	-	**SMD 3.95 higher** (3.52 higher to 4.38 higher)	⊕⊕◯◯ Low

BRIEF Subdomains – Caregiver Report: Organisation of Materials

Confirmed Unquantifiable

2	serious[a]	not serious	not serious	serious[e]	none	101	302	-	**SMD 2.18 higher** (1.82 higher to 2.55 higher)	⊕⊕◯◯ Low

DIAGNOSED STUDIES

NEPSY: Speeded Naming

FASD

4	serious[a]	serious[b]	not serious	serious[e]	none	156	935	-	**SMD 0.84 lower** (1.33 lower to 0.34 lower)	⊕◯◯◯ Very Low

FAS

1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.53 higher** (0.35 lower to 1.41 higher)	⊕⊕◯◯ Low

pFAS

1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 0.41 lower** (0.71 lower to 0.1 lower)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.06 lower** (0.37 lower to 0.24 higher)	⊕⊕◯◯ Low

NEPSY: INN

FASD

8	serious[a]	serious[b]	not serious	not serious	none	428	1258	-	**SMD 0.78 lower** (1.02 lower to 0.53 lower)	⊕⊕◯◯ Low

FAS

1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.00** (0.88 lower to 0.88 higher)	⊕⊕◯◯ Low

pFAS

1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.03 lower** (0.33 lower to 0.28 higher)	⊕⊕◯◯ Low

ARND/Others

2	serious[a]	not serious	not serious	serious[d,e]	none	66	860	-	**SMD 0.32 lower** (0.65 lower to 0.01 higher)	⊕⊕◯◯ Low

NEPSY: INI

FASD

9	serious[a]	serious[b]	not serious	not serious	none	431	1336	-	**SMD 0.81 lower** (1.00 lower to 0.61 lower)	⊕⊕◯◯ Low

FAS

1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.34 lower** (1.22 lower to 0.54 higher)	⊕⊕◯◯ Low

pFAS

1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.20 lower** (0.50 lower to 0.10 higher)	⊕⊕◯◯ Low

ARND/Other

2	serious[a]	not serious	not serious	not serious	none	66	851	-	**SMD 0.32 lower** (0.58 lower to 0.07 lower)	⊕⊕⊕◯ Moderate

NEPSY: INS

FASD

8	serious[a]	serious[b]	not serious	serious[e]	none	424	1262	-	**SMD 0.85 lower** (1.19 lower to 0.51 lower)	⊕◯◯◯ Very Low

FAS

1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.44 higher** (0.44 lower to 1.32 higher)	⊕⊕◯◯ Low

pFAS

1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.16 lower** (0.46 lower to 0.15 higher)	⊕⊕◯◯ Low

ARND/Other

2	serious[a]	serious[b]	not serious	serious[d,e]	none	66	851	-	**SMD 0.34 lower** (0.94 lower to 0.26 higher)	⊕◯◯◯ Very Low

NEPSY: INN vs INI										
FASD										
4	serious[a]	not serious	not serious	not serious	none	129	987	-	**SMD 0.32 lower** (0.50 lower to 0.13 lower)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.36 lower** (1.24 lower to 0.52 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.24 lower** (0.55 lower to 0.06 higher)	⊕⊕◯◯ Low
ARND/Other										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.21 lower** (0.51 lower to 0.09 higher)	⊕⊕◯◯ Low
NEPSY: Animal Sorting										
FASD										
6	serious[a]	serious[b]	not serious	serious[e]	none	330	407	-	**SMD 1.02 lower** (1.40 lower to 0.65 lower)	⊕◯◯◯ Very Low
WCST: Perseverative Errors (ss), Total Errors (ss), Preservative responses (ss), Preservative responses (raw), No. of Categories Completed (ss)										
FASD (Perseverative Errors - ss)										
1	serious[a]	not serious	not serious	serious[e,f]	none	20	20	-	**SMD 0.89 higher** (0.24 higher to 1.55 higher)	⊕⊕◯◯ Low
pFAS (Total Errors - ss)										
1	serious[a]	not serious	not serious	serious[e,f]	none	18	16	-	**SMD 1.29 lower** (2.03 lower to 0.54 lower)	⊕⊕◯◯ Low
ARND/Others (Total Errors - ss)										
1	serious[a]	not serious	not serious	serious[e,f]	none	24	16	-	**SMD 1.42 lower** (2.14 lower to 0.71 lower)	⊕⊕◯◯ Low
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	21	7	-	**SMD 1.16 lower** (2.07 lower to 0.24 lower)	⊕⊕◯◯ Low
pFAS (Preservative responses – Raw)										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	25	14	-	**SMD 0.59 higher** (0.08 lower to 1.26 higher)	⊕◯◯◯ Very Low
ARND/Others (Preservative responses – Raw)										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	62	14	-	**SMD 0.12 lower** (0.70 lower to 0.46 higher)	⊕◯◯◯ Very Low
Verbal Fluency: D-KEFS, NEPSY-II (total correct Letter)										
FAS										
3	serious[a]	not serious	not serious	serious[e]	none	143	252	-	**SMD 1.09 lower** (1.46 lower to 0.71 lower)	⊕⊕◯◯ Low
pFAS										

1	seriousª	not serious	not serious	serious^(e,f)	none	24	32	-	**SMD 0.80 lower** (1.35 lower to 0.25 lower)	⊕⊕◯◯ Low
ARND/Others										
1	seriousª	not serious	not serious	serious^f	none	117	185	-	**SMD 0.83 lower** (1.07 lower to 0.59 lower)	⊕⊕◯◯ Low
Letter Fluency: D-KEFS (speed)										
FAS										
1	seriousª	not serious	not serious	very serious^(d,e,f)	none	10	10	-	**SMD 0.85 lower** (1.77 lower to 0.08 higher)	⊕◯◯◯ Very Low
ARND/Others										
1	seriousª	not serious	not serious	very serious^(d,e,f)	none	8	10	-	**SMD 0.74 lower** (1.71 lower to 0.23 higher)	⊕◯◯◯ Very Low
Letter Fluency: F-A-S test (words/mins)										
FASD										
1	seriousª	not serious	not serious	serious^(e,f)	none	21	21	-	**SMD 1.72 lower** (2.43 lower to 1.00 lower)	⊕⊕◯◯ Low
Verbal Fluency: D-KEFS (Verbal Fluency Switching)										
FASD										
1	seriousª	not serious	not serious	serious^(e,f)	none	47	46	-	**SMD 0.44 lower** (0.85 lower to 0.03 lower)	⊕⊕◯◯ Low
FAS										
2	seriousª	not serious	not serious	serious^f	none	120	231	-	**SMD 0.97 lower** (1.21 lower to 0.74 lower)	⊕⊕◯◯ Low
ARND/Others										
1	seriousª	not serious	not serious	serious^f	none	117	185	-	**SMD 0.85 lower** (1.09 lower to 0.61 lower)	⊕⊕◯◯ Low
Category Fluency: D-KEFS (total correct)										
FASD										
1	seriousª	not serious	not serious	serious^(e,f)	none	73	47	-	**SMD 0.77 lower** (1.15 lower to 0.39 lower)	⊕⊕◯◯ Low
FAS										
2	seriousª	not serious	not serious	serious^(e,f)	none	64	67	-	**SMD 0.60 lower** (1.11 lower to 0.09 lower)	⊕⊕◯◯ Low
Category Fluency: F-A-S test (words/min)										
FASD										
1	seriousª	not serious	not serious	serious^(e,f)	none	21	21	-	**SMD 0.94 lower** (1.58 lower to 0.30 lower)	⊕⊕◯◯ Low
Other D-KEFS Measures: Tower Test (total achievement)										
FASD										
2	seriousª	not serious	not serious	serious^(e,f)	none	112	76	-	**SMD 0.94 lower** (1.24 lower to 0.63 lower)	⊕⊕◯◯ Low

pFAS

1	serious[a]	not serious	not serious	serious[e,f]	none	20	6	-	**SMD 1.37 lower** (2.37 lower to 0.37 lower)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	serious[e,f]	none	24	16	-	**SMD 1.04 lower** (1.72 lower to 0.37 lower)	⊕⊕◯◯ Low

Other Measures: Trail Making Test Trial B

FASD

2	serious[a]	not serious	not serious	very serious[d,e,f]	none	68	81	-	**SMD 0.28 higher** (0.07 lower to 0.63 higher)	⊕◯◯◯ Very Low

Other Measures: Test of Executive Control - Non-Inhibitory Condition: Incorrect

FASD

1	serious[a]	not serious	not serious	serious[e,f]	none	26	19	-	**SMD 2.36 higher** (1.58 higher to 3.15 higher)	⊕⊕◯◯ Low

BRIEF Global Executive Composite – Caregiver Report

FASD

3	serious[a]	serious[b]	not serious	serious[e,f]	none	177	201	-	**SMD 2.05 higher** (1.48 higher to 2.62 higher)	⊕◯◯◯ Very Low

pFAS

2	serious[a]	serious[b]	not serious	serious[e,f]	none	35	42	-	**SMD 2.07 higher** (0.20 higher to 3.95 higher)	⊕◯◯◯ Very Low

ARND/Other

2	serious[a]	serious[b]	not serious	serious[e,f]	none	34	42	-	**SMD 2.78 higher** (1.67 higher to 3.88 higher)	⊕◯◯◯ Very Low

BRIEF Behaviour Regulation Index – Caregiver Report

FASD

3	serious[a]	not serious	not serious	serious[e]	none	304	227	-	**SMD 2.14 higher** (1.81 higher to 2.47 higher)	⊕⊕◯◯ Low

pFAS

2	serious[a]	serious[b]	not serious	serious[e,f]	none	35	42	-	**SMD 1.72 higher** (0.17 higher to 3.28 higher)	⊕◯◯◯ Very Low

ARND/Other

2	serious[a]	not serious	not serious	serious[e,f]	none	34	42	-	**SMD 2.34 higher** (1.72 higher to 2.96 higher)	⊕⊕◯◯ Low

BRIEF Behaviour Regulation Index – Teacher Report

FASD

1	serious[a]	not serious	not serious	serious[e,f]	none	55	23	-	**SMD 1.12 higher** (0.60 higher to 1.64 higher)	⊕⊕◯◯ Low

BRIEF Metacognition Index – Caregiver Report

FASD

3	serious[a]	serious[b]	not serious	serious[e]	none	304	226	-	**SMD 1.46 higher** (0.89 higher to 2.03 higher)	⊕◯◯◯ Very Low

pFAS

2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	35	42	-	**SMD 1.93 higher** (0.10 lower to 3.95 higher)	⊕◯◯◯ Very Low

ARND/Other

2	serious[a]	serious[b]	not serious	serious[e,f]	none	34	42	-	**SMD 2.61 higher** (1.03 higher to 4.19 higher)	⊕◯◯◯ Very Low

BRIEF Metacognition Index – Teacher Report

FASD

1	serious[a]	not serious	not serious	serious[e,f]	none	55	23	-	**SMD 0.69 higher** (0.19 higher to 1.19 higher)	⊕⊕◯◯ Low

Other BRIEF Measures: Inhibit, Shift, Plan/Organise, Monitor – Caregiver Report

FASD (Inhibit)

2	serious[a]	serious[b]	not serious	serious[e,f]	none	83	110	-	**SMD 2.22 higher** (1.32 higher to 3.12 higher)	⊕◯◯◯ Very Low

FASD (Shift)

2	serious[a]	not serious	not serious	serious[e,f]	none	83	110	-	**SMD 1.77 higher** (1.43 higher to 2.11 higher)	⊕⊕◯◯ Low

FASD (Monitor)

1	serious[a]	not serious	not serious	serious[e,f]	none	47	70	-	**SMD 2.51 higher** (2.02 higher to 3.00 higher)	⊕⊕◯◯ Low

FASD (Plan/Organise)

1	serious[a]	not serious	not serious	serious[e,f]	none	46	70	-	**SMD 2.53 higher** (2.03 higher to 3.03 higher)	⊕⊕◯◯ Low

FASD (Working Memory)

1	serious[a]	not serious	not serious	serious[e,f]	none	46	70	-	**SMD 2.95 higher** (2.41 higher to 3.48 higher)	⊕⊕◯◯ Low

ARND/Others (Working Memory)

1	serious[a]	not serious	not serious	serious[e,f]	none	22	21	-	**SMD 2.59 higher** (1.76 higher to 3.42 higher)	⊕⊕◯◯ Low

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.

Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CI for overall estimate crossed the line of no effect; e) Wide 95% CIs for overall estimate; f) Optimal information size criteria not met.

Meta-analyses for executive functioning

EXPOSURE STUDIES

NEPSY Speeded Naming (mean/SD)

Heavy PAE and NEPSY Speeded Naming (mean/SD) (1 study)

Study or Subgroup	Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 2021 (3.5-4.5yrs; NEPSY-II)	8.18	2.88	82	9.92	2.62	132	100.0%	-0.64 [-0.92, -0.35]		🔴
Total (95% CI)			82			132	100.0%	-0.64 [-0.92, -0.35]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.42 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Coles et al 2021 also reports other measures, including AB game (mean/SD).

Confirmed PAE Level Unquantifiable and NEPSY Speeded Naming (mean/SD) (3 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Doyle et al 2018 (10-16yrs; NEPSY-II)	8.2	2.78	142	9	2.41	160	41.8%	-0.31 [-0.54, -0.08]		🔴
Glass et al 2015 (8-16yrs; NEPSY-II)	7.8	2.4	49	9.9	2.07	47	31.2%	-0.93 [-1.35, -0.51]		🔴
Gomez et al 2022 (8-16yrs; NEPSY)	9	4	31	11	3	31	26.9%	-0.56 [-1.07, -0.05]		🔴
Total (95% CI)			222			238	100.0%	-0.57 [-0.96, -0.17]		

Heterogeneity: Tau² = 0.08; Chi² = 6.59, df = 2 (P = 0.04); I² = 70%
Test for overall effect: Z = 2.82 (P = 0.005)

Risk of bias legend
(A) Overall RoB

NEPSY Inhibition Errors (ss) (mean/SD)

Confirmed PAE Level Unquantifiable and NEPSY Inhibition Errors (ss) (mean/SD) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Doyle et al 2018 (10-16yrs; NEPSY-II)	5.5	3.94	142	8.1	3.73	160	100.0%	-0.68 [-0.91, -0.44]		🔴
Total (95% CI)			142			160	100.0%	-0.68 [-0.91, -0.44]		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.71 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

NEPSY Inhibition Errors (raw) (mean/SD)

Confirmed PAE Level Unquantifiable and NEPSY Inhibition Errors (raw) (mean/SD) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Migliorini et al 2015 (12-17yrs; NEPSY-II)	3.7	4	25	2.7	3.6	16	100.0%	0.25 [-0.38, 0.88]		🔴
Total (95% CI)			25			16	100.0%	0.25 [-0.38, 0.88]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)

Risk of bias legend
(A) Overall RoB

Note: Migliorini et al 2015 also reports NEPSY Inhibition (timed score).

Wisconsin Card Sorting Test (WCST): Composite Percentage (mean/SD)

Confirmed PAE Level Unquantifiable and WCST Composite (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McGee et al 2008b (8-18yrs; WSCT)	97.25	12.13	47	107.97	15.25	60	49.3%	-0.76 [-1.16, -0.37]		🔴
Vaurio et al 2011 (6-16yrs; WCST)	94.45	13.69	53	99.9	16.12	53	50.7%	-0.36 [-0.75, 0.02]		🔴
Total (95% CI)			100			113	100.0%	-0.56 [-0.95, -0.17]		

Heterogeneity: Tau² = 0.04; Chi² = 2.02, df = 1 (P = 0.15); I² = 51%
Test for overall effect: Z = 2.79 (P = 0.005)

Risk of bias legend
(A) Overall RoB

Note: Vaurio et al 2011 also reports COWAT Letter Fluency and COWAT Category Fluency (mean/SD).

Wisconsin Card Sorting Test (WCST): Total Errors (raw) (mean/SD)

Any PAE and WCST: Total Errors (raw) (mean/SD) (1 study)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Furtado et al 2016 (11-12yrs; WCST)	30.3	18.83	28	23.93	15.73	28	100.0%	0.36 [-0.17, 0.89]		🔴
Total (95% CI)			28			28	100.0%	**0.36 [-0.17, 0.89]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.34 (P = 0.18)

Risk of bias legend
(A) Overall RoB

Note: Furtado et al 2016 also reports Animal Test, WCST Perseverative Errors, Non- Perseverative Errors, Failure to keep context, and number of completed categories (raw) (mean/SD).

NIH Toolbox: Dimensional Change Card Sort (mean/SD)

Light PAE and NIH Toolbox: Dimensional Change Card Sort (mean/SD) (1 study)

Study or Subgroup	Light PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; NIH Toolbox)	99.2	14.4	93	96.5	15.2	6669	100.0%	0.18 [-0.03, 0.38]		🔴
Total (95% CI)			93			6669	100.0%	**0.18 [-0.03, 0.38]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.70 (P = 0.09)

Risk of bias legend
(A) Overall RoB

Moderate PAE and NIH Toolbox: Dimensional Change Card Sort (mean/SD) (1 study)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; NIH Toolbox)	98.9	15.7	755	96.5	15.2	6669	100.0%	0.16 [0.08, 0.23]		🔴
Total (95% CI)			755			6669	100.0%	**0.16 [0.08, 0.23]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.10 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

Any PAE and NIH Toolbox: Dimensional Change Card Sort (mean/SD) (1 study)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; NIH Toolbox)	98.3	15.3	2518	96.4	15.1	7501	100.0%	0.13 [0.08, 0.17]		🔴
Total (95% CI)			2518			7501	100.0%	**0.13 [0.08, 0.17]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.44 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports NIH Flanker test (mean/SD).

Verbal Fluency: D-KEFS (total correct Letter) (mean/SD)

Confirmed PAE Level Unquantifiable and D-KEFS Letter Fluency (total words) (mean/SD) (3 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2010 (7-21yrs; D-KEFS)	8.32	3.1	38	11.1	3.33	60	14.0%	-0.85 [-1.27, -0.43]		🔴
Mattson et al 2013 (8-17yrs; D-KEFS)	7.05	3.43	209	10.17	3.35	185	58.1%	-0.92 [-1.13, -0.71]		🔴
Nguyen et al 2014 (8-16yrs; D-KEFS)	8	3.12	141	10.7	2.82	69	27.9%	-0.89 [-1.19, -0.59]		🔴
Total (95% CI)			388			314	100.0%	**-0.90 [-1.06, -0.74]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 2 (P = 0.96); I² = 0%
Test for overall effect: Z = 11.12 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Mattson et al 2010 also reports D-KEFS Trail Making Test (combined number/letter, switch vs number, switch vs visual, switch errors) and verbal fluency (second interval correct and set loss errors). Nguyen et al 2014 also reports D-KEFS Colour Interference and Trail Making Test (completion time and total errors). Mattson et al 2013 also reports D-KEFS Tower Test (rule violation per item ratio), Colour Word Interference (Inhibit/Switch Completion time), Trail Making Test (Switching ss), and Twenty Questions Total Initial Abstraction (scaled score). Nguyen et al 2014 reports it as D-KEFS letter fluency whilst Mattson et al 2010 and 2013 report D-KEFS verbal fluency – letter.

Verbal Fluency: D-KEFS (Verbal Fluency Switching)

Confirmed PAE Level Unquantifiable and D-KEFS Verbal Fluency Switching (mean/SD) (3 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Mattson et al 2010 (7-21yrs; D-KEFS)	6.95	2.44	38	10.62	2.6	60	20.3%	-1.43 [-1.89, -0.98]		●
Mattson et al 2013 (8-17yrs; D-KEFS)	8.4	2.97	209	11.09	3.01	185	42.5%	-0.90 [-1.11, -0.69]		●
Ware et al 2012 (6-18yrs; D-KEFS)	8.25	3.41	142	11.68	2.9	133	37.2%	-1.08 [-1.33, -0.82]		●
Total (95% CI)			**389**			**378**	**100.0%**	**-1.07 [-1.33, -0.82]**		

Heterogeneity: Tau² = 0.03; Chi² = 4.70, df = 2 (P = 0.10); I² = 57%
Test for overall effect: Z = 8.33 (P < 0.00001)

Confirmed Unquantifiable   Control

Risk of bias legend
(A) Overall RoB

Note: Mattson et al 2010 also reports D-KEFS Trail Making Test (combined number/letter, switch vs number, switch vs visual, switch errors). Ware et al 2012 also reports D-KEFS design fluency (switching), trail making test (switching), and colour interference (switching) (mean/SD). Mattson et al 2013 also reports D-KEFS Tower Test (rule violation per item ratio), Colour Word Interference (Inhibit/Switch Completion time), Trail Making Test (Switching ss), and Twenty Questions Total Initial Abstraction (scaled score).

Category Fluency: McCarthy/D-KEFS (mean/SD)

Confirmed PAE Level Unquantifiable and McCarthy/D-KEFS Category Fluency (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Noland et al 2003 (~4yrs; McCarthy)	4.8	3.4	46	5.3	3.3	213	51.3%	-0.15 [-0.47, 0.17]		●
Mattson et al 2010 (7-21yrs; D-KEFS)	9.03	2.96	38	12.52	3.26	60	48.7%	-1.10 [-1.54, -0.66]		●
Total (95% CI)			**84**			**273**	**100.0%**	**-0.61 [-1.54, 0.32]**		

Heterogeneity: Tau² = 0.41; Chi² = 11.89, df = 1 (P = 0.0006); I² = 92%
Test for overall effect: Z = 1.29 (P = 0.20)

Confirmed Unquantifiable   Control

Risk of bias legend
(A) Overall RoB

Note: Mattson et al 2010 also reports D-KEFS Trail Making Test (combined number/letter, switch vs number, switch vs visual, switch errors).

D-KEFS: Tower Test (total)

Confirmed PAE Level Unquantifiable (2 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Glass et al 2013 (8-16yrs; D-KEFS)	8.03	2.98	90	10.24	2.48	136	53.4%	-0.82 [-1.10, -0.54]		●
Nguyen et al 2014 (8-16yrs; D-KEFS)	8.1	2.93	141	10.1	2.24	69	46.6%	-0.73 [-1.03, -0.44]		●
Total (95% CI)			**231**			**205**	**100.0%**	**-0.78 [-0.98, -0.58]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 1 (P = 0.67); I² = 0%
Test for overall effect: Z = 7.54 (P < 0.00001)

Confirmed Unquantifiable   Control

Risk of bias legend
(A) Overall RoB

Note: Nguyen et al 2014 also reports D-KEFS Colour Interference and Trail Making Test (completion time and total errors).

BRIEF Global Executive Composite – Caregiver Report (SMD)

Light PAE and BRIEF Global Executive Composite – Caregiver (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kesmodel et al 2012 (~5yrs; BRIEF-C)	0.0645	0.0529	100.0%	0.06 [-0.04, 0.17]		✚
Total (95% CI)			**100.0%**	**0.06 [-0.04, 0.17]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.22 (P = 0.22)

Control   Light PAE

Risk of bias legend
(A) Overall RoB

Moderate PAE and BRIEF Global Executive Composite – Caregiver (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kesmodel et al 2012 (~5yrs; BRIEF-C)	-0.0013	0.0839	100.0%	-0.00 [-0.17, 0.16]		✚
Total (95% CI)			**100.0%**	**-0.00 [-0.17, 0.16]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.02 (P = 0.99)

Control   Moderate PAE

Risk of bias legend
(A) Overall RoB

Heavy PAE and BRIEF Global Executive Composite – Caregiver (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kesmodel et al 2012 (~5yrs; BRIEF-C)	0.0522	0.2265	100.0%	0.05 [-0.39, 0.50]		+
Total (95% CI)			**100.0%**	**0.05 [-0.39, 0.50]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.23 (P = 0.82)

Control ↔ Heavy PAE

Risk of bias legend
(A) Overall RoB

Confirmed Unquantifiable PAE and BRIEF Global Executive Composite – Caregiver (SMD) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McGee et al 2008a (13-18yrs; BRIEF-C)	82.5	8.28	28	47.6	5.28	15	100.0%	4.63 [3.43, 5.84]		?
Total (95% CI)			**28**			**15**	**100.0%**	**4.63 [3.43, 5.84]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 7.54 (P < 0.00001)

Control ↔ Confirmed Unquantifiable

Risk of bias legend
(A) Overall RoB

Note: Kesmodel et al 2012 reports adjusted mean difference. Mean and the low CI were added into revman, with the upper CI autogenerated by revman. This value differs from the reported upper CI by 0.01. SMD autogenerated by revman.

BRIEF Behaviour Regulation Index – Caregiver Report (SMD)

Light PAE and BRIEF Behaviour Regulation Index – Caregiver (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-C)	0.067	0.0529	100.0%	0.07 [-0.04, 0.17]		+
Total (95% CI)			**100.0%**	**0.07 [-0.04, 0.17]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.27 (P = 0.21)

Control ↔ Light PAE

Risk of bias legend
(A) Overall RoB

Moderate PAE and BRIEF Behaviour Regulation Index – Caregiver (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-C)	-0.0113	0.0839	100.0%	-0.01 [-0.18, 0.15]		+
Total (95% CI)			**100.0%**	**-0.01 [-0.18, 0.15]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.13 (P = 0.89)

Control ↔ Moderate PAE

Risk of bias legend
(A) Overall RoB

Heavy PAE and BRIEF Behaviour Regulation Index – Caregiver (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-C)	0.2004	0.2266	100.0%	0.20 [-0.24, 0.64]		+
Total (95% CI)			**100.0%**	**0.20 [-0.24, 0.64]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.88 (P = 0.38)

Control ↔ Heavy PAE

Risk of bias legend
(A) Overall RoB

Confirmed PAE Level Unquantifiable and BRIEF Behaviour Regulation Index – Caregiver (SMD) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McGee et al 2008a (13-18yrs; BRIEF-C)	81.14	12.23	28	47.67	7.88	15	100.0%	3.00 [2.09, 3.92]		?
Total (95% CI)			**28**			**15**	**100.0%**	**3.00 [2.09, 3.92]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 6.43 (P < 0.00001)

Control ↔ Confirmed Unquantifiable

Risk of bias legend
(A) Overall RoB

Note: Skogerbo et al 2012 reports adjusted mean difference. SMD autogenerated by revman.

BRIEF Behaviour Regulation Index – Teacher Report (SMD)

Light PAE and BRIEF Behaviour Regulation Index – Teacher (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-T)	-0.0098	0.0529	100.0%	-0.01 [-0.11, 0.09]	+
Total (95% CI)			100.0%	-0.01 [-0.11, 0.09]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.19 (P = 0.85)

Risk of bias legend
(A) Overall RoB

Moderate PAE and BRIEF Behaviour Regulation Index – Teacher (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-T)	-0.0811	0.0839	100.0%	-0.08 [-0.25, 0.08]	+
Total (95% CI)			100.0%	-0.08 [-0.25, 0.08]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.97 (P = 0.33)

Risk of bias legend
(A) Overall RoB

Heavy PAE and BRIEF Behaviour Regulation Index – Teacher (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-T)	-0.1878	0.2266	100.0%	-0.19 [-0.63, 0.26]	+
Total (95% CI)			100.0%	-0.19 [-0.63, 0.26]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)

Risk of bias legend
(A) Overall RoB

Note: Skogerbo et al 2012 reports adjusted mean difference. SMD autogenerated by revman.

BRIEF Metacognition Index – Caregiver Report (SMD)

Light PAE and BRIEF Metacognition Index – Caregiver (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-C)	0.0933	0.053	100.0%	0.09 [-0.01, 0.20]	+
Total (95% CI)			100.0%	0.09 [-0.01, 0.20]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.76 (P = 0.08)

Risk of bias legend
(A) Overall RoB

Moderate PAE and BRIEF Metacognition Index – Caregiver (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-C)	0.0933	0.053	100.0%	0.09 [-0.01, 0.20]	+
Total (95% CI)			100.0%	0.09 [-0.01, 0.20]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.76 (P = 0.08)

Risk of bias legend
(A) Overall RoB

Heavy PAE and BRIEF Metacognition Index – Caregiver (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-C)	0.3789	0.2267	100.0%	0.38 [-0.07, 0.82]		+
Total (95% CI)			100.0%	**0.38 [-0.07, 0.82]**		
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.67 (P = 0.09)						

Risk of bias legend
(A) Overall RoB

Confirmed Unquantifiable PAE and BRIEF Metacognition Index – Caregiver (SMD) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McGee et al 2008a (13-18yrs; BRIEF-C)	79.89	6.48	28	48.07	5.01	15	100.0%	5.19 [3.88, 6.50]		?
Total (95% CI)			28			15	100.0%	**5.19 [3.88, 6.50]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 7.76 (P < 0.00001)										

Risk of bias legend
(A) Overall RoB

Note: Skogerbo et al 2012 reports adjusted mean difference. SMD autogenerated by revman.

BRIEF Metacognition Index – Teacher Report (SMD)

Light PAE and BRIEF Metacognition Index – Teacher (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-T)	0.0202	0.0529	100.0%	0.02 [-0.08, 0.12]		+
Total (95% CI)			100.0%	**0.02 [-0.08, 0.12]**		
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.38 (P = 0.70)						

Risk of bias legend
(A) Overall RoB

Moderate PAE and BRIEF Metacognition Index – Teacher (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-T)	-0.018	0.0839	100.0%	-0.02 [-0.18, 0.15]		+
Total (95% CI)			100.0%	**-0.02 [-0.18, 0.15]**		
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.83)						

Risk of bias legend
(A) Overall RoB

Heavy PAE and BRIEF Metacognition Index – Teacher (SMD) (1 study)

Study or Subgroup	Std. Mean Difference	SE	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2012 (~5yrs; BRIEF-T)	-0.2127	0.2266	100.0%	-0.21 [-0.66, 0.23]		+
Total (95% CI)			100.0%	**-0.21 [-0.66, 0.23]**		
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.94 (P = 0.35)						

Risk of bias legend
(A) Overall RoB

Note: Skogerbo et al 2012 reports adjusted mean difference. SMD autogenerated by revman.

BRIEF Subdomains – Caregiver Report (mean/SD)

Confirmed PAE-Level Unquantifiable and BRIEF Inhibit – Caregiver (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McGee et al 2008a (13-18yrs; BRIEF-C)	81.21	17.26	28	48.87	9.3	15	47.8%	2.11 [1.33, 2.90]	?
Nguyen et al 2014 (8-16yrs; BRIEF-C)	75.8	12.4	73	44.7	5.51	151	52.2%	3.69 [3.25, 4.14]	−
Total (95% CI)			101			166	100.0%	2.94 [1.39, 4.49]	

Heterogeneity: Tau² = 1.15; Chi² = 11.86, df = 1 (P = 0.0006); I² = 92%
Test for overall effect: Z = 3.72 (P = 0.0002)

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and BRIEF Shift – Caregiver (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McGee et al 2008a (13-18yrs; BRIEF-C)	79.86	12.81	28	47.33	6.39	15	15.5%	2.89 [1.99, 3.79]	?
Nguyen et al 2014 (8-16yrs; BRIEF-C)	67.6	12.6	73	43.1	5.83	151	84.5%	2.83 [2.45, 3.21]	−
Total (95% CI)			101			166	100.0%	2.84 [2.49, 3.19]	

Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0%
Test for overall effect: Z = 15.74 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and BRIEF Emotional Control – Caregiver (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McGee et al 2008a (13-18yrs; BRIEF-C)	72.04	10.87	28	47.6	7.85	15	15.4%	2.41 [1.59, 3.24]	?
Nguyen et al 2014 (8-16yrs; BRIEF-C)	64.2	13.7	73	42.9	6.21	151	84.6%	2.28 [1.93, 2.63]	−
Total (95% CI)			101			166	100.0%	2.30 [1.97, 2.62]	

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.77); I² = 0%
Test for overall effect: Z = 13.94 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and BRIEF Initiate – Caregiver (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McGee et al 2008a (13-18yrs; BRIEF-C)	75.68	6.84	28	48.4	6.1	15	33.0%	4.06 [2.96, 5.16]	?
Nguyen et al 2014 (8-16yrs; BRIEF-C)	67.5	9.21	73	43.3	6.71	151	67.0%	3.17 [2.76, 3.58]	−
Total (95% CI)			101			166	100.0%	3.46 [2.64, 4.28]	

Heterogeneity: Tau² = 0.22; Chi² = 2.23, df = 1 (P = 0.14); I² = 55%
Test for overall effect: Z = 8.27 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and BRIEF Working Memory – Caregiver (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McGee et al 2008a (13-18yrs; BRIEF-C)	80.25	11.66	28	46.53	5.48	15	49.1%	3.31 [2.35, 4.28]	?
Nguyen et al 2014 (8-16yrs; BRIEF-C)	74.5	5.13	73	43.3	5.13	151	50.9%	6.06 [5.43, 6.69]	−
Total (95% CI)			101			166	100.0%	4.71 [2.02, 7.41]	

Heterogeneity: Tau² = 3.60; Chi² = 21.78, df = 1 (P < 0.00001); I² = 95%
Test for overall effect: Z = 3.43 (P = 0.0006)

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and BRIEF Plan/Organise – Caregiver (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McGee et al 2008a (13-18yrs; BRIEF-C)	78	6.96	28	48	5.57	15	13.8%	4.52 [3.34, 5.70]	?
Nguyen et al 2014 (8-16yrs; BRIEF-C)	71.8	7.52	73	43.3	6.68	151	86.2%	4.08 [3.61, 4.55]	−
Total (95% CI)			101			166	100.0%	4.14 [3.70, 4.58]	

Heterogeneity: Tau² = 0.00; Chi² = 0.46, df = 1 (P = 0.50); I² = 0%
Test for overall effect: Z = 18.49 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and BRIEF Monitor – Caregiver (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
McGee et al 2008a (13-18yrs; BRIEF-C)	77.71	6.45	28	49.47	6.23	15	13.7%	4.35 [3.20, 5.50]		?
Nguyen et al 2014 (8-16yrs; BRIEF-C)	71.6	7.94	73	41.6	7.57	151	86.3%	3.89 [3.43, 4.35]		−
Total (95% CI)			101			166	100.0%	3.95 [3.52, 4.38]		

Heterogeneity: Tau² = 0.00; Chi² = 0.53, df = 1 (P = 0.47); I² = 0%
Test for overall effect: Z = 18.19 (P < 0.00001)

Scale: -10 -5 0 5 10 — Control / Confirmed Unquantifiable

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and BRIEF Organisation of Materials – Caregiver (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
McGee et al 2008a (13-18yrs; BRIEF-C)	64.79	7.96	28	49.27	7.82	151	42.6%	1.97 [1.52, 2.42]		?
Nguyen et al 2014 (8-16yrs; BRIEF-C)	64.4	7.44	73	45.6	8.25	151	57.4%	2.34 [1.99, 2.70]		−
Total (95% CI)			101			302	100.0%	2.18 [1.82, 2.55]		

Heterogeneity: Tau² = 0.03; Chi² = 1.61, df = 1 (P = 0.20); I² = 38%
Test for overall effect: Z = 11.87 (P < 0.00001)

Scale: -4 -2 0 2 4 — Control / Confirmed Unquantifiable

Risk of bias legend
(A) Overall RoB

DIAGNOSED STUDIES

NEPSY: Speeded Naming (mean/SD)
FASD and NEPSY: Speeded Naming (mean/SD) (4 studies)

Study or Subgroup	FASD			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
May et al 2020a (6-7yrs; NEPSY-II)	7.8	3	49	9.2	3.1	302	27.0%	-0.45 [-0.76, -0.15]		●
May et al 2020b (6-7yrs; NEPSY-II)	8.2	3.2	38	10	3	273	26.3%	-0.59 [-0.94, -0.25]		●
May et al 2020c (6-7yrs; NEPSY-II)	7.8	2.1	37	9.3	2.7	330	26.3%	-0.57 [-0.91, -0.22]		●
Rasmussen et al 2013 (6-16yrs; NEPSY-II)	7.38	1.31	32	10.29	1.55	30	20.4%	-2.01 [-2.63, -1.39]		●
Total (95% CI)			156			935	100.0%	-0.84 [-1.33, -0.34]		

Heterogeneity: Tau² = 0.21; Chi² = 20.52, df = 3 (P = 0.0001); I² = 85%
Test for overall effect: Z = 3.33 (P = 0.0009)

Scale: -4 -2 0 2 4 — FASD / Control

Risk of bias legend
(A) Overall RoB

FAS and NEPSY: Speeded Naming (mean/SD) (1 study)

Study or Subgroup	FAS			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Chambers et al 2019 (6-7yrs; NEPSY)	10.6	4.7	5	8.9	3.2	761	100.0%	0.53 [-0.35, 1.41]		●
Total (95% CI)			5			761	100.0%	0.53 [-0.35, 1.41]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.18 (P = 0.24)

Scale: -4 -2 0 2 4 — FAS / Control

Risk of bias legend
(A) Overall RoB

pFAS and NEPSY: Speeded Naming (mean/SD) (1 study)

Study or Subgroup	pFAS			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Chambers et al 2019 (6-7yrs; NEPSY)	7.6	3	44	8.9	3.2	761	100.0%	-0.41 [-0.71, -0.10]		●
Total (95% CI)			44			761	100.0%	-0.41 [-0.71, -0.10]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.62 (P = 0.009)

Scale: -4 -2 0 2 4 — pFAS / Control

Risk of bias legend
(A) Overall RoB

ARND/Others and NEPSY: Speeded Naming (mean/SD) (1 study)

Study or Subgroup	ARND/Others			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Chambers et al 2019 (6-7yrs; NEPSY)	8.7	3.3	44	8.9	3.2	761	100.0%	-0.06 [-0.37, 0.24]		●
Total (95% CI)			44			761	100.0%	-0.06 [-0.37, 0.24]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.40 (P = 0.69)

Scale: -4 -2 0 2 4 — ARND/Others / Control

Risk of bias legend
(A) Overall RoB

NEPSY: Inhibition – Naming (mean/SD)

FASD and NEPSY: Inhibition – Naming (mean/SD) (8 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; NEPSY-II)	8.2	4.2	49	9.7	3.6	302	14.0%	-0.41 [-0.71, -0.10]		🔴
May et al 2020b (6-7yrs; NEPSY-II)	8.2	4.2	38	10.2	3.3	273	13.2%	-0.58 [-0.93, -0.24]		🔴
May et al 2020c (6-7yrs; NEPSY-II)	7.9	3.5	37	10.1	3.5	330	13.2%	-0.63 [-0.97, -0.28]		🔴
McLachlan et al 2020 (7-19yrs; NEPSY-II)	7	3.9	64	9.7	3.2	68	13.0%	-0.75 [-1.11, -0.40]		🟡
Paolozza et al 2014a (5-17yrs; NEPSY-II)	6.6	3.3941	72	9.6	2.846	90	13.5%	-0.96 [-1.29, -0.64]		🔴
Rasmussen et al 2013 (6-16yrs; NEPSY-II)	6.68	1.37	32	9.91	1.69	30	8.2%	-2.08 [-2.71, -1.45]		🔴
Treit et al 2016 (5-19yrs; NEPSY-II)	6.6	4	99	9.3	3.5	135	14.7%	-0.72 [-0.99, -0.46]		🔴
Ware et al 2021 (6-18yrs; NEPSY-II)	8	4	37	10	3	30	10.3%	-0.55 [-1.04, -0.06]		🔴
Total (95% CI)			**428**			**1258**	**100.0%**	**-0.78 [-1.02, -0.53]**		

Heterogeneity: Tau² = 0.09; Chi² = 25.79, df = 7 (P = 0.0005); I² = 73%
Test for overall effect: Z = 6.25 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Paolozza et al 2014a also reports NEPSY-II Direction Errors and Timing Errors.

FAS and NEPSY: Inhibition – Naming (mean/SD) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	9.3	2.3	5	9.3	3.6	761	100.0%	0.00 [-0.88, 0.88]		🔴
Total (95% CI)			**5**			**761**	**100.0%**	**0.00 [-0.88, 0.88]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

Risk of bias legend
(A) Overall RoB

pFAS and NEPSY: Inhibition – Naming (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	9.3	3.7	44	9.4	3.6	761	100.0%	-0.03 [-0.33, 0.28]		🔴
Total (95% CI)			**44**			**761**	**100.0%**	**-0.03 [-0.33, 0.28]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.18 (P = 0.86)

Risk of bias legend
(A) Overall RoB

ARND/Others and NEPSY: Inhibition – Naming (mean/SD) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	8.7	4.2	44	9.4	3.6	761	63.6%	-0.19 [-0.50, 0.11]		🔴
Paolozza et al 2014a (5-17yrs; NEPSY-II)	7.9	3.7523	22	9.6	2.985	99	36.4%	-0.54 [-1.01, -0.07]		🔴
Total (95% CI)			**66**			**860**	**100.0%**	**-0.32 [-0.65, 0.01]**		

Heterogeneity: Tau² = 0.02; Chi² = 1.49, df = 1 (P = 0.22); I² = 33%
Test for overall effect: Z = 1.91 (P = 0.06)

Risk of bias legend
(A) Overall RoB

NEPSY: Inhibition – Inhibition (mean/SD)

FASD and NEPSY: Inhibition – Inhibition (mean/SD) (9 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; NEPSY-II)	7.5	3.3	49	9.3	3.4	302	13.8%	-0.53 [-0.83, -0.23]	🔴
May et al 2020b (6-7yrs; NEPSY-II)	8.3	3.7	38	9.8	3.3	273	12.7%	-0.45 [-0.79, -0.11]	🔴
May et al 2020c (6-7yrs; NEPSY-II)	7.8	3.1	37	9.6	3.4	330	12.7%	-0.53 [-0.87, -0.19]	🔴
May et al 2021 (6-7yrs; NEPSY-II)	6.4	1.8	5	9.1	3.2	68	3.6%	-0.85 [-1.77, 0.07]	🔴
McLachlan et al 2020 (7-19yrs; NEPSY-II)	6.7	3.2	63	10.2	3.2	68	11.9%	-1.09 [-1.46, -0.72]	🟡
Paolozza et al 2014a (5-17yrs; NEPSY-II)	6.2	3.3941	72	10.1	3.7947	90	13.0%	-1.07 [-1.40, -0.74]	🔴
Rasmussen et al 2013 (6-16yrs; NEPSY-II)	7.39	1.37	32	9.34	1.76	30	7.9%	-1.23 [-1.77, -0.68]	🔴
Treit et al 2016 (5-19yrs; NEPSY-II)	6.1	3.6	98	9.7	3.8	135	14.8%	-0.97 [-1.24, -0.69]	🔴
Ware et al 2021 (6-18yrs; NEPSY-II)	7	4	37	10	4	40	9.5%	-0.74 [-1.21, -0.28]	🔴
Total (95% CI)			431			1336	100.0%	**-0.81 [-1.00, -0.61]**	

Heterogeneity: Tau² = 0.05; Chi² = 18.20, df = 8 (P = 0.02); I² = 56%
Test for overall effect: Z = 8.20 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Paolozza et al 2014a also reports NEPSY-II Direction Errors and Timing Errors.

FAS and NEPSY: Inhibition – Inhibition (mean/SD) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	8.2	4.8	5	9.4	3.5	761	100.0%	-0.34 [-1.22, 0.54]	🔴
Total (95% CI)			5			761	100.0%	**-0.34 [-1.22, 0.54]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.76 (P = 0.45)

Risk of bias legend
(A) Overall RoB

pFAS and NEPSY: Inhibition – Inhibition (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	8.7	3.7	44	9.4	3.5	761	100.0%	-0.20 [-0.50, 0.10]	🔴
Total (95% CI)			44			761	100.0%	**-0.20 [-0.50, 0.10]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.28 (P = 0.20)

Risk of bias legend
(A) Overall RoB

ARND/Others and NEPSY: Inhibition – Inhibition (mean/SD) (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	8.4	3.7	44	9.4	3.5	761	70.4%	-0.28 [-0.59, 0.02]	🔴
Paolozza et al 2014a (5-17yrs; NEPSY-II)	8.9	3.2833	22	10.1	2.846	90	29.6%	-0.41 [-0.88, 0.06]	🔴
Total (95% CI)			66			851	100.0%	**-0.32 [-0.58, -0.07]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 1 (P = 0.67); I² = 0%
Test for overall effect: Z = 2.46 (P = 0.01)

Risk of bias legend
(A) Overall RoB

NEPSY: Inhibition – Switching (mean/SD)

FASD and NEPSY: Inhibition – Switching (mean/SD) (8 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; NEPSY-II)	8	3	49	9	3	302	13.3%	-0.33 [-0.64, -0.03]	🔴
May et al 2020b (6-7yrs; NEPSY-II)	7.3	4.5	38	7.9	3.8	273	12.9%	-0.15 [-0.49, 0.19]	🔴
May et al 2020c (6-7yrs; NEPSY-II)	7.9	2.6	37	10	3.1	330	12.9%	-0.69 [-1.03, -0.34]	🔴
McLachlan et al 2020 (7-19yrs; NEPSY-II)	6.7	3.2	63	10.8	2.7	68	12.5%	-1.38 [-1.76, -1.00]	🟡
Paolozza et al 2014a (5-17yrs; NEPSY-II)	6.7	3.3941	72	10.6	2.846	90	12.9%	-1.25 [-1.59, -0.91]	🔴
Rasmussen et al 2013 (6-16yrs; NEPSY-II)	7.66	1.26	32	10.1	1.72	30	10.3%	-1.61 [-2.18, -1.03]	🔴
Treit et al 2016 (5-19yrs; NEPSY-II)	6.4	4.1	96	10.2	3.8	129	13.5%	-0.96 [-1.24, -0.68]	🔴
Ware et al 2021 (6-18yrs; NEPSY-II)	8	4	37	10	3	40	11.7%	-0.56 [-1.02, -0.11]	🔴
Total (95% CI)			**424**			**1262**	**100.0%**	**-0.85 [-1.19, -0.51]**	

Heterogeneity: Tau² = 0.20; Chi² = 49.00, df = 7 (P < 0.00001); I² = 86%
Test for overall effect: Z = 4.94 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Paolozza et al 2014a also reports NEPSY-II Direction Errors and Timing Errors.

FAS and NEPSY: Inhibition – Switching (mean/SD) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	10.5	3.5	5	9.1	3.2	761	100.0%	0.44 [-0.44, 1.32]	🔴
Total (95% CI)			**5**			**761**	**100.0%**	**0.44 [-0.44, 1.32]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.97 (P = 0.33)

Risk of bias legend
(A) Overall RoB

pFAS and NEPSY: Inhibition – Switching (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	8.6	3	44	9.1	3.2	761	100.0%	-0.16 [-0.46, 0.15]	🔴
Total (95% CI)			**44**			**761**	**100.0%**	**-0.16 [-0.46, 0.15]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.01 (P = 0.31)

Risk of bias legend
(A) Overall RoB

ARND/Others and NEPSY: Inhibition – Switching (mean/SD) (2 studies)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	8.9	3.3	44	9.1	3.2	761	54.6%	-0.06 [-0.37, 0.24]	🔴
Paolozza et al 2014a (5-17yrs; NEPSY-II)	8.6	3.2833	22	10.6	2.846	90	45.4%	-0.68 [-1.15, -0.20]	🔴
Total (95% CI)			**66**			**851**	**100.0%**	**-0.34 [-0.94, 0.26]**	

Heterogeneity: Tau² = 0.15; Chi² = 4.57, df = 1 (P = 0.03); I² = 78%
Test for overall effect: Z = 1.12 (P = 0.26)

Risk of bias legend
(A) Overall RoB

Note: Paolozza et al 2014a also reports NEPSY-II Direction Errors and Timing Errors.

NEPSY: Inhibition - Naming vs Inhibition – Inhibition (mean/SD)

FASD and NEPSY: Inhibition – Naming vs Inhibition – Inhibition (mean/SD) (4 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; NEPSY-II)	8	3.3	49	9.3	3.3	302	37.0%	-0.39 [-0.70, -0.09]	🔴
May et al 2020b (6-7yrs; NEPSY-II)	9	3.4	38	9.7	3.3	287	29.6%	-0.21 [-0.55, 0.13]	🔴
May et al 2020c (6-7yrs; NEPSY-II)	8.6	3.4	37	9.5	3.3	330	29.4%	-0.27 [-0.61, 0.07]	🔴
May et al 2021 (6-7yrs; NEPSY-II)	7	1.9	5	9.5	3.2	68	4.0%	-0.79 [-1.71, 0.13]	🔴
Total (95% CI)			**129**			**987**	**100.0%**	**-0.32 [-0.50, -0.13]**	

Heterogeneity: Tau² = 0.00; Chi² = 1.70, df = 3 (P = 0.64); I² = 0%
Test for overall effect: Z = 3.39 (P = 0.0007)

Risk of bias legend
(A) Overall RoB

FAS and NEPSY: Inhibition – Naming vs Inhibition – Inhibition (mean/SD) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	8.4	5.1	5	9.6	3.3	761	100.0%	-0.36 [-1.24, 0.52]		🔴
Total (95% CI)			5			761	100.0%	-0.36 [-1.24, 0.52]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.81 (P = 0.42)

Risk of bias legend
(A) Overall RoB

pFAS and NEPSY: Inhibition – Naming vs Inhibition – Inhibition (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	8.8	3.5	44	9.6	3.3	761	100.0%	-0.24 [-0.55, 0.06]		🔴
Total (95% CI)			44			761	100.0%	-0.24 [-0.55, 0.06]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.56 (P = 0.12)

Risk of bias legend
(A) Overall RoB

ARND/Others and NEPSY: Inhibition – Naming vs Inhibition – Inhibition (mean/SD) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; NEPSY)	8.9	3.6	44	9.6	3.3	761	100.0%	-0.21 [-0.51, 0.09]		🔴
Total (95% CI)			44			761	100.0%	-0.21 [-0.51, 0.09]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.36 (P = 0.17)

Risk of bias legend
(A) Overall RoB

NEPSY: Animal Sorting (mean/SD)
FASD and NEPSY: Animal Sorting (mean/SD) (6 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Crawford et al 2020 (8-12yrs; NEPSY-II)	4.69	3.22	39	10.48	2.59	29	14.1%	-1.93 [-2.51, -1.34]		🔴
McLachlan et al 2020 (7-19yrs; NEPSY-II)	7.3	3	65	9.7	3.4	68	18.0%	-0.74 [-1.10, -0.39]		🟡
Paolozza et al 2014c (5-17yrs; NEPSY-II)	6.7	2.5278	71	9.3	4.2143	111	18.7%	-0.71 [-1.02, -0.40]		🟡
Rasmussen et al 2013 (6-16yrs; NEPSY-II)	6.51	1.45	32	9.38	1.67	30	13.9%	-1.82 [-2.41, -1.22]		🔴
Treit et al 2016 (5-19yrs; NEPSY-II)	7	3.4	86	9.4	3.8	129	19.1%	-0.66 [-0.94, -0.38]		🔴
Ware et al 2021 (6-18yrs; NEPSY-II)	8	3	37	10	3	40	16.2%	-0.66 [-1.12, -0.20]		🔴
Total (95% CI)			330			407	100.0%	-1.02 [-1.40, -0.65]		

Heterogeneity: Tau² = 0.17; Chi² = 26.74, df = 5 (P < 0.0001); I² = 81%
Test for overall effect: Z = 5.33 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Crawford et al 2020 also reports an executive function composite (combination of three measures) and NEPSY-II Inhibition Total Errors (ss).

WCST: Perseverative Errors (ss)
FAS and WCST: Perseverative Errors (ss) (1 study)

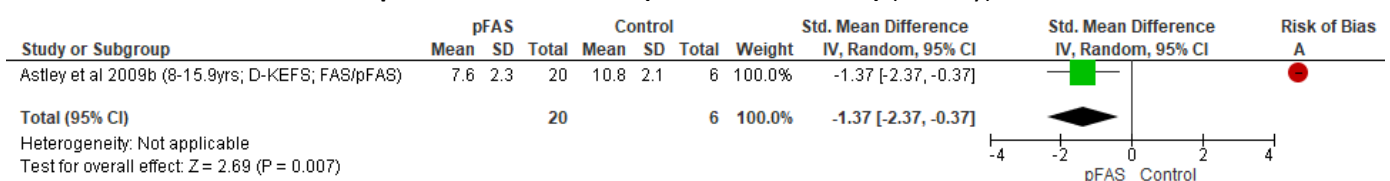| Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kodituwakku et al 2001 (7-19yrs; WCST)	23.75	15.46	20	12.75	7.18	20	100.0%	0.89 [0.24, 1.55]		🔴
Total (95% CI)			20			20	100.0%	0.89 [0.24, 1.55]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.68 (P = 0.007)

Risk of bias legend
(A) Overall RoB

Note: Kodituwakku et al 2001 also reports WCST no. categories completed (ss) and response set loss.

WCST: Total Errors (ss)

pFAS and WCST: Total Errors (ss) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; WCST; FAS/pFAS)	91.2	17	18	112.8	15.7	16	100.0%	-1.29 [-2.03, -0.54]	−
Total (95% CI)			18			16	100.0%	-1.29 [-2.03, -0.54]	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.37 (P = 0.0008)

Risk of bias legend
(A) Overall RoB

ARND/Others and WCST: Total Errors (ss) (1 study)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; WCST; SE/AE)	90	15.7	24	112.8	15.7	16	100.0%	-1.42 [-2.14, -0.71]	−
Total (95% CI)			24			16	100.0%	-1.42 [-2.14, -0.71]	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.91 (P < 0.0001)
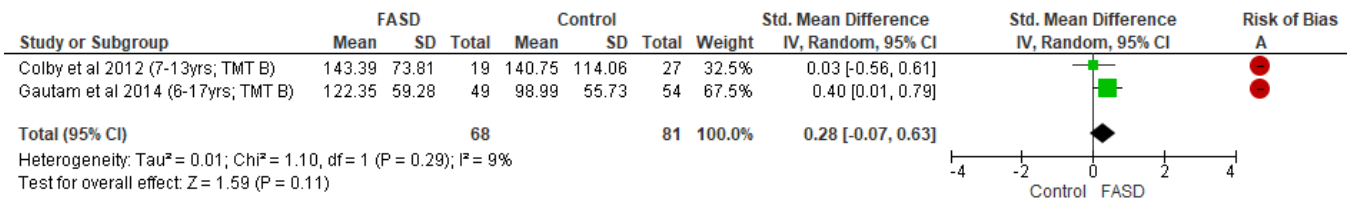
Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009b also reports ND/AE. Astley 2009b also reports D-KEFS tower test total rule violations, colour word interference (inhibit/switch completion time), and Verbal Fluency Conds 1-3% Switch Accuracy (scaled).

WCST: Preservative Responses (ss)

FASD and WCST: Preservative responses (ss) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Fryer et al 2012 (~13yrs; WCST)	90.79	15.77	21	107.71	6.58	7	100.0%	-1.16 [-2.07, -0.24]	−
Total (95% CI)			21			7	100.0%	-1.16 [-2.07, -0.24]	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.48 (P = 0.01)

Risk of bias legend
(A) Overall RoB

pFAS and WCST: Preservative responses (raw) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 1997 (7-8yrs; WCST; FAS/pFAS)	73.39	38.94	25	51	32.97	14	100.0%	0.59 [-0.08, 1.26]	−
Total (95% CI)			25			14	100.0%	0.59 [-0.08, 1.26]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.74 (P = 0.08)

Risk of bias legend
(A) Overall RoB

ARND/Others and WCST: Preservative responses (raw) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 1997 (7-8yrs; WCST; Non-syndromal)	46.86	32.86	62	51	32.97	14	100.0%	-0.12 [-0.70, 0.46]	−
Total (95% CI)			62			14	100.0%	-0.12 [-0.70, 0.46]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.42 (P = 0.67)

Risk of bias legend
(A) Overall RoB

Note: Coles 1997 also reports WCST total errors (raw), Perseverative errors (ss), non-perseverative errors (ss), no. of completed categories, and no. correct (mean/SD).

Verbal Fluency: D-KEFS/NEPSY-II (total correct Letter)

FAS and Verbal/Letter Fluency: D-KEFS/NEPSY-II (total correct) (3 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kodituwakku et al 2006a (8-9yrs; NEPSY-II)	8.78	5.9	23	11.9	5.22	21	23.6%	-0.55 [-1.15, 0.06]	red
Mattson et al 2010 (7-21yrs; D-KEFS)	7.73	2.82	41	11.43	2.99	46	31.5%	-1.26 [-1.72, -0.80]	red
Mattson et al 2013 (8-17yrs; D-KEFS)	6.01	3.28	79	10.17	3.35	185	44.9%	-1.25 [-1.53, -0.96]	red
Total (95% CI)			143			252	100.0%	-1.09 [-1.46, -0.71]	

Heterogeneity: Tau² = 0.06; Chi² = 4.47, df = 2 (P = 0.11); I² = 55%
Test for overall effect: Z = 5.67 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Kodituwakku et al 2006a also reports measures at 6 and 7yrs. Mattson et al 2010 also reports D-KEFS Trail Making Test (combined number-letter, switch vs number, switch vs visual, switch errors) and Verbal Fluency (Second Interval Correct and Set Loss Errors). Mattson et al 2013 also reports D-KEFS Tower Test (rule violation per item ratio), Colour Word Interference (Inhibit/Switch Completion time), Trail Making Test (Switching ss), and Twenty Questions Total Initial Abstraction (scaled score).

pFAS and D-KEFS Verbal Fluency (total correct Letter) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008b (7-17yrs; D-KEFS; FAS/pFAS)	7.61	3.01	24	9.72	2.24	32	100.0%	-0.80 [-1.35, -0.25]	?
Total (95% CI)			24			32	100.0%	-0.80 [-1.35, -0.25]	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.85 (P = 0.004)

Risk of bias legend
(A) Overall RoB

Note: Aragon 2008b also reports D-KEFS Category Fluency (total correct and switching).

ARND/Others and Verbal Fluency: D-KEFS (total correct Letter) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2013 (8-17yrs; D-KEFS; not FAS)	7.52	3.41	117	10.17	3.01	185	100.0%	-0.83 [-1.07, -0.59]	red
Total (95% CI)			117			185	100.0%	-0.83 [-1.07, -0.59]	

Heterogeneity: Not applicable
Test for overall effect: Z = 6.78 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Letter Fluency: F-A-S test (words/mins)

FASD and F-A-S Test Letter Fluency (words/min) (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson & Riley 1999 (8-18yrs; F-A-S test)	6.19	1.82	21	10.33	2.81	21	100.0%	-1.72 [-2.43, -1.00]	red
Total (95% CI)			21			21	100.0%	-1.72 [-2.43, -1.00]	

Heterogeneity: Not applicable
Test for overall effect: Z = 4.69 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Letter Fluency: D-KEFS (speed)

FAS and Letter Fluency: D-KEFS (speed) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Schonfeld et al 2001 (8-15yrs; D-KEFS)	6.5	2.63	10	8.7	2.34	10	100.0%	-0.85 [-1.77, 0.08]	red
Total (95% CI)			10			10	100.0%	-0.85 [-1.77, 0.08]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.80 (P = 0.07)

Risk of bias legend
(A) Overall RoB

ARND/Others and Letter Fluency: D-KEFS (speed) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Schonfeld et al 2001 (8-15yrs; D-KEFS; PEA)	7	1.99	8	8.7	2.34	10	100.0%	-0.74 [-1.71, 0.23]	🔴
Total (95% CI)			8			10	100.0%	-0.74 [-1.71, 0.23]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.49 (P = 0.14)

Risk of bias legend
(A) Overall RoB

Note: Schonfeld et al 2001 also reports D-KEFS Category Fluency, Set-shifting, Four lines, Empty dots only (All speed measures).

Verbal Fluency: D-KEFS (Verbal Fluency Switching)
FASD and Verbal Fluency (Switching): D-KEFS (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Rockhold et al 2021 (11-12yrs; D-KEFS)	7.7	6.9242	47	10.5	5.6293	46	100.0%	-0.44 [-0.85, -0.03]	🔴
Total (95% CI)			47			46	100.0%	-0.44 [-0.85, -0.03]	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.09 (P = 0.04)

Risk of bias legend
(A) Overall RoB

Note: Rockhold et al 2021 also reports D-KEFS Colour Word Interference Inhibition, Trail Making Task Inhibition and NIH Dimensional Card Sort, Flanker Task and List Sort.

FAS and Verbal Fluency (Switching): D-KEFS (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2010 (7-21yrs; D-KEFS)	7.98	2.66	41	10.96	2.73	46	27.0%	-1.10 [-1.55, -0.64]	🔴
Mattson et al 2013 (8-17yrs; D-KEFS)	8.15	3.51	79	11.09	3.01	185	73.0%	-0.93 [-1.20, -0.65]	🔴
Total (95% CI)			120			231	100.0%	-0.97 [-1.21, -0.74]	

Heterogeneity: Tau² = 0.00; Chi² = 0.39, df = 1 (P = 0.53); I² = 0%
Test for overall effect: Z = 8.10 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and Verbal Fluency (Switching): D-KEFS (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2013 (8-17yrs; D-KEFS; not FAS)	8.4	2.97	117	11.09	3.25	185	100.0%	-0.85 [-1.09, -0.61]	🔴
Total (95% CI)			117			185	100.0%	-0.85 [-1.09, -0.61]	

Heterogeneity: Not applicable
Test for overall effect: Z = 6.93 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Mattson et al 2010 also reports D-KEFS Trail Making Test (combined number-letter, switch vs number, switch vs visual, switch errors) and Verbal Fluency (Second Interval Correct and Set Loss Errors). Mattson et al 2013 also reports D-KEFS Tower Test (rule violation per item ratio), Colour Word Interference (Inhibit/Switch Completion time), Trail Making Test (Switching ss), and Twenty Questions Total Initial Abstraction (scaled score).

Category Fluency: D-KEFS/NEPSY-II (total correct)
FASD and Category Fluency (total correct): D-KEFS (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bernes et al 2021 (5-18yrs; D-KEFS)	7.9	3.4	73	10.4	2.93	47	100.0%	-0.77 [-1.15, -0.39]	🔴
Total (95% CI)			73			47	100.0%	-0.77 [-1.15, -0.39]	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.98 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

FAS and Category Fluency (total correct): D-KEFS/NEPSY-II (2 studies)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kodituwakku et al 2006a (8-9yrs; NEPSY-II)	16.26	4.47	23	17.66	4.91	21	42.4%	-0.29 [-0.89, 0.30]		🔴
Mattson et al 2010 (7-21yrs; D-KEFS)	9.71	3.19	41	12.46	3.44	46	57.6%	-0.82 [-1.26, -0.38]		🔴
Total (95% CI)			64			67	100.0%	-0.60 [-1.11, -0.09]		

Heterogeneity: Tau² = 0.07; Chi² = 1.95, df = 1 (P = 0.16); I² = 49%
Test for overall effect: Z = 2.29 (P = 0.02)

Risk of bias legend
(A) Overall RoB

Note: Kodituwakku et al 2006a also reports measures at 6 and 7yrs. Mattson et al 2010 also reports D-KEFS Trail Making Test (combined number-letter, switch vs number, switch vs visual, switch errors) and Verbal Fluency (Second Interval Correct and Set Loss Errors).

Category Fluency: F-A-S test (words/min)

FASD and F-A-S Test Category Fluency (words/min) (mean/SD) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson & Riley 1999 (8-18yrs; F-A-S test)	13.34	3.71	21	16.98	3.87	21	100.0%	-0.94 [-1.58, -0.30]		🔴
Total (95% CI)			21			21	100.0%	-0.94 [-1.58, -0.30]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.88 (P = 0.004)

Risk of bias legend
(A) Overall RoB

Other D-KEFS Measures: Tower Test (total achievement)

FASD and Tower Test (total achievement) (2 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bernes et al 2021 (5-18yrs; D-KEFS)	7.1	3.36	73	9.9	2.72	47	64.0%	-0.89 [-1.27, -0.51]		🔴
Crawford et al 2020 (8-12yrs; D-KEFS)	8.92	2.92	39	11.35	1.23	29	36.0%	-1.02 [-1.53, -0.51]		🔴
Total (95% CI)			112			76	100.0%	-0.94 [-1.24, -0.63]		

Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 1 (P = 0.69); I² = 0%
Test for overall effect: Z = 5.98 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Crawford et al 2020 also reports an executive function composite (combination of three measures) and NEPSY-II Inhibition Total Errors (ss).

pFAS and Tower Test (total achievement) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; D-KEFS; FAS/pFAS)	7.6	2.3	20	10.8	2.1	6	100.0%	-1.37 [-2.37, -0.37]		🔴
Total (95% CI)			20			6	100.0%	-1.37 [-2.37, -0.37]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.69 (P = 0.007)

Risk of bias legend
(A) Overall RoB

ARND/Others and Tower Test (total achievement) (1 study)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; D-KEFS; SE/AE)	8.3	2.5	24	10.8	2.1	16	100.0%	-1.04 [-1.72, -0.37]		🔴
Total (95% CI)			24			16	100.0%	-1.04 [-1.72, -0.37]		

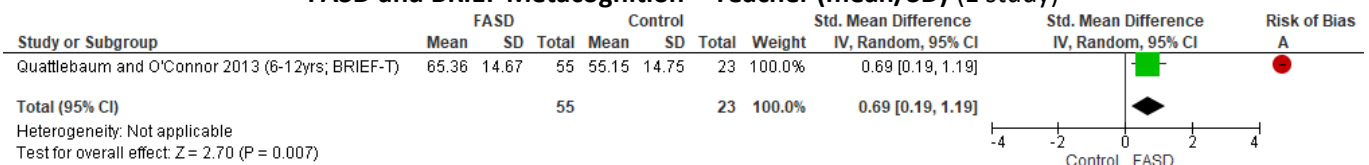Heterogeneity: Not applicable
Test for overall effect: Z = 3.02 (P = 0.003)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009b also reports ND/AE. Astley 2009 also reports D-KEFS tower test total rule violations, colour word interference (inhibit/switch completion time), and Verbal Fluency Conds 1-3% Switch Accuracy (scaled).

Other Measures: Trail Making Test Trial B

FASD and Trail Making Test Trial B (2 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Colby et al 2012 (7-13yrs; TMT B)	143.39	73.81	19	140.75	114.06	27	32.5%	0.03 [-0.56, 0.61]
Gautam et al 2014 (6-17yrs; TMT B)	122.35	59.28	49	98.99	55.73	54	67.5%	0.40 [0.01, 0.79]
Total (95% CI)			68			81	100.0%	0.28 [-0.07, 0.63]

Heterogeneity: Tau² = 0.01; Chi² = 1.10, df = 1 (P = 0.29); I² = 9%
Test for overall effect: Z = 1.59 (P = 0.11)

Risk of bias legend
(A) Overall RoB

Other Measures: Test of Executive Control

FASD and Test of Executive Control: Non-Inhibitory Condition: Incorrect (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Barrett et al 2019 (6-18yrs; TEC)	49.88	1.49	26	46.63	1.13	19	100.0%	2.36 [1.58, 3.15]
Total (95% CI)			26			19	100.0%	2.36 [1.58, 3.15]

Heterogeneity: Not applicable
Test for overall effect: Z = 5.92 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Barrett et al 2019 also reports TEC Non-Inhibitory Condition: Target Response Time, Non-Inhibitory Condition: Standard Response Time, Inhibitory Condition: Incorrect, Inhibitory Condition: Target Response Time, and Inhibitory condition: Standard Response Time.

BRIEF Global Executive Composite – Caregiver Report (mean/SD)

FASD and BRIEF Global Executive Composite – Caregiver (mean/SD) (3 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Treit et al 2016 (5-19yrs; BRIEF-C)	70	10	37	53	12	40	33.2%	1.52 [1.01, 2.03]
Ware et al 2021 (6-18yrs; BRIEF-C)	73	10	116	49	10	130	39.3%	2.39 [2.06, 2.72]
Wozniak et al 2013 (10-17yrs; BRIEF-C)	71	16.3	24	44	7.4	31	27.4%	2.20 [1.52, 2.88]
Total (95% CI)			177			201	100.0%	2.05 [1.48, 2.62]

Heterogeneity: Tau² = 0.19; Chi² = 8.00, df = 2 (P = 0.02); I² = 75%
Test for overall effect: Z = 7.04 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Ware et al 2021 also reports BRIEF emotional control.

pFAS and BRIEF Global Executive Composite – Caregiver (mean/SD) (2 studies)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Astley et al 2009b (8-15.9yrs; BRIEF-C; FAS/pFAS)	73.2	10.7	20	44.2	7	16	48.1%	3.06 [2.07, 4.06]
Candelaria-Cook et al 2021 (8-12yrs; BRIEF-C; FAS/pF)	62.5	10.1085	15	50.31	10.504	26	51.9%	1.15 [0.47, 1.84]
Total (95% CI)			35			42	100.0%	2.07 [0.20, 3.95]

Heterogeneity: Tau² = 1.64; Chi² = 9.56, df = 1 (P = 0.002); I² = 90%
Test for overall effect: Z = 2.17 (P = 0.03)

Risk of bias legend
(A) Overall RoB

ARND/Others and BRIEF Global Executive Composite – Caregiver (mean/SD) (2 studies)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Astley et al 2009b (8-15.9yrs; BRIEF-C; SE/AE)	73	9.2	24	44.2	7	16	48.2%	3.36 [2.36, 4.36]
Candelaria-Cook et al 2021 (8-12yrs; BRIEF-C;ARND)	73.89	9.8347	10	50.31	10.504	26	51.8%	2.23 [1.32, 3.14]
Total (95% CI)			34			42	100.0%	2.78 [1.67, 3.88]

Heterogeneity: Tau² = 0.40; Chi² = 2.67, df = 1 (P = 0.10); I² = 63%
Test for overall effect: Z = 4.92 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009b also reports ND/AE. Astley 2009b also reports D-KEFS tower test total rule violations, colour word interference (inhibit/switch completion time), and Verbal Fluency Conds 1-3% Switch Accuracy (scaled).

BRIEF Behaviour Regulation Index – Caregiver Report (mean/SD)

FASD and BRIEF Behaviour Regulation Index – Caregiver (mean/SD) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McLachlan et al 2020 (7-19yrs; BRIEF)	68.4	12.1	63	46.9	7.2	68	30.9%	2.17 [1.73, 2.60]	?
Quattlebaum and O'Connor 2013 (6-12yrs; BRIEF-C)	69.89	12.07	125	47.79	13.19	28	29.2%	1.79 [1.33, 2.25]	−
Treit et al 2016 (5-19yrs; BRIEF-C)	72	12	116	48	8	131	39.9%	2.37 [2.05, 2.70]	−
Total (95% CI)			304			227	100.0%	2.14 [1.81, 2.47]	

Heterogeneity: Tau² = 0.05; Chi² = 4.13, df = 2 (P = 0.13); I² = 52%
Test for overall effect: Z = 12.54 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Quattlebaum and O'Connor 2013 also reports CCT Form 1 and Form 2.

pFAS and BRIEF Behaviour Regulation Index – Caregiver (mean/SD) (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; BRIEF-C; FAS/pFAS)	73.1	13.2	20	43.9	8	16	48.1%	2.55 [1.64, 3.45]	−
Candelaria-Cook et al 2021 (8-12yrs;BRIEF-C;FAS/pF)	61.86	16.2665	15	49.41	10.147	26	51.9%	0.96 [0.29, 1.63]	
Total (95% CI)			35			42	100.0%	1.72 [0.17, 3.28]	

Heterogeneity: Tau² = 1.09; Chi² = 7.58, df = 1 (P = 0.006); I² = 87%
Test for overall effect: Z = 2.18 (P = 0.03)

Risk of bias legend
(A) Overall RoB

ARND/Others and BRIEF Behaviour Regulation Index – Caregiver (mean/SD) (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; BRIEF-C; SE/AE)	70.1	13.4	24	43.9	8	16	57.9%	2.22 [1.40, 3.03]	−
Candelaria-Cook et al 2021 (8-12yrs; BRIEF-C;ARND)	75.38	9.9296	10	49.41	10.147	26	42.1%	2.52 [1.56, 3.47]	−
Total (95% CI)			34			42	100.0%	2.34 [1.72, 2.96]	

Heterogeneity: Tau² = 0.00; Chi² = 0.22, df = 1 (P = 0.64); I² = 0%
Test for overall effect: Z = 7.42 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009 also reports ND/AE. Astley 2009 also reports D-KEFS tower test total rule violations, colour word interference (inhibit/switch completion time), and Verbal Fluency Conds 1-3% Switch Accuracy (scaled).

BRIEF Behaviour Regulation Index – Teacher Report (mean/SD)

FASD and BRIEF Behaviour Regulation Index – Teacher (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Quattlebaum and O'Connor 2013 (6-12yrs; BRIEF-T)	68.2	18.72	55	49.91	6.87	23	100.0%	1.12 [0.60, 1.64]	−
Total (95% CI)			55			23	100.0%	1.12 [0.60, 1.64]	

Heterogeneity: Not applicable
Test for overall effect: Z = 4.22 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

Note: Quattlebaum and O'Connor 2013 also reports CCT Form 1 and Form 2.

BRIEF Metacognition – Caregiver Report (mean/SD)

FASD and BRIEF Metacognition – Caregiver (mean/SD) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McLachlan et al 2020 (7-19yrs; BRIEF)	65.4	11.2	63	54	14	68	33.7%	0.89 [0.53, 1.25]	?
Quattlebaum and O'Connor 2013 (6-12yrs; BRIEF-C)	71.1	9.59	125	50.46	13.04	28	30.8%	2.00 [1.53, 2.46]	−
Treit et al 2016 (5-19yrs; BRIEF-C)	68	10	116	51	12	130	35.5%	1.53 [1.24, 1.81]	−
Total (95% CI)			304			226	100.0%	1.46 [0.89, 2.03]	

Heterogeneity: Tau² = 0.22; Chi² = 14.66, df = 2 (P = 0.0007); I² = 86%
Test for overall effect: Z = 5.01 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Quattlebaum and O'Connor 2013 also reports CCT Form 1 and Form 2.

pFAS and BRIEF Metacognition – Caregiver (mean/SD) (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; BRIEF-C; FAS/pFAS)	70.8	9.4	20	44.9	7.1	16	48.4%	2.99 [2.01, 3.98]		
Candelaria-Cook et al 2021 (8-12yrs;BRIEF-C;FAS/pF)	62.64	9.4501	15	52.14	11.9827	26	51.6%	0.92 [0.25, 1.59]		
Total (95% CI)			35			42	100.0%	1.93 [-0.10, 3.95]		

Heterogeneity: Tau² = 1.95; Chi² = 11.60, df = 1 (P = 0.0007); I² = 91%
Test for overall effect: Z = 1.86 (P = 0.06)

Risk of bias legend
(A) Overall RoB

ARND/Others and BRIEF Metacognition – Caregiver (mean/SD) (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; BRIEF-C; SE/AE)	72.2	8.2	24	44.9	7.1	16	48.5%	3.44 [2.42, 4.45]		
Candelaria-Cook et al 2021 (8-12yrs; BRIEF-C;ARND)	72.88	8.2535	10	52.14	11.9827	26	51.5%	1.82 [0.97, 2.68]		
Total (95% CI)			34			42	100.0%	2.61 [1.03, 4.19]		

Heterogeneity: Tau² = 1.07; Chi² = 5.68, df = 1 (P = 0.02); I² = 82%
Test for overall effect: Z = 3.23 (P = 0.001)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009b also reports ND/AE. Astley 2009b also reports D-KEFS tower test total rule violations, colour word interference (inhibit/switch completion time), and Verbal Fluency Conds 1-3% Switch Accuracy (scaled).

BRIEF Metacognition – Teacher Report (mean/SD)
FASD and BRIEF Metacognition – Teacher (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Quattlebaum and O'Connor 2013 (6-12yrs; BRIEF-T)	65.36	14.67	55	55.15	14.75	23	100.0%	0.69 [0.19, 1.19]		
Total (95% CI)			55			23	100.0%	0.69 [0.19, 1.19]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.70 (P = 0.007)

Risk of bias legend
(A) Overall RoB

Note: Quattlebaum and O'Connor 2013 also reports CCT Form 1 and Form 2.

Other BRIEF Measures: Inhibit – Caregiver Report (mean/SD)
FASD and BRIEF: Inhibit – Caregiver (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bernes et al 2021 (5-18yrs; BRIEF-C)	70.8	13.49	46	45	5.73	70	50.3%	2.68 [2.17, 3.19]		
Ware et al 2021 (6-18yrs; BRIEF-C)	69	13	37	50	8	40	49.7%	1.76 [1.23, 2.29]		
Total (95% CI)			83			110	100.0%	2.22 [1.32, 3.12]		

Heterogeneity: Tau² = 0.35; Chi² = 5.97, df = 1 (P = 0.01); I² = 83%
Test for overall effect: Z = 4.84 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Other BRIEF Measures: Shift – Caregiver Report (mean/SD)
FASD and BRIEF: Shift – Caregiver (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bernes et al 2021 (5-18yrs; BRIEF-C)	64.2	13.89	46	44.9	7.27	70	58.1%	1.84 [1.40, 2.29]		
Ware et al 2021 (6-18yrs; BRIEF-C)	67	13	37	49	8	40	41.9%	1.67 [1.14, 2.19]		
Total (95% CI)			83			110	100.0%	1.77 [1.43, 2.11]		

Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 10.26 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Summary of available outcomes for **working memory**

Working Memory			
Study type	**Outcome**	**Data**	**# studies**
Exposure	**Working Memory Index**	N/A	
	Freedom From Distractibility Index: WISC-III	mean/SD	**2 studies:** confirmed unquantifiable
	Digit Span Total Score/Scaled Score	N/A	
	Block Recall: WMTB-C	N/A	
	Digit Span: WISC-III	mean/SD	**1 study:** Any PAE
	Forward Digit Span: WISC-III	mean/SD	**1 study:** confirmed unquantifiable
	Backwards Digit Span: WISC-III	mean/SD	**2 studies:** confirmed unquantifiable
	Spatial WM: CANTAB, WISC-III spatial span backwards	mean/SD	**3 studies:** confirmed unquantifiable
	Spatial WM: CANTAB total errors, spatial span length	z-scores	**2 studies:** confirmed unquantifiable
Diagnosed	**Working Memory Index/ Freedom from Distractibility Index:** WISC-IV & WISC-III	mean/SD	**4 studies:** 2 FASD, 1 pFAS, 2 ARND/Other
	Freedom from Distractibility Index: WISC-III	Frequency	**1 study:** 1 pFAS, 1 ARND/Others
	Digit Span Total Scaled Score: WISC-III, WISC-IV	mean/SD	**2 studies:** 2 FAS, 2 pFAS, 2 ARND/Others
	Digit Span Total: WISC-III, WISC-IV, WISC-V, JSAIS	mean/SD	**7 studies:** 4 FASD, 3 pFAS, 2 ARND/Others
	Block Recall: WMTB-C	mean/SD	**4 studies:** FASD
	Digit Recall: WMTB-C	mean/SD	**3 studies:** FASD
	Forward Digit Span: WISC-III, JSAIS, TOMAL, WMTB-C	mean/SD	**9 studies:** 7 FASD, 1 pFAS, 1 ARND/Others
	Backwards Digit Span: WISC-IV, JSAIS	mean/SD	**6 studies:** 4 FASD, 1, pFAS, 1 ARND/Others
	Other Spatial Working Memory Measures: spatial WM strategy	mean/SD	**3 studies:** 2 FASD, 1 ARND/Others
	Other Spatial Working Memory Measures: CANTAB –-Spatial WM Total Errors	z-scores	**2 studies:** 2 FAS, 1 ARND/Others
	Other Working Memory Measures: DAS working memory percentile	mean/SD	**2 studies:** 2 FASD (different measures)

GRADE ratings for working memory

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	Certainty
Certainty assessment						**№ of patients**		**Effect**		**Certainty**
EXPOSURE STUDIES										
Freedom From Distractibility Index: WISC-III										
Confirmed unquantifiable										
2	serious[a]	not serious	not serious	serious[e,f]	none	51	40	-	**SMD 1.65 lower** (2.14 lower to 1.16 lower)	⊕⊕◯◯ Low
Digit Span: WISC-III										
Any PAE										
1	serious[a]	not serious	serious[c]	very serious[d,e,f]	none	28	28	-	**SMD 0.22 higher** (0.31 lower to 0.75 higher)	⊕◯◯◯ Very Low
Forward Digit Span: WISC-III										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	serious[e,f]	none	29	27	-	**SMD 0.99 lower** (1.55 lower to 0.43 lower)	⊕⊕◯◯ Low
Backwards Digit Span: WISC-III										
Confirmed unquantifiable										
2	serious[a]	not serious	not serious	serious[e,f]	none	98	168	-	**SMD 0.78 lower** (1.04 lower to 0.52 lower)	⊕⊕◯◯ Low
Spatial WM: CANTAB/WISC-III spatial span backwards (mean/SD), CANTAB total errors (z-score)										
Confirmed unquantifiable (SS backwards)										
3	serious[a]	serious[b]	not serious	serious[e]	none	261	323	-	**SMD 0.90 lower** (1.25 lower to 0.54 lower)	⊕◯◯◯ Very Low
Confirmed unquantifiable (total errors)										
2	serious[a]	not serious	not serious	serious[e]	none	247	245		**SMD 0.71 lower** (1.24 lower to 0.18 lower)	⊕⊕◯◯ Low
DIAGNOSED STUDIES										
Working Memory Index/ Freedom from Distractibility Index: WISC-IV & WISC-III										
FASD										
2	serious[a]	not serious	not serious	serious[e,f]	none	54	99	-	**SMD 1.18 lower** (2.36 lower to 0.00 lower)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	20	16	-	**SMD 2.68 lower** (3.61 lower to 1.75 lower)	⊕⊕◯◯ Low
ARND/Other										
2	serious[a]	serious[b]	not serious	serious[e,f]	none	46	37	-	**SMD 2.83 lower** (4.38 lower to 1.28 lower)	⊕◯◯◯ Very Low
Freedom from Distractibility Index: WISC-III										
pFAS										

No. studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	n	n	Relative effect (OR)	Absolute effect (SMD)	Certainty
1	serious[a]	not serious	not serious	serious[e,f]	none	8/20	0/16	**OR 22.04** (1.18 to 426.72)	-	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	5/24	0/16	**OR 9.31** (0.48 to 181.13)	-	⊕◯◯◯ Very Low
Digit Span Scaled Score: WISC-IV & WISC-III										
FAS										
2	serious[a]	not serious	serious[c]	not serious	none	135	293	-	**SMD 0.86 lower** (1.08 lower to 0.65 lower)	⊕⊕◯◯ Low
pFAS										
2	serious[a]	not serious	serious[c]	not serious	none	139	293	-	**SMD 0.43 lower** (0.63 lower to 0.22 lower)	⊕⊕◯◯ Low
ARND/Other										
2	serious[a]	not serious	serious[c]	serious[e,f]	none	74	293	-	**SMD 0.80 lower** (1.09 lower to 0.51 lower)	⊕◯◯◯ Very Low
Digit Span Total: WISC-IV, WISC-III, JSAIS										
FASD										
4	serious[a]	serious[b]	not serious	serious[e]	none	228	206	-	**SMD 0.70 lower** (1.05 lower to 0.35 lower)	⊕◯◯◯ Very Low
pFAS										
3	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	85	112	-	**SMD 0.42 lower** (1.01 lower to 0.17 higher)	⊕◯◯◯ Very Low
ARND/Others										
2	serious[a]	not serious	not serious	very serious[d,e,f]	none	96	80	-	**SMD 0.04 lower** (0.34 lower to 0.27 higher)	⊕◯◯◯ Very Low
Block Recall: WMTB-C (raw), WMTB-C (ss)										
FASD (raw)										
3	serious[a]	not serious	not serious	not serious	none	241	298	-	**SMD 0.80 lower** (0.98 lower to 0.63 lower)	⊕⊕⊕◯ Moderate
FAS (ss)										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	25	28	-	**SMD 0.41 higher** (0.14 lower to 0.95 higher)	⊕◯◯◯ Very Low
Digit Recall: WMTB-C										
FASD										
3	serious[a]	not serious	not serious	not serious	none	244	300	-	**SMD 0.96 lower** (1.14 lower to 0.78 lower	⊕⊕⊕◯ Moderate
Forward Digit Span: WISC-III, JSAIS, TOMAL, WMTB-C										
FASD										
7	serious[a]	not serious	not serious	not serious	none	378	449	-	**SMD 0.83 lower** (0.98 lower to 0.69 lower)	⊕⊕⊕◯ Moderate
pFAS										

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n1	n2		Effect (95% CI)	Certainty
1	serious[a]	not serious	not serious	serious[e,f]	none	24	32	-	**SMD 0.90 lower** (1.45 lower to 0.34 lower)	⊕⊕◯◯ Low

ARND/Other

| 1 | serious[a] | not serious | not serious | serious[e,f] | none | 18 | 17 | - | **SMD 1.01 lower** (1.72 lower to 0.3 lower) | ⊕⊕◯◯ Low |

Backwards Digit Span: WISC-IV, JSAIS

FASD

| 4 | serious[a] | not serious | not serious | serious[f] | none | 177 | 199 | - | **SMD 0.60 lower** (0.81 lower to 0.39 lower) | ⊕⊕◯◯ Low |

pFAS

| 1 | serious[a] | not serious | not serious | serious[e,f] | none | 24 | 32 | - | **SMD 0.82 lower** (1.37 lower to 0.26 lower) | ⊕⊕◯◯ Low |

ARND/Other

| 1 | serious[a] | not serious | not serious | serious[e,f] | none | 18 | 17 | - | **SMD 0.85 lower** (1.55 lower to 0.16 lower) | ⊕⊕◯◯ Low |

Other Spatial Working Memory Measures: CANTAB – Spatial Working Memory Strategy

FASD (Spatial Working Memory Strategy)

| 2 | serious[a] | not serious | not serious | serious[e,f] | none | 31 | 48 | - | **SMD 0.65 higher** (0.18 higher to 1.12 higher) | ⊕⊕◯◯ Low |

Other Spatial Working Memory Measures: CANTAB – Spatial Working Memory Total Errors (z-scores)

FAS

| 2 | serious[a] | not serious | not serious | serious[e,f] | none | 120 | 231 | - | **SMD 1.07 lower** (1.30 lower to 0.83 lower) | ⊕⊕◯◯ Low |

ARND/Others

| 1 | serious[a] | not serious | not serious | serious[f] | none | 117 | 185 | - | **SMD 0.82 lower** (1.06 lower to 0.58 lower) | ⊕⊕◯◯ Low |

Other Spatial Working Memory Measures: DAS Working Memory Percentile

FASD (DAS)

| 1 | serious[a] | not serious | not serious | serious[e,f] | none | 36 | 98 | - | **SMD 0.74 lower** (1.14 lower to 0.35 lower) | ⊕⊕◯◯ Low |

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.

Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I^2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CI for overall estimate crossed the line of no effect. ; e) Wide 95% Cis for overall estimate; f) Optimal information size criteria not met.

Meta-analyses for working memory

EXPOSURE STUDIES

Freedom From Distractibility Index: WISC-III (mean/SD)

Confirmed PAE Level Unquantifiable and Freedom from Distractibility Index (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bjorkquist et al 2010 (8-16yrs; WISC-III FfD)	81.48	15.79	21	111.6	11.47	10	28.1%	-2.01 [-2.94, -1.09]		🔴
Lee et al 2004 (9-17yrs; WISC-III FfD)	85.4	13.68	30	105.5	12.57	30	71.9%	-1.51 [-2.09, -0.93]		🔴
Total (95% CI)			**51**			**40**	**100.0%**	**-1.65 [-2.14, -1.16]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.81, df = 1 (P = 0.37); I² = 0%
Test for overall effect: Z = 6.60 (P < 0.00001)

-4 -2 0 2 4
Confirmed Unquantifiable   Control

Risk of bias legend
(A) Overall RoB

Digit Span: WISC-III (mean/SD)

Any PAE and WISC-III Digit Span (mean/SD) (1 study)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Furtado et al 2016 (11-12yrs; WISC-III)	9.3	3.21	28	8.68	2.28	28	100.0%	0.22 [-0.31, 0.75]		🔴
Total (95% CI)			**28**			**28**	**100.0%**	**0.22 [-0.31, 0.75]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.82 (P = 0.41)

-4 -2 0 2 4
Control   Any PAE

Risk of bias legend
(A) Overall RoB

Forward Digit Span: WISC-III (mean/SD)

Confirmed PAE Level Unquantifiable and WISC-III Forward Digit Span (mean/SD) (1 study)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Crocker et al 2015 (7-12yrs; WISC-III-Digit Span)	7.69	2.33	29	10.37	2.99	27	100.0%	-0.99 [-1.55, -0.43]		🔴
Total (95% CI)			**29**			**27**	**100.0%**	**-0.99 [-1.55, -0.43]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.48 (P = 0.0005)

-4 -2 0 2 4
Confirmed Unquantifiable   Control

Risk of bias legend
(A) Overall RoB

Backwards Digit Span: WISC-III (mean/SD)

Confirmed PAE Level Unquantifiable and Backwards Digit Span (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Crocker et al 2015 (7-12yrs; WISC-III)	7.62	3.28	29	9.81	3.63	27	23.6%	-0.63 [-1.16, -0.09]		🔴
Nguyen et al 2014 (8-16yrs; WISC-IV)	8.1	2.93	69	10.4	2.68	141	76.4%	-0.83 [-1.13, -0.53]		🔴
Total (95% CI)			**98**			**168**	**100.0%**	**-0.78 [-1.04, -0.52]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.42, df = 1 (P = 0.52); I² = 0%
Test for overall effect: Z = 5.86 (P < 0.00001)

-4 -2 0 2 4
Confirmed Unquantifiable   Control

Risk of bias legend
(A) Overall RoB

Spatial Working Memory: CANTAB, WISC-III spatial span backwards (mean/SD)

Confirmed PAE Level Unquantifiable and SWM (mean/SD) (3 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Crocker et al 2015 (7-12yrs; WISC-III)	8.07	4.18	29	10.41	3.27	27	23.1%	-0.61 [-1.15, -0.07]		🔴
Doyle et al 2018 (10-16yrs; CANTAB)	0.1	0.79	142	0.7	0.77	160	40.1%	-0.77 [-1.00, -0.53]		🔴
Glass et al 2013 (8-16yrs; CANTAB)	-0.16	0.76	90	0.72	0.69	136	36.8%	-1.22 [-1.51, -0.93]		🔴
Total (95% CI)			**261**			**323**	**100.0%**	**-0.90 [-1.25, -0.54]**		

Heterogeneity: Tau² = 0.07; Chi² = 7.01, df = 2 (P = 0.03); I² = 71%
Test for overall effect: Z = 4.94 (P < 0.00001)

-4 -2 0 2 4
Confirmed Unquantifiable   Control

Risk of bias legend
(A) Overall RoB

Spatial Working Memory (Total Errors): CANTAB (z-scores)

Confirmed PAE Level Unquantifiable and Spatial Working Memory (total errors) (z-scores) (2 studies)

Study or Subgroup	Confirmed Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2010 (7-21yrs; CANTAB)	-0.35	1.14	38	0.08	0.99	60	44.5%	-0.41 [-0.82, 0.00]		−
Mattson et al 2013 (8-17yrs; CANTAB)	-0.31	0.77	209	0.431	0.79	185	55.5%	-0.95 [-1.16, -0.74]		−
Total (95% CI)			247			245	100.0%	**-0.71 [-1.24, -0.18]**		

Heterogeneity: Tau² = 0.12; Chi² = 5.33, df = 1 (P = 0.02); I² = 81%
Test for overall effect: Z = 2.62 (P = 0.009)

Risk of bias legend
(A) Overall RoB

Note: Mattson et al 2010 also reports CANTAB SWM Strategy, Spatial Recognition Memory Percent Correct, and SWM legnth (z-scores). Mattson et al 2013 also reports other CANTAB measures.

DIAGNOSED STUDIES

Working Memory Index/Freedom from Distractibility Index: WISC-IV & WISC-III (mean/SD)

FASD and WMI/FfDI (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Popova et al 2019 (7-9yrs; WISC-IV)	87.91	23.22	21	104.73	28.76	80	51.9%	-0.60 [-1.09, -0.11]		●
Wozniak et al 2009 (10-17yrs; WISC-IV)	78.7	14.8	33	102.3	8.5	19	48.1%	-1.80 [-2.47, -1.13]		●
Total (95% CI)			54			99	100.0%	**-1.18 [-2.36, -0.00]**		

Heterogeneity: Tau² = 0.63; Chi² = 8.07, df = 1 (P = 0.004); I² = 88%
Test for overall effect: Z = 1.97 (P = 0.05)

Risk of bias legend
(A) Overall RoB

pFAS and WMI/FfDI (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; WISC-III; FAS/pFAS)	78.9	17.1	20	120.9	12.7	16	100.0%	-2.68 [-3.61, -1.75]		●
Total (95% CI)			20			16	100.0%	**-2.68 [-3.61, -1.75]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.66 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and WMI/FfDI (mean/SD) (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; WISC-III; SE/AE)	79	10.1	24	120.9	12.7	16	47.2%	-3.67 [-4.72, -2.61]		−
Malisza et al 2012 (10-14yrs; WISC-IV; ARND)	69.62	16.49	22	100.86	12.65	21	52.8%	-2.08 [-2.84, -1.32]		−
Total (95% CI)			46			37	100.0%	**-2.83 [-4.38, -1.28]**		

Heterogeneity: Tau² = 1.04; Chi² = 5.74, df = 1 (P = 0.02); I² = 83%
Test for overall effect: Z = 3.57 (P = 0.0004)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009 also reports ND/AE.

Frequency of Freedom from Distractibility Index: WISC-III <2SD (%)

pFAS and Frequency of FfDI <2SD (%) (1 study)

Study or Subgroup	pFAS Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; WISC-III; FAS/pFAS)	8	20	0	16	100.0%	22.44 [1.18, 426.74]		●
Total (95% CI)		20		16	100.0%	**22.44 [1.18, 426.74]**		
Total events	8		0					

Heterogeneity: Not applicable
Test for overall effect: Z = 2.07 (P = 0.04)

Risk of bias legend
(A) Overall RoB

ARND/Others and Frequency of FfDI <2SD (%) (1 study)

Study or Subgroup	ARND/Others Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; WISC-III; SE/AE)	5	24	0	16	100.0%	9.31 [0.48, 181.13]		🔴
Total (95% CI)		24		16	100.0%	9.31 [0.48, 181.13]		
Total events	5		0					

Heterogeneity: Not applicable
Test for overall effect: Z = 1.47 (P = 0.14)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009b also reports ND/AE.

Digit Span Scaled Score: WISC-IV & WISC-III (mean/SD)

FAS and Digit Span (ss) (mean/SD) (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2013a (6-7yrs; WISC-IV)	4.4	2.6	66	6.7	3.3	87	42.3%	-0.76 [-1.09, -0.43]		🔴
May et al 2016 (6-7yrs; WISC-III)	3.5	2.4	69	5.9	2.6	206	57.7%	-0.94 [-1.22, -0.65]		🔴
Total (95% CI)			135			293	100.0%	-0.86 [-1.08, -0.65]		

Heterogeneity: Tau² = 0.00; Chi² = 0.65, df = 1 (P = 0.42); I² = 0%
Test for overall effect: Z = 7.84 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

pFAS and Digit Span (ss) (mean/SD) (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2013a (6-7yrs; WISC-IV)	5.1	2.8	51	6.7	3.3	87	33.9%	-0.51 [-0.86, -0.16]		🔴
May et al 2016 (6-7yrs; WISC-III)	4.9	2.6	88	5.9	2.6	206	66.1%	-0.38 [-0.64, -0.13]		🔴
Total (95% CI)			139			293	100.0%	-0.43 [-0.63, -0.22]		

Heterogeneity: Tau² = 0.00; Chi² = 0.32, df = 1 (P = 0.57); I² = 0%
Test for overall effect: Z = 4.09 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

ARND/Others Digit Span (ss) (mean/SD) (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2013a (6-7yrs; WISC-IV)	4.7	2.7	35	6.7	3.3	87	44.7%	-0.63 [-1.03, -0.23]		🔴
May et al 2016 (6-7yrs; WISC-III)	3.5	2.4	39	5.9	2.6	206	55.3%	-0.93 [-1.28, -0.58]		🔴
Total (95% CI)			74			293	100.0%	-0.80 [-1.09, -0.51]		

Heterogeneity: Tau² = 0.01; Chi² = 1.20, df = 1 (P = 0.27); I² = 17%
Test for overall effect: Z = 5.38 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Digit Span Total: WISC-IV, WISC-III, JSAIS (mean/SD)

FASD and Digit Span (mean/SD) (4 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kalberg et al 2013 (6-8yrs; JSAIS)	6.9	2.9	61	10.3	3.2	52	26.5%	-1.11 [-1.51, -0.71]		🔴
Popova et al 2019 (7-9yrs; WISC-IV)	9.23	4.83	21	11.1	6.09	80	22.8%	-0.32 [-0.80, 0.17]		🔴
Quattlebaum & O'Connor 2013 (6-12yrs; WISC-III)	8.68	3.07	97	10.14	2.72	28	25.3%	-0.48 [-0.91, -0.06]		🔴
Rockhold et al 2021 (8yrs; WISC-V)	8.52	3.03	49	10.89	2.6	46	25.5%	-0.83 [-1.25, -0.41]		🔴
Total (95% CI)			228			206	100.0%	-0.70 [-1.05, -0.35]		

Heterogeneity: Tau² = 0.08; Chi² = 7.82, df = 3 (P = 0.05); I² = 62%
Test for overall effect: Z = 3.95 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

pFAS and Digit Span (mean/SD) (3 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008b (7-17yrs; WISC-IV; FAS/pFAS)	6.79	2.79	24	9.5	2.6	32	32.3%	-1.00 [-1.56, -0.43]	?
Howell et al 2006 (15yrs; WISC-III; dysmorphic)	7.83	3.21	46	7.95	3.13	56	38.1%	-0.04 [-0.43, 0.35]	−
Miles et al 2021 (9-14yrs; WISC-IV; FAS/pFAS)	7.1	3.2	15	7.9	2.6	24	29.5%	-0.28 [-0.92, 0.37]	−
Total (95% CI)			**85**			**112**	**100.0%**	**-0.42 [-1.01, 0.17]**	

Heterogeneity: Tau² = 0.20; Chi² = 7.57, df = 2 (P = 0.02); I² = 74%
Test for overall effect: Z = 1.38 (P = 0.17)

Risk of bias legend
(A) Overall RoB

Note: Aragon et al 2008b also reports DRST Spatial measures and Lhermitte measures.

ARND/Others and Digit Span (mean/SD) (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Howell et al 2006 (15yrs; WISC-III; non-syndromal)	8.01	2.32	83	7.95	3.13	56	80.0%	0.02 [-0.32, 0.36]	−
Miles et al 2021 (9-14yrs; HE)	7.2	2.4	13	7.9	2.6	24	20.0%	-0.27 [-0.95, 0.41]	−
Total (95% CI)			**96**			**80**	**100.0%**	**-0.04 [-0.34, 0.27]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.57, df = 1 (P = 0.45); I² = 0%
Test for overall effect: Z = 0.23 (P = 0.81)

Risk of bias legend
(A) Overall RoB

Block Recall: WMTB-C (raw) (mean/SD)
FASD and Block Recall (raw) (mean/SD) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McLachlan et al 2020 (7-19, WMTB-C)	90.3	16	63	103	16.2	63	23.9%	-0.78 [-1.15, -0.42]	?
Paolozza et al 2014c (5-17yrs; WMTB-C)	87.1	16.9706	72	100.5	18.9642	111	33.5%	-0.73 [-1.04, -0.43]	?
Treit et al 2016 (5-19yrs; WMTB-C)	86	16	106	100	16	124	42.6%	-0.87 [-1.14, -0.60]	−
Total (95% CI)			**241**			**298**	**100.0%**	**-0.80 [-0.98, -0.63]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.46, df = 2 (P = 0.79); I² = 0%
Test for overall effect: Z = 8.90 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Block Recall: WMTB-C (ss) (mean/SD)
FASD and Block Recall (ss) (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Rasmussen et al 2009b (4-8yrs; WMTB-C)	84.8	19.38	25	69.16	48.84	28	100.0%	0.41 [-0.14, 0.95]	−
Total (95% CI)			**25**			**28**	**100.0%**	**0.41 [-0.14, 0.95]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.46 (P = 0.14)

Risk of bias legend
(A) Overall RoB

Digit Recall: WMTB-C (mean/SD)
FASD and Digit Recall (mean/SD) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
McLachlan et al 2020 (7-19, WMTB-C)	86.3	13.4	64	100.5	17	64	24.1%	-0.92 [-1.29, -0.56]	?
Paolozza et al 2014c (5-17yrs; WMTB-C)	82.9	13.5765	72	100.1	18.9642	111	32.5%	-1.00 [-1.32, -0.69]	?
Treit et al 2016 (5-19yrs; WMTB-C)	85	13	108	99	16	125	43.4%	-0.95 [-1.22, -0.68]	−
Total (95% CI)			**244**			**300**	**100.0%**	**-0.96 [-1.14, -0.78]**	

Heterogeneity: Tau² = 0.00; Chi² = 0.12, df = 2 (P = 0.94); I² = 0%
Test for overall effect: Z = 10.52 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Forward Digit Span: WISC-III, JSAIS, TOMAL, WMTB-C (mean/SD)
FASD and Forward Digit Span (mean/SD) (7 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Gautem et al 2014 (6-18yrs; WISC-III Digit Span)	7.64	1.95	49	8.86	1.99	54	13.1%	-0.61 [-1.01, -0.22]		🔴
Kalberg et al 2013 (6-7yrs; JSAIS Digit Span A)	5.8	2.2	61	7.6	2.3	52	13.9%	-0.80 [-1.18, -0.41]		🔴
O'Hare et al 2009 (7-15yrs; WISC-IV Digit Span)	7.1	1.7	20	8.6	2.1	20	5.0%	-0.77 [-1.41, -0.12]		🔴
Paolozza et al 2014c (5-17yrs; WMTB-C)	82.9	13.5765	72	100.1	18.9642	111	20.9%	-1.00 [-1.32, -0.69]		🟡?
Rasmussen et al 2009b (4-8yrs; WMTB-C)	88.44	13.64	25	98.84	28	28	6.9%	-0.46 [-1.00, 0.09]		🔴
Treit et al 2016 (5-19yrs; WMTB-C)	85	13	108	99	16	125	27.9%	-0.95 [-1.22, -0.68]		🔴
Treit et al 2017 (5-32yrs; WMTB-C)	86	13	43	98	16	59	12.3%	-0.80 [-1.21, -0.40]		🔴
Total (95% CI)			378			449	100.0%	-0.83 [-0.98, -0.69]		

Heterogeneity: Tau² = 0.00; Chi² = 4.93, df = 6 (P = 0.55); I² = 0%
Test for overall effect: Z = 11.40 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

pFAS and Forward Digit Span (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008b (7-17yrs; WISC-III; FAS/pFAS)	6.29	1.79	24	8.25	2.39	32	100.0%	-0.90 [-1.45, -0.34]		🟡?
Total (95% CI)			24			32	100.0%	-0.90 [-1.45, -0.34]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.16 (P = 0.002)

Risk of bias legend
(A) Overall RoB

Note: Aragon et al 2008b also reports DRST Spatial Measures.

ARND/Others and Forward Digit Span (mean/SD) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Dudek et al 2014 (11-14yrs; TOMAL-Digits Forward)	5.4	2.5	18	8.2	2.9	17	100.0%	-1.01 [-1.72, -0.30]		🔴
Total (95% CI)			18			17	100.0%	-1.01 [-1.72, -0.30]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.80 (P = 0.005)

Risk of bias legend
(A) Overall RoB

Note: Dudek et al 2014 also reports other CANTAB Spatial Span (ss) and CANTAB SWM (mean/SD).

Backwards Digit Span: WISC-IV, JSAIS (mean/SD)
FASD and Backward Digit Span (mean/SD) (4 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bernes et al 2021 (8-16yrs; WISC-IV)	8.1	3.29	47	10.3	2.76	73	30.4%	-0.73 [-1.11, -0.36]		🔴
Gautam et al 2014 (6-17yrs; WISC-IV)	6.81	2.14	49	7.73	2.53	54	28.6%	-0.39 [-0.78, 0.00]		🔴
Kalberg et al 2013 (6-8yrs; JSAIS)	1.1	1.4	61	2.1	1.7	52	30.2%	-0.64 [-1.02, -0.26]		🔴
O'Hare et al 2009 (7-15yrs; WISC-IV)	6.3	1.9	20	7.7	2.4	20	10.7%	-0.63 [-1.27, 0.00]		🔴
Total (95% CI)			177			199	100.0%	-0.60 [-0.81, -0.39]		

Heterogeneity: Tau² = 0.00; Chi² = 1.67, df = 3 (P = 0.64); I² = 0%
Test for overall effect: Z = 5.60 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

pFAS and Backward Digit Span (mean/SD) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008b (7-17yrs; WISC-IV; FAS/pFAS)	5.58	1.81	24	7.15	1.96	32	100.0%	-0.82 [-1.37, -0.26]		🟡?
Total (95% CI)			24			32	100.0%	-0.82 [-1.37, -0.26]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.90 (P = 0.004)

Risk of bias legend
(A) Overall RoB

Note: Aragon et al 2008b also reports DRST Spatial Measures

ARND/Others and Backward Digit Span (mean/SD) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Dudek et al 2014 (11-14yrs; TOMAL)	8.4	2.5	18	10.9	3.2	17	100.0%	-0.85 [-1.55, -0.16]		
Total (95% CI)			18			17	100.0%	-0.85 [-1.55, -0.16]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.40 (P = 0.02)

Risk of bias legend
(A) Overall RoB

Note: Dudek et al 2014 also reports other CANTAB Spatial Span (ss) and CANTAB SWM (mean/SD).

Other Spatial Working Memory Measures: CANTAB – Spatial Working Memory Strategy

FASD and CANTAB SWM Strategy (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Pinner et al 2020 (12-21yrs; CANTAB)	33.73	4.7	19	29.85	5.73	22	54.6%	0.72 [0.09, 1.36]		
Rasmussen et al 2011b (6-17yrs; CANTAB)	37.6	2.8	12	34.4	6.3	26	45.4%	0.57 [-0.13, 1.27]		
Total (95% CI)			31			48	100.0%	0.65 [0.18, 1.12]		

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.76); I² = 0%
Test for overall effect: Z = 2.73 (P = 0.006)

Risk of bias legend
(A) Overall RoB

Note: Pinner et al 2020 also reports CANTAB SWM Latency, and other CANTAB CGT and IED measures (mean/SD). Rasmussen et al 2011b also reports CANTAB SWM Between Errors and CANTAB Spatial Span Length (mean/SD).

Other Spatial Working Memory Measures: CANTAB – Spatial Working Memory Total Errors

FAS and CANTAB SWM Total Errors (z-scores) (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2010 (7-21yrs; CANTAB)	-0.84	0.93	41	0.05	1.02	46	28.7%	-0.90 [-1.34, -0.46]		
Mattson et al 2013 (8-17yrs; CANTAB)	-0.45	0.79	79	0.431	0.77	185	71.3%	-1.13 [-1.41, -0.85]		
Total (95% CI)			120			231	100.0%	-1.07 [-1.30, -0.83]		

Heterogeneity: Tau² = 0.00; Chi² = 0.74, df = 1 (P = 0.39); I² = 0%
Test for overall effect: Z = 8.81 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Mattson et al 2010 also reports CANTAB – SWM Strategy, Spatial Recognition Memory % correct, and total errors (z-scores). Mattson et al 2013 also reports other CANTAB measures.

ARND/Others and CANTAB SWM Total Errors (z-scores) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson et al 2013 (8-17yrs; CANTAB; not FAS)	-0.2	0.73	117	0.431	0.79	185	100.0%	-0.82 [-1.06, -0.58]		
Total (95% CI)			117			185	100.0%	-0.82 [-1.06, -0.58]		

Heterogeneity: Not applicable
Test for overall effect: Z = 6.68 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Other Spatial Working Memory Measures: DAS Working Memory Percentile

FASD and DAS WM Percentile (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2014 (6-7yrs; DAS)	39.6	27	36	57.6	22.9	98	100.0%	-0.74 [-1.14, -0.35]		
Total (95% CI)			36			98	100.0%	-0.74 [-1.14, -0.35]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.71 (P = 0.0002)

Risk of bias legend
(A) Overall RoB

Summary of available outcomes for **academic**

Academic			
Study Type	**Outcome**	**Data**	**# of studies**
Exposure Studies (light, moderate, heavy, very heavy, any level, confirmed-unquantifiable)	Overall academic achievement	Mean and SDs	**2 studies:** 1 light, 1 moderate, 1 heavy, 1 very heavy, 0 any, 0 confirmed-unquantifiable
	Literacy/Reading	Mean and SDs; adjusted mean difference and 95% CIs	**4 studies:** 0 light, 1 moderate, 1 heavy, 1 very heavy, 0 any, 2 confirmed-unquantifiable
		OR/aOR and 95% CIs; % or n cases with event	**2 studies:**
	Numeracy/Maths	Mean and SDs; adjusted mean difference and 95% CIs	**3 studies:** 0 light, 0 moderate, 0 heavy, 1 very heavy, 0 any, 2 confirmed-unquantifiable
		OR/aOR and 95% CIs; % or n cases with event	**1 study:**
Diagnosed Studies (FASD, FAS, pFAS, Other FASDs)	Overall academic achievement	Mean and SDs	**8 studies:** 4 FASD, 2 FAS, 2 pFAS, 2 Other
	Literacy/Reading	Mean and SDs	**5 studies:** 5 FASD, 2 FAS, 1 pFAS, 1 Other
	Numeracy/Maths	Mean and SDs	**8 studies:** 6 FASD, 3 FAS, 2 pFAS, 2 Other

Note. No specific age groups all studies included a range of ages from 5 to 19 years.

GRADE ratings for academic

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	Certainty
		Certainty assessment				**№ of patients**		**Effect**		**Certainty**
EXPOSURE STUDIES										
Overall academic achievement (m/sd)										
Light prenatal alcohol exposure (1-20g/w in at least one trimester)										
1	serious[a]	not serious	not serious	not serious	none	2928	3332	-	**SMD 0.09 higher** (0.04 higher to 0.14 higher)	⊕⊕⊕◯ Moderate
Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)										
1	serious[a]	not serious	not serious	not serious	none	947	3332	-	**SMD 0.08 higher** (0.01 higher to 0.15 higher)	⊕⊕⊕◯ Moderate
Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)										
1	serious[a]	not serious	not serious	serious[d]	none	106	3332	-	**SMD 0.19 lower** (0.38 lower to 0.01 higher)	⊕⊕◯◯ Low
Very heavy prenatal alcohol exposure (201g+g/w in at least one trimester)										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	25	21	-	**SMD 0.92 lower** (1.53 lower to 0.30 lower)	⊕◯◯◯ Very Low
Any level, Confirmed-Unquantifiable – no studies										
Literacy/Reading (m/sd)										
Light prenatal alcohol exposure – no studies										
Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)										
1	serious[a]	not serious	not serious	serious[d]	none	1561	1536	-	**SMD 0.05 higher** (0.02 lower to 0.12 higher)	⊕⊕◯◯ Low
Heavy prenatal alcohol exposure (101g-200g/w in at least one trimester)										
1	serious[a]	not serious	not serious	serious[d]	none	39	1536	-	**SMD 0.17 lower** (0.48 lower to 0.15 higher)	⊕⊕◯◯ Low
Very heavy prenatal alcohol exposure (201g+/w in at least one trimester)										
1	serious[a]	not serious	not serious	serious[e,f]	none	25	21	-	**SMD 0.70 lower** (1.30 lower to 0.10 lower)	⊕⊕◯◯ Low
Any level prenatal alcohol exposure – no studies										
Confirmed prenatal alcohol exposure-Level Unquantifiable										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	112	116	-	**SMD 0.44 lower** (1.00 lower to 0.12 higher)	⊕◯◯◯ Very Low
Literacy/Reading (ORs/aOR/Frequency)										
Low reading achievement (WRAT-R scores < 85)										
Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)										
1	serious[a]	not serious	not serious	serious[d]	none	1561	1563	**OR 0.70** (0.30 to 1.63)	-	⊕⊕◯◯ Low
Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)										
1	serious[a]	not serious	not serious	serious[d,f]	none	39	1563	**OR 1.10** (0.50 to 2.42)	-	⊕⊕◯◯ Low

126

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n1	n2	OR	SMD	Certainty
0 studies for light, very heavy, any level, confirmed-unquantifiable										
Reading achievement below minimum standards (based on Western Australian minimum standards)										
Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)										
1	serious[a]	not serious	not serious	serious[d,f]	none	12	52	**OR 0.85** (0.44 to 1.64)	-	⊕⊕◯◯ Low
Heavy prenatal alcohol exposure (101-200g/w in at least one trimester)										
1	serious[a]	not serious	not serious	serious[e,f]	none	12	52	**OR 2.27** (1.11 to 4.64)	-	⊕⊕◯◯ Low
0 studies for light, very heavy, any level, confirmed-unquantifiable										
Numeracy/Maths (m/sd)										
Very heavy prenatal alcohol exposure (201+g/w in at least one trimester)										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	25	21	-	**SMD 0.88 lower** (1.49 lower to 0.27 lower)	⊕◯◯◯ Very Low
Confirmed prenatal alcohol exposure-Level Unquantifiable										
3	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	195	176	-	**SMD 0.76 lower** (1.36 lower to 0.17 lower)	⊕◯◯◯ Very Low
0 studies for light, moderate, heavy, any level										
Numeracy/Maths (ORs/aOR/Frequency)										
Maths achievement below minimum standards (based on Western Australian minimum standards)										
Moderate prenatal alcohol exposure (21-100g/w in at least one trimester)										
1	not serious	not serious	not serious	serious[d,f]	none	27	135	**OR 0.71** (0.46 to 1.10)	-	⊕⊕⊕◯ Moderate
Heavy prenatal alcohol exposure (101-200g/w in eat least one trimester)										
1	not serious	not serious	not serious	serious[d,f]	none	13	135	**OR 0.98** (0.52 to 1.85)	-	⊕⊕⊕◯ Moderate
0 studies for light, very heavy, any level, confirmed-unquantifiable										
DIAGNOSED STUDIES										
Academic Achievement										
FASD										
4	serious[a]	not serious	not serious	not serious	none	102	892	-	**SMD 0.56 lower** (0.79 lower to 0.32 lower)	⊕⊕⊕◯ Moderate
FAS										
2	serious[a]	serious[b]	not serious	serious[d,e]	none	43	428	-	**SMD 0.29 lower** (1.07 lower to 0.50 higher)	⊕◯◯◯ Very Low
pFAS (pFAS or pFAS/FAS or dysmorphic)										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	68	190	-	**SMD 0.35 lower** (0.88 lower to 0.18 higher)	⊕◯◯◯ Very Low
Other FASDs (ARND, ND-AE, SE-AE, Non-syndromal)										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	103	190	-	**SMD 0.04 higher** (0.40 lower to 0.47 higher)	⊕◯◯◯ Very Low
Reading Ability										

FASD										
5	serious[a]	not serious	not serious	not serious	none	282	331	-	**SMD 1.05 lower** (1.29 lower to 0.82 lower)	⊕⊕⊕◯ Moderate

FAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	7	186	-	**SMD 0.82 lower** (1.60 lower to 0.08 lower)	⊕⊕◯◯ Low

pFAS (pFAS, pFAS/FAS, dysmorphic)										
2	serious[a]	not serious	not serious	serious[e,f]	none	39	202	-	**SMD 1.59 lower** (2.27 lower to 0.91 lower)	⊕⊕◯◯ Low

Other FASDs (ARND, ND-AE, SE-AE, Non-syndromal)										
1	serious[a]	not serious	not serious	serious[e,f]	none	21	16	-	**SMD 1.05 lower** (1.75 lower to 0.35 lower)	⊕⊕◯◯ Low

Maths Ability

FASD										
5	serious[a]	not serious	not serious	serious[e]	none	298	320	-	**SMD 1.49 lower** (1.69 lower to 1.29 lower)	⊕⊕◯◯ Low

FAS										
2	serious[a]	not serious	not serious	serious[e,f]	none	15	209	-	**SMD 1.04 lower** (1.61 lower to 0.48 lower)	⊕⊕◯◯ Low

pFAS (pFAS, pFAS/FAS, dysmorphic)										
3	serious[a]	serious[b]	not serious	serious[e,f]	none	47	225	-	**SMD 1.65 lower** (2.71 lower to 0.58 lower)	⊕◯◯◯ Very Low

Other FASDs (ARND, ND-AE, SE-AE, Non-syndromal)										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	30	39	-	**SMD 0.87 lower** (2.79 lower to 1.05 higher)	⊕◯◯◯ Very Low

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.
Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CI for overall estimate crossed the line of no effect. ; e) Wide 95% CIs for overall estimate; f) Optimal information size criteria not met.

Meta-analyses for academic

EXPOSURE STUDIES

Overall academic achievement (m/SD)
Light PAE and Academic Achievement (1 study)

Study or Subgroup	Light PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Alati et al 2013 (KeyStages2, 11yrs)	102.8	8.7	2928	102	9.1	3332	100.0%	0.09 [0.04, 0.14]		●
Total (95% CI)			**2928**			**3332**	**100.0%**	**0.09 [0.04, 0.14]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.54 (P = 0.0004)

Risk of bias legend
(A) Overall Risk of Bias

Note. Key Stages 2 of the UK National Curriculum that covers English, Mathematics and Science.

Moderate PAE and Academic Achievement (1 study)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Alati et al 2013 (KeyStages2, 11yrs)	102.7	8.7	947	102	9.1	3332	100.0%	0.08 [0.01, 0.15]		●
Total (95% CI)			**947**			**3332**	**100.0%**	**0.08 [0.01, 0.15]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.11 (P = 0.04)

Risk of bias legend
(A) Overall Risk of Bias

Note. Key Stages 2 of the UK National Curriculum that covers English, Mathematics and Science.

Heavy PAE and Academic Achievement (1 study)

Study or Subgroup	Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Alati et al 2013 (KeyStages2, 11yrs)	100.3	10.7	106	102	9.1	3332	100.0%	-0.19 [-0.38, 0.01]		●
Total (95% CI)			**106**			**3332**	**100.0%**	**-0.19 [-0.38, 0.01]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.88 (P = 0.06)

Risk of bias legend
(A) Overall Risk of Bias

Note. Key Stages 2 of the UK National Curriculum that covers English, Mathematics and Science.

Very Heavy PAE and Academic Achievement (1 study)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al. 1991 (K-ABC acad composite; 5-6yrs)	85.65	10.53	25	94.65	8.49	21	100.0%	-0.92 [-1.53, -0.30]		●
Total (95% CI)			**25**			**21**	**100.0%**	**-0.92 [-1.53, -0.30]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.93 (P = 0.003)

Risk of bias legend
(A) Overall Risk of Bias

Literacy/Reading (m/SD)
Moderate PAE and Reading Ability (1 study)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
O'Callaghan et al. 2007 (WRAT-R reading; 14yrs)	101.7	62.6846	1561	99.5	15.1	1536	100.0%	0.05 [-0.02, 0.12]		?
Total (95% CI)			1561			1536	100.0%	0.05 [-0.02, 0.12]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.34 (P = 0.18)

<u>Risk of bias legend</u>
(A) Overall Risk of Bias

Note. O'Callaghan et al 2007 = mean and SD estimated from adjusted mean difference and 95% CIs.

Heavy PAE and Reading Ability (1 study)

Study or Subgroup	Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
O'Callaghan et al. 2007 (WRAT-R reading; 14yrs)	97	14.4581	39	99.5	15.1	1536	100.0%	-0.17 [-0.48, 0.15]		?
Total (95% CI)			39			1536	100.0%	-0.17 [-0.48, 0.15]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.02 (P = 0.31)

<u>Risk of bias legend</u>
(A) Overall Risk of Bias

Note. O'Callaghan et al 2007 = mean and SD estimated from adjusted mean difference and 95% CIs.

Very Heavy PAE and Reading Ability (1 study)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al 1991 (K-ABC reading/decoding; 5-6yrs)	91.62	15.63	25	101.76	12.38	21	100.0%	-0.70 [-1.30, -0.10]		●
Total (95% CI)			25			21	100.0%	-0.70 [-1.30, -0.10]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.29 (P = 0.02)

<u>Risk of bias legend</u>
(A) Overall Risk of Bias

Confirmed PAE Level Unquantifiable and Reading Ability (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Glass et al 2017 (WIAT-II word reading; 8-16yrs)	94.7	17.32	67	105.9	13.03	61	50.5%	-0.72 [-1.08, -0.36]		●
Vaurio et al 2011 (WRAT-3 reading; 6-16yrs)	96.58	14.82	55	99.04	17.93	55	49.5%	-0.15 [-0.52, 0.23]		●
Total (95% CI)			122			116	100.0%	-0.44 [-1.00, 0.12]		

Heterogeneity: Tau² = 0.13; Chi² = 4.70, df = 1 (P = 0.03); I² = 79%
Test for overall effect: Z = 1.53 (P = 0.13)

<u>Risk of bias legend</u>
(A) Overall Risk of Bias

Literacy/Reading (OR/aOR/frequency)

LOW READING ACHIEVEMENT (WRAT-R SCORES <85)

Moderate PAE and Low Reading Achievement (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Moderate PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Callaghan et al. 2007 (WRAT-R reading; 14yrs)	-0.3567	0.4323	1561	1536	100.0%	0.70 [0.30, 1.63]		?
Total (95% CI)			1561	1536	100.0%	0.70 [0.30, 1.63]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)

<u>Risk of bias legend</u>
(A) Overall Risk of Bias

Note. O'Callaghan et al 2007 = mean and SD estimated from adjusted mean difference and 95% CIs.

Heavy PAE and Low Reading Achievement (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Heavy PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Callaghan et al. 2007 (WRAT-R reading; 14yrs)	0.0953	0.4023	39	1536	100.0%	1.10 [0.50, 2.42]		?
Total (95% CI)			**39**	**1536**	**100.0%**	**1.10 [0.50, 2.42]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)

Risk of bias legend
(A) Overall Risk of Bias

Note. O'Callaghan et al 2007 = mean and SD estimated from adjusted mean difference and 95% CIs.

READING ACHIEVEMENT BELOW MINIMUM STANDARD (BASED ON WESTERN AUSTRALIAN MINIMUM STANDARDS)

Moderate PAE and Reading Achievement below Minimum Standard (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Moderate PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al. 2013 (WALNA reading; 8-9yrs)	-0.1625	0.336	12	52	100.0%	0.85 [0.44, 1.64]		+
Total (95% CI)			**12**	**52**	**100.0%**	**0.85 [0.44, 1.64]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.48 (P = 0.63)

Risk of bias legend
(A) Overall Risk of Bias

Note. O'Leary et al. 2013 = adjusted ORs; WALNA: Western Australian Literacy and Numeracy Assessment state-wide education testing program.

Heavy PAE and Reading Achievement below Minimum Standard (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Heavy PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al. 2013 (WALNA reading; 8-9yrs)	0.8198	0.365	12	52	100.0%	2.27 [1.11, 4.64]		+
Total (95% CI)			**12**	**52**	**100.0%**	**2.27 [1.11, 4.64]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.25 (P = 0.02)

Risk of bias legend
(A) Overall Risk of Bias

Note. O'Leary et al. 2013 = adjusted ORs; WALNA: Western Australian Literacy and Numeracy Assessment state-wide education testing program.

Numeracy/Maths (m/SD)

Very Heavy PAE and Maths Ability (1 study)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Coles et al. 1991 (K-ABC math subtest; 5-6yrs)	84.83	13.31	25	96.52	12.76	21	100.0%	-0.88 [-1.49, -0.27]		–
Total (95% CI)			**25**			**21**	**100.0%**	**-0.88 [-1.49, -0.27]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.83 (P = 0.005)

Risk of bias legend
(A) Overall Risk of Bias

Confirmed PAE Level Unquantifiable and Maths Ability (3 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Gautum Lebel etal 2015 (WISC-IV arithmetic; 7-16yr)	6.8	2.5	73	8.3	3.5	60	33.9%	-0.50 [-0.85, -0.15]		●
Glass et al 2017 (WIAT-II maths composit; 8-16yrs)	86.7	18.1	67	110.8	16.3	61	32.9%	-1.39 [-1.77, -1.00]		●
Vaurio et al 2011 (WRAT-3 arithmetic; 6-16yrs)	90.72	16.57	55	98.28	19.92	55	33.2%	-0.41 [-0.79, -0.03]		●
Total (95% CI)			**195**			**176**	**100.0%**	**-0.76 [-1.36, -0.17]**		

Heterogeneity: Tau² = 0.24; Chi² = 15.53, df = 2 (P = 0.0004); I² = 87%
Test for overall effect: Z = 2.51 (P = 0.01)

Risk of bias legend
(A) Overall Risk of Bias

Numeracy/Maths (OR/aOR/frequency)

NUMERACY ACHIEVEMENT BELOW MINIMUM STANDARD (BASED ON WESTERN AUSTRALIAN MINIMUM STANDARDS)

Moderate PAE and Numeracy Achievement below Minimum Standard (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Moderate PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al. 2013 (WALNA numeracy; 8-9yrs)	-0.3425	0.2215	27	135	100.0%	0.71 [0.46, 1.10]		+
Total (95% CI)			27	135	100.0%	**0.71 [0.46, 1.10]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.55 (P = 0.12)

Risk of bias legend
(A) Overall Risk of Bias

Note. O'Leary et al. 2013 = adjusted ORs; WALNA: Western Australian Literacy and Numeracy Assessment state-wide education testing program.

Heavy PAE and Numeracy Achievement below Minimum Standard (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Heavy PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al. 2013 (WALNA numeracy; 8-9yrs)	-0.0202	0.3233	13	135	100.0%	0.98 [0.52, 1.85]		+
Total (95% CI)			13	135	100.0%	**0.98 [0.52, 1.85]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.06 (P = 0.95)

Risk of bias legend
(A) Overall Risk of Bias

Note. O'Leary et al. 2013 = adjusted ORs; WALNA: Western Australian Literacy and Numeracy Assessment state-wide education testing program.

DIAGNOSED STUDIES

Academic Achievement (m/SD)

FASD and Academic Achievement (4 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
1.1.1 Low-Moderate Risk of Bias										
Aragon et al 2008a (IPDA; 6-7yrs)	16.42	5.69	23	20.96	6.03	57	20.1%	-0.76 [-1.26, -0.26]		?
Kodituwakku et al 2006b (IPDA; 6-7yrs)	16.9	3.41	22	21.25	5.6	60	19.6%	-0.84 [-1.35, -0.34]		?
Subtotal (95% CI)			45			117	39.8%	**-0.80 [-1.15, -0.44]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = 0.82); I² = 0%
Test for overall effect: Z = 4.41 (P < 0.0001)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
1.1.2 High Risk of Bias										
May et al 2020b (BBCS school readiness; 6-7yrs)	101.5	14.5	49	106.4	12.9	444	49.6%	-0.37 [-0.67, -0.08]		−
May et al 2020c (BBCS school readiness; 6-7yrs)	107	13.3	8	112.3	10.4	331	10.6%	-0.51 [-1.21, 0.20]		−
Subtotal (95% CI)			57			775	60.2%	**-0.39 [-0.67, -0.12]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.11, df = 1 (P = 0.74); I² = 0%
Test for overall effect: Z = 2.83 (P = 0.005)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Total (95% CI)			102			892	100.0%	**-0.56 [-0.79, -0.32]**		

Heterogeneity: Tau² = 0.01; Chi² = 3.31, df = 3 (P = 0.35); I² = 9%
Test for overall effect: Z = 4.67 (P < 0.00001)
Test for subgroup differences: Chi² = 3.14, df = 1 (P = 0.08), I² = 68.2%

FAS and Academic Achievement (2 studies)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (BBCS school readiness; 7yrs)	105.6	18.1	5	102	15.2	155	37.1%	0.23 [-0.66, 1.13]		−
May et al 2020a (BBCS school readiness; 6-7yrs)	105.4	16.2	38	111.8	9.8	273	62.9%	-0.59 [-0.94, -0.25]		−
Total (95% CI)			43			428	100.0%	**-0.29 [-1.07, 0.50]**		

Heterogeneity: Tau² = 0.22; Chi² = 2.89, df = 1 (P = 0.09); I² = 65%
Test for overall effect: Z = 0.71 (P = 0.47)

Risk of bias legend
(A) Risk of Bias

pFAS and Academic Achievement (2 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (BBCS school readiness; 7yrs)	100.2	15.2	43	102	15.2	155	57.2%	-0.12 [-0.46, 0.22]		🔴
Coles et 1997 FAS/FAE(K-ABC acad composite; 7-8yrs)	84.8	12.91	25	92.26	9.63	35	42.8%	-0.66 [-1.19, -0.14]		🔴
Total (95% CI)			**68**			**190**	**100.0%**	**-0.35 [-0.88, 0.18]**		

Heterogeneity: Tau² = 0.10; Chi² = 2.91, df = 1 (P = 0.09); I² = 66%
Test for overall effect: Z = 1.30 (P = 0.19)

Risk of bias legend
(A) Risk of Bias

Other FASDs and Academic Achievement (2 studies)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 ARND (BBCS school readi; 7yrs)	105.7	14.9	41	102	15.2	155	53.5%	0.24 [-0.10, 0.59]		🔴
Coles et 1997 Non-dys (K-ABC acad composite; 7-8yr)	90.08	11.47	62	92.26	9.63	35	46.5%	-0.20 [-0.61, 0.22]		🔴
Total (95% CI)			**103**			**190**	**100.0%**	**0.04 [-0.40, 0.47]**		

Heterogeneity: Tau² = 0.06; Chi² = 2.58, df = 1 (P = 0.11); I² = 61%
Test for overall effect: Z = 0.17 (P = 0.86)

Risk of bias legend
(A) Risk of Bias

Reading Ability (m/SD)

FASD and Reading Ability (4 studies/5 samples)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Jirikowic Olson 2008a (WRAT3 reading; 5-8yrs)	93	16.7	25	101.5	14.8	26	13.2%	-0.53 [-1.09, 0.03]		🔴
Little et al 2020_CHIR (WRMT-R Word ID; 5-16yrs)	89	14	52	108	13	66	20.4%	-1.40 [-1.81, -1.00]		🔴
Little et al 2020_NDN (WRMT-R Word ID; 5-16yrs)	91	14	78	106	13	80	25.4%	-1.11 [-1.44, -0.77]		🔴
Sowell et al 2008 (WRAT3 reading; 7-15yrs)	33.77	8.9	17	39.95	4.98	19	9.6%	-0.85 [-1.54, -0.16]		🔴
Treit et al 2016 (WRMT-R-Word ID ; 5-19yrs)	90	15	110	106	15	140	31.4%	-1.06 [-1.33, -0.80]		🔴
Total (95% CI)			**282**			**331**	**100.0%**	**-1.05 [-1.29, -0.82]**		

Heterogeneity: Tau² = 0.03; Chi² = 6.59, df = 4 (P = 0.16); I² = 39%
Test for overall effect: Z = 8.79 (P < 0.00001)

Risk of bias legend
(A) Risk of Bias

FAS and Reading Ability (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2015 (WRAT3 reading; 6-7yrs)	99.9	8.92	7	111.8	14.26	186	100.0%	-0.84 [-1.60, -0.08]		🔴
Total (95% CI)			**7**			**186**	**100.0%**	**-0.84 [-1.60, -0.08]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.17 (P = 0.03)

Risk of bias legend
(A) Risk of Bias

pFAS and Reading Ability (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley Olson et al 2009 (WIAT basic read; 13yrs)	86.5	15.8	20	115.8	11.7	16	38.8%	-2.03 [-2.85, -1.20]		🔴
May et al 2015 (WRAT3 reading; 6-7yrs)	92.6	17.53	19	111.8	14.26	186	61.2%	-1.31 [-1.80, -0.82]		🔴
Total (95% CI)			**39**			**202**	**100.0%**	**-1.59 [-2.27, -0.91]**		

Heterogeneity: Tau² = 0.14; Chi² = 2.14, df = 1 (P = 0.14); I² = 53%
Test for overall effect: Z = 4.57 (P < 0.00001)

Risk of bias legend
(A) Risk of Bias

Other FASDs and Reading Ability (1 study)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley Olson et al 2009 ND/AE (WIATbasicread; 13yr)	102.4	14.9	21	115.8	8.2	16	100.0%	-1.05 [-1.75, -0.35]		🔴
Total (95% CI)			**21**			**16**	**100.0%**	**-1.05 [-1.75, -0.35]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.95 (P = 0.003)

Math Ability (m/SD)

FASD and Maths Ability (4 studies/5 samples)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Fryer et al. 2012 (WRAT3 arithmetic; 9-21yrs)	83	16.56	21	104	13.98	7	4.4%	-1.27 [-2.20, -0.35]		⊖
Jirikowic Olson 2008a (WRAT3 arithmetic; 5-8yrs)	81.2	14	25	101.2	13.05	26	9.4%	-1.46 [-2.08, -0.83]		⊖
Little et al 2020_CIHR (WJ Quant Concept; 5-16yrs)	82	13	52	107	13	66	18.0%	-1.91 [-2.35, -1.47]		⊖
Little et al 2020_NDN (WJ Quant Concepts; 5-16yrs)	83	19	78	105	12	80	27.2%	-1.38 [-1.73, -1.03]		⊖
Treit et al 2016 (WJ Quant Concepts; 5-19yrs)	82	19	122	106	15	141	41.0%	-1.41 [-1.68, -1.14]		⊖
Total (95% CI)			**298**			**320**	**100.0%**	**-1.49 [-1.69, -1.29]**		

Heterogeneity: Tau² = 0.01; Chi² = 4.43, df = 4 (P = 0.35); I² = 10%
Test for overall effect: Z = 14.90 (P < 0.00001)

Risk of bias legend
(A) Risk of Bias

FAS and Maths Ability (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Ben-Shachar 2020 (WIATnum operations, 16yrs)	57.5	16.5	8	74.1	18.4	23	45.3%	-0.90 [-1.74, -0.06]		⊖
May et al 2015 (WRAT3 arithmetic; 6-7yrs)	89.1	21.12	7	107.8	15.81	186	54.7%	-1.16 [-1.93, -0.40]		⊖
Total (95% CI)			**15**			**209**	**100.0%**	**-1.04 [-1.61, -0.48]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 3.62 (P = 0.0003)

Risk of bias legend
(A) Risk of Bias

pFAS and Maths Ability (3 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley Olson et al 2009 (KeyMaths; 13yrs)	78.3	14.6	20	118.4	11.7	16	30.3%	-2.93 [-3.90, -1.95]		⊖
Ben-Shachar 2020 (WIATnum operations, 16yrs)	62.3	12.2	8	74.1	18.4	23	32.6%	-0.67 [-1.50, 0.15]		⊖
May et al 2015 (WRAT3 arithmetic; 6-7yrs)	84.8	14.84	19	107.8	15.81	186	37.2%	-1.46 [-1.95, -0.96]		⊖
Total (95% CI)			**47**			**225**	**100.0%**	**-1.65 [-2.71, -0.58]**		

Heterogeneity: Tau² = 0.74; Chi² = 12.17, df = 2 (P = 0.002); I² = 84%
Test for overall effect: Z = 3.02 (P = 0.003)

Risk of bias legend
(A) Risk of Bias

Other FASDs and Maths Ability (2 studies)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley Olson et al 2009 ND/AE (KeyMaths; 13yrs)	96.7	11.3	21	118.4	11.7	16	49.9%	-1.85 [-2.64, -1.06]		⊖
Ben-Shachar 2020 Non-syn (WIATnum operations, 16yr	76.1	17.7	9	74.1	18.4	23	50.1%	0.11 [-0.66, 0.88]		⊖
Total (95% CI)			**30**			**39**	**100.0%**	**-0.87 [-2.79, 1.05]**		

Heterogeneity: Tau² = 1.76; Chi² = 12.10, df = 1 (P = 0.0005); I² = 92%
Test for overall effect: Z = 0.89 (P = 0.37)

Risk of bias legend
(A) Risk of Bias

Summary of available outcomes for **adaptive behaviour**

Adaptive behaviour			
Study type	**Measures**	**Data**	**# studies**
Exposure Studies	**Adaptive Composite – Caregiver**: VABS, BSID	mean/SD	**4 studies:** 4 confirmed unquantifiable
	Adaptive Composite – Teacher -	N/A	
	Adaptive: Socialisation – Caregiver: VABS	mean/SD	**3 studies:** 3 confirmed unquantifiable
	Adaptive: Socialisation – Teacher	N/A	
	Adaptive: Daily Living Skills – Caregiver: VABS	mean/SD	**3 studies:** 3 confirmed unquantifiable
	Adaptive: Daily Living Skills – Teacher	N/A	
	Adaptive: Communication – Caregiver: VABS, BSID	mean/SD	**4 studies:** 4 confirmed unquantifiable
	Adaptive: Communication – Teacher	N/A	
	~~Adaptive: More Sub-Domains~~	~~N/A~~	
Diagnosed Studies	**Adaptive Composite – Caregiver**: SIB-R, VABS, ABAS	mean/SD	**4 studies:** 4 FASD, 2 pFAS, 2 ARND/Others
	Adaptive Composite – Teacher: VABS, ABAS	mean/SD	**6 studies:** 4 FASD, 2 pFAS, 2 ARND/Others
	Adaptive: Socialisation – Teacher: VABS	mean/SD	**1 study:** 1 FAS, 1 pFAS
	Adaptive: Socialisation – Caregiver: VABS, ABAS	mean/SD	**14 studies:** 11 FASD, 1 FAS, 3 pFAS, 3 ARND/Others
	Adaptive: Daily Living Skills – Teacher: VABS	mean/SD	**4 studies:** 3 FASD, 1 FAS, 1 pFAS
	Adaptive: Daily Living Skills – Caregiver: VABS	mean/SD	**8 studies:** 8 FASD, 1 FAS, 2 pFAS, 2 ARND/Others
	Adaptive: Communication – Teacher: VABS	mean/SD	**4 studies:** 3 FASD, 1 FAS, 1 pFAS
	Adaptive: Communication – Caregiver: VABS	mean/SD	**9 studies:** 8 FASD, 1 FAS, 2 pFAS, 2 ARND/Others

GRADE ratings for adaptive behaviour

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	Certainty
Certainty assessment						**№ of patients**		**Effect**		**Certainty**
EXPOSURE STUDIES										
Adaptive Composite – Caregiver: VABS, BSID										
Confirmed unquantifiable										
4	serious[a]	serious[b]	not serious	serious[e]	none	336	485	-	**SMD 0.84 lower** (1.47 lower to 0.20 lower)	⊕◯◯◯ Very low
Adaptive: Socialisation – Caregiver: VABS										
Confirmed unquantifiable										
3	serious[a]	serious[b]	not serious	serious[e]	none	218	327	-	**SMD 0.73 lower** (1.22 lower to 0.25 lower)	⊕◯◯◯ Very low
Adaptive: Daily Living Skills – Caregiver: VABS										
Confirmed unquantifiable										
3	serious[a]	serious[b]	not serious	serious[e]	none	218	327	-	**SMD 0.88 lower** (1.50 lower to 0.26 lower)	⊕◯◯◯ Very low
Adaptive: Communication – Caregiver: VABS, BSID										
Confirmed unquantifiable										
4	serious[a]	serious[b]	not serious	serious[e]	none	360	487	-	**SMD 1.06 lower** (1.78 lower to 0.35 lower)	⊕◯◯◯ Very low
DIAGNOSED STUDIES										
Adaptive Composite – Caregiver: SIB-R, VABS, ABAS										
FASD										
4	serious[a]	serious[b]	not serious	serious[e,f]	none	156	114	-	**SMD 2.12 lower** (2.70 lower to 1.55 lower)	⊕◯◯◯ Very low
pFAS										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	66	73	-	**SMD 1.09 lower** (3.39 lower to 1.21 higher)	⊕◯◯◯ Very low
ARND/Other										
2	serious[a]	not serious	not serious	serious[e,f]	none	58	73	-	**SMD 2.43 lower** (3.21 lower to 1.65 lower)	⊕⊕◯◯ Low
Adaptive Composite – Teacher: VABS, SIB-R, ABAS										
FAS										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	7	186	-	**SMD 0.59 lower** (1.35 lower to 0.17 higher)	⊕◯◯◯ Very low
pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	19	186	-	**SMD 1.18 lower** (1.66 lower to 0.69 lower)	⊕⊕◯◯ Low
Adaptive: Socialisation – Caregiver: VABS										
FASD										

No.	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n1	n2		Effect	Certainty
11	serious[a]	serious[b]	not serious	serious[e]	none	502	880	-	**SMD 1.25 lower** (1.70 lower to 0.81 lower)	⊕◯◯◯ Very low
FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.18 higher** (0.70 lower to 1.06 higher)	⊕⊕◯◯ Low
pFAS										
3	serious[a]	serious[b]	not serious	serious[d,e]	none	109	830	-	**SMD 0.64 lower** (1.44 lower to 0.17 higher)	⊕◯◯◯ Very low
ARND/Others										
3	serious[a]	serious[b]	not serious	serious[d,e]	none	144	831	-	**SMD 0.87 lower** (1.77 lower to 0.03 higher)	⊕◯◯◯ Very low
Adaptive: Socialisation – Teacher: VABS										
FASD										
3	serious[a]	not serious	not serious	not serious	none	116	1052	-	**SMD 0.58 lower** (0.78 lower to 0.39 lower)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	7	186	-	**SMD 0.35 lower** (1.11 lower to 0.40 higher)	⊕◯◯◯ Very low
pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	19	186	-	**SMD 0.79 lower** (1.27 lower to 0.32 lower)	⊕⊕◯◯ Low
Adaptive: Daily Living Skills – Caregiver: VABS										
FASD										
8	serious[a]	serious[b]	not serious	not serious	none	323	811	-	**SMD 1.16 lower** (1.71 lower to 0.62 lower)	⊕⊕◯◯ Low
FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.59 higher** (0.29 lower to 1.47 higher)	⊕⊕◯◯ Low
pFAS										
2	serious[a]	not serious	not serious	not serious	none	85	815	-	**SMD 0.36 lower** (0.60 lower to 0.11 lower)	⊕⊕⊕◯ Moderate
ARND/Others										
2	serious[a]	not serious	not serious	serious[d]	none	120	815	-	**SMD 0.22 lower** (0.45 lower to 0.01 higher)	⊕⊕◯◯ Low
Adaptive: Daily Living Skills – Teacher: VABS										
FASD										
3	serious[a]	not serious	not serious	not serious	none	116	1052	-	**SMD 0.43 lower** (0.64 lower to 0.21 lower)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	7	186	-	**SMD 0.50 lower** (1.26 lower to 0.25 higher)	⊕◯◯◯ Very low

pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	19	186	-	**SMD 1.01 lower** (1.49 lower to 0.53 lower)	⊕⊕◯◯ Low
Adaptive: Communication – Caregiver: VABS										
FASD										
9	serious[a]	serious[b]	not serious	not serious	none	372	815	-	**SMD 1.58 lower** (2.15 lower to 1.02 lower)	⊕⊕◯◯ Low
FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.35 higher** (0.53 lower to 1.23 higher)	⊕⊕◯◯ Low
pFAS										
2	serious[a]	not serious	not serious	not serious	none	89	815	-	**SMD 4.69 lower** (7.98 lower to 1.40 lower)	⊕⊕⊕◯ Moderate
ARND/Other										
2	serious[a]	not serious	not serious	serious[e]	none	120	815	-	**SMD 6.16 lower** (10.84 lower to 1.48 lower)	⊕⊕◯◯ Low
Adaptive: Communication – Teacher: VABS										
FASD										
3	serious[a]	not serious	not serious	not serious	none	116	1052	-	**SMD 0.49 lower** (0.69 lower to 0.30 lower)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	7	186	-	**SMD 0.70 lower** (1.46 lower to 0.06 higher)	⊕◯◯◯ Very low
pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	19	186	-	**SMD 1.28 lower** (1.76 lower to 0.79 lower)	⊕⊕◯◯ Low

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.

Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I^2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CI for overall estimate crossed the line of no effect; e) Wide CIs for overall estimate; f) Optimal information size criteria not met.

Meta-analyses for adaptive behaviour

EXPSOURE STUDIES

Adaptive Composite – Caregiver: VABS, BSID

Confirmed PAE Level Unquantifiable and Adaptive Composite - Caregiver (4 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Doyle et al 2019a (8-16yrs; VABS-II)	83.4	18	163	103.6	17.81	274	26.6%	-1.13 [-1.34, -0.92]		🔴
Donald et al 2016 (6mnths; BSID-III)	103.81	8.82	28	106.26	8.34	45	23.8%	-0.28 [-0.76, 0.19]		🔴
Ware et al 2012 (8-18yrs; VABS-II)	84.78	17.27	142	111.44	13.81	133	26.0%	-1.69 [-1.97, -1.42]		🔴
Whaley et al 2001 (20 mnths-10.5 yrs; VABS-II)	70.85	17.17	33	73.06	18.98	33	23.6%	-0.12 [-0.60, 0.36]		🔴
Total (95% CI)			366			485	100.0%	-0.84 [-1.47, -0.20]		

Heterogeneity: Tau² = 0.38; Chi² = 44.98, df = 3 (P < 0.00001); I² = 93%
Test for overall effect: Z = 2.58 (P = 0.010)

Risk of bias legend
(A) Overall risk of bias

Adaptive Socialisation – Caregiver: VABS

Confirmed PAE Level Unquantifiable and Adaptive Socialisation – Caregiver (3 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Crocker et al 2009 (6-13yrs; VABS)	81.5	20.85	22	102.45	10.75	20	24.9%	-1.22 [-1.89, -0.56]		🔴
Doyle et al 2019a (8-16yrs; VABS-II)	85	21.86	163	102.1	19.15	274	43.2%	-0.85 [-1.05, -0.64]		🔴
Whaley et al 2001 (20 mnths-10.5 yrs; VABS-II)	74.94	15.11	33	77.94	14.04	33	31.9%	-0.20 [-0.69, 0.28]		🔴
Total (95% CI)			218			327	100.0%	-0.73 [-1.22, -0.25]		

Heterogeneity: Tau² = 0.13; Chi² = 7.55, df = 2 (P = 0.02); I² = 74%
Test for overall effect: Z = 2.96 (P = 0.003)

Risk of bias legend
(A) Overall risk of bias

Adaptive Daily Living – Caregiver: VABS

Confirmed PAE Level Unquantifiable and Adaptive Daily Living – Caregiver (3 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Crocker et al 2009 (6-13yrs; VABS)	69.41	19.83	22	98.15	13.02	20	26.8%	-1.66 [-2.38, -0.95]		🔴
Doyle et al 2019a (8-16yrs; VABS-II)	89.2	20.15	163	106.6	19.03	274	39.9%	-0.89 [-1.10, -0.69]		🔴
Whaley et al 2001 (20 mnths-10.5 yrs; VABS-II)	73.12	20.18	33	78.21	24.03	33	33.2%	-0.23 [-0.71, 0.26]		🔴
Total (95% CI)			218			327	100.0%	-0.88 [-1.50, -0.26]		

Heterogeneity: Tau² = 0.24; Chi² = 11.57, df = 2 (P = 0.003); I² = 83%
Test for overall effect: Z = 2.79 (P = 0.005)

Risk of bias legend
(A) Overall risk of bias

Adaptive: Communication – Caregiver: VABS

Confirmed PAE Level Unquantifiable and Adaptive Communication – Caregiver (4 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Crocker et al 2009 (6-13yrs; VABS)	77.23	22.89	22	103.25	11.73	20	22.1%	-1.38 [-2.06, -0.70]		🔴
Doyle et al 2019a (8-16yrs; VABS-II)	82.2	15.17	163	101.1	17.78	274	26.9%	-1.12 [-1.33, -0.91]		🔴
Doyle et al 2018 (10-16yrs; VABS-II)	76.6	10.69	142	102.4	16.39	160	26.5%	-1.84 [-2.11, -1.57]		🔴
Whaley et al 2001 (20 mnths-10.5 yrs; VABS-II)	77.61	17.04	33	75.09	20.7	33	24.5%	0.13 [-0.35, 0.61]		🔴
Total (95% CI)			360			487	100.0%	-1.06 [-1.78, -0.35]		

Heterogeneity: Tau² = 0.48; Chi² = 51.28, df = 3 (P < 0.00001); I² = 94%
Test for overall effect: Z = 2.91 (P = 0.004)

Risk of bias legend
(A) Overall risk of bias

DIAGNOSED STUDIES

Adaptive Composite – Caregiver: SIB-R, VABS, ABAS

FASD and Adaptive Composite – Caregiver (4 studies)

Study or Subgroup	FASD			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Kerns et al 2016 (8-14yrs; VABS-II)	78.2	10.3	22	107.6	14.2	22	21.8%	-2.33 [-3.11, -1.55]		🟡
Crawford et al 2020 (8-12yrs; VABS-II)	72.61	5.42	36	106.07	16.92	29	23.8%	-2.76 [-3.45, -2.07]		🔴
Fagerlund et al 2012 (8-20yrs; VABS)	75.25	17.55	73	109.56	11.92	40	29.0%	-2.16 [-2.64, -1.68]		🔴
Jirikowic et al 2008a (5-8yrs; SIB-R)	81.7	23.7	25	107.9	14.02	23	25.4%	-1.31 [-1.94, -0.68]		🔴
Total (95% CI)			156			114	100.0%	-2.12 [-2.70, -1.55]		

Heterogeneity: Tau² = 0.24; Chi² = 9.93, df = 3 (P = 0.02); I² = 70%
Test for overall effect: Z = 7.21 (P < 0.00001)

Risk of bias legend
(A) Overall ROB Rating

pFAS and Adaptive Composite – Caregiver (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; VABS; FAS/pFAS)	59	17.5	20	95.3	12.3	16	48.6%	-2.30 [-3.17, -1.44]		🔴
Lynch et al 2015 (~22yrs; ABAS-II; dysmorphic)	98.1	1.57	46	98.03	1.43	57	51.4%	0.05 [-0.34, 0.44]		🔴
Total (95% CI)			66			73	100.0%	-1.09 [-3.39, 1.21]		

Heterogeneity: Tau² = 2.64; Chi² = 23.52, df = 1 (P < 0.00001); I² = 96%
Test for overall effect: Z = 0.93 (P = 0.35)

Control   pFAS

Risk of bias legend
(A) Overall ROB Rating

ARND/Others and Adaptive Composite – Caregiver (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; VABS; SE/AE)	55	14.2	24	95.3	12.3	16	38.7%	-2.93 [-3.86, -2.00]		🔴
Lynch et al 2015 (~22yrs; ABAS-II; non-syndromal)	94.34	2.15	34	98.03	1.43	57	61.3%	-2.11 [-2.64, -1.58]		🔴
Total (95% CI)			58			73	100.0%	-2.43 [-3.21, -1.65]		

Heterogeneity: Tau² = 0.19; Chi² = 2.26, df = 1 (P = 0.13); I² = 56%
Test for overall effect: Z = 6.10 (P < 0.00001)

Control   ARND/Others

Risk of bias legend
(A) Overall ROB Rating

Note: Fagerlund et al 2012 also reports other VABS minor subdomains (m/SD). Lynch et al 2015 also reports other ABAS minor subdomains (m/SD).

Adaptive Composite – Teacher: VABS

FAS and Adaptive Composite – Teacher (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2015 (6-7yrs; VABS - Classroom Ed.)	97	8.81	7	107.2	17.41	186	100.0%	-0.59 [-1.35, 0.17]		🔴
Total (95% CI)			7			186	100.0%	-0.59 [-1.35, 0.17]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.53 (P = 0.13)

FAS   Control

Risk of bias legend
(A) Overall ROB Rating

pFAS and Adaptive Composite – Teacher (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2015 (6-7yrs; VABS - Classroom Ed.)	86.9	14.44	19	107.2	17.41	186	100.0%	-1.18 [-1.66, -0.69]		🔴
Total (95% CI)			19			186	100.0%	-1.18 [-1.66, -0.69]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.75 (P < 0.00001)

pFAS   Control

Risk of bias legend
(A) Overall ROB Rating

Adaptive Socialisation – Caregiver: VABS

FASD and Adaptive Socialisation – Caregiver (11 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kerns et al 2016 (8-14yrs; VABS-II)	82.2	13.5	22	105.4	14.4	22	8.4%	-1.63 [-2.32, -0.94]		🟡
Crawford et al 2020 (8-12yrs; VABS-II)	74.42	9.17	36	104.76	16.78	29	8.7%	-2.29 [-2.92, -1.65]		🔴
de Water et al 2021 (8-16yrs; VABS-III)	74.85	15.4	41	102.42	10.24	43	9.1%	-2.10 [-2.64, -1.56]		🔴
Fagerlund et al 2012 (8-20yrs; VABS)	88.13	18.29	73	114.15	9.24	40	9.6%	-1.64 [-2.09, -1.20]		🔴
May et al 2020a (6-7yrs; VABS-II)	99.6	16.9	24	108.4	14.6	150	9.6%	-0.59 [-1.02, -0.15]		🔴
May et al 2020b (6-7yrs; VABS-II)	97.7	22.3	24	102.9	17.1	150	9.6%	-0.29 [-0.72, 0.14]		🔴
May et al 2020c (6-7yrs; VABS)	100.1	17	32	104.8	13.4	292	9.9%	-0.34 [-0.71, 0.03]		🔴
May et al 2021 (6-7yrs; VABS-II)	78.3	13.4	4	101.1	15.9	50	6.6%	-1.43 [-2.48, -0.37]		🔴
Quattlebaum et al 2013 (6-12yrs; VABS)	62.78	8.12	97	70.36	9	28	9.6%	-0.91 [-1.34, -0.47]		🔴
Rockhold et al 2021 (11-12yrs; VABS)	75.11	14.94	49	102.42	10.24	46	9.3%	-2.10 [-2.61, -1.60]		🔴
Walthall et al 2008 (6-12yrs; VABS)	62.83	8.04	100	69.43	9.57	30	9.7%	-0.78 [-1.20, -0.36]		🔴
Total (95% CI)			502			880	100.0%	-1.25 [-1.70, -0.81]		

Heterogeneity: Tau² = 0.49; Chi² = 88.60, df = 10 (P < 0.00001); I² = 89%
Test for overall effect: Z = 5.53 (P < 0.00001)

FASD   Control

Risk of bias legend
(A) Overall ROB Rating

Funnel Plot: FASD diagnosis and Adaptive Socialisation

FAS and Adaptive Socialisation – Caregiver (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; VABS)	102.4	17	5	100.4	11	761	100.0%	0.18 [-0.70, 1.06]	–
Total (95% CI)			5			761	100.0%	0.18 [-0.70, 1.06]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.40 (P = 0.69)

Risk of bias legend
(A) Overall ROB Rating

pFAS and Adaptive Socialisation – Caregiver (3 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; VABS; FAS/pFAS)	67	18.5	20	100.8	13.7	16	27.7%	-2.00 [-2.82, -1.18]	–
Chambers et al 2019 (6-7yrs; VABS)	97.8	10.4	44	100.4	11	761	36.8%	-0.24 [-0.54, 0.07]	–
Howell et al 2006 (15yrs; VABS; dysmorphic)	102.2	15.43	45	101.93	17.34	54	35.5%	0.02 [-0.38, 0.41]	–
Total (95% CI)			109			831	100.0%	-0.64 [-1.44, 0.17]	

Heterogeneity: Tau² = 0.44; Chi² = 19.09, df = 2 (P < 0.0001); I² = 90%
Test for overall effect: Z = 1.54 (P = 0.12)

Risk of bias legend
(A) Overall ROB Rating

ARND/Others and Adaptive Socialisation – Caregiver (3 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-15.9yrs; VABS; SE/AE)	64.3	17.8	24	100.8	13.7	16	28.7%	-2.19 [-3.00, -1.38]	–
Chambers et al 2019 (6-7yrs; VABS; ARND)	92.9	9.2	44	100.4	11	761	35.9%	-0.69 [-0.99, -0.38]	–
Howell et al 2006 (15yrs; VABS; HE)	102.29	16.77	76	101.93	17.34	54	35.4%	0.02 [-0.33, 0.37]	–
Total (95% CI)			144			831	100.0%	-0.87 [-1.77, 0.03]	

Heterogeneity: Tau² = 0.56; Chi² = 26.78, df = 2 (P < 0.00001); I² = 93%
Test for overall effect: Z = 1.89 (P = 0.06)

Risk of bias legend
(A) Overall ROB Rating

Adaptive: Socialisation – Teacher: VABS, ABAS

FASD and Adaptive Socialisation – Teacher (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; VABS-II)	93.7	13.6	38	103.6	15.4	273	31.9%	-0.65 [-0.99, -0.31]	–
May et al 2020b (6-7yrs; VABS-II)	96.2	17.5	43	105.4	15.4	342	36.7%	-0.59 [-0.91, -0.27]	–
May et al 2020c (6-7yrs; VABS)	96.1	15.4	35	103.8	15	437	31.4%	-0.51 [-0.86, -0.17]	–
Total (95% CI)			116			1052	100.0%	-0.58 [-0.78, -0.39]	

Heterogeneity: Tau² = 0.00; Chi² = 0.31, df = 2 (P = 0.86); I² = 0%
Test for overall effect: Z = 5.90 (P < 0.00001)

Risk of bias legend
(A) Overall ROB Rating

FAS and Adaptive Socialisation – Teacher (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2015 (6-7yrs; VABS - Classroom Ed.)	99.1	10.3	7	104.5	15.4	186	100.0%	-0.35 [-1.11, 0.40]	●
Total (95% CI)			7			186	100.0%	-0.35 [-1.11, 0.40]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.91 (P = 0.36)

Risk of bias legend
(A) Overall ROB Rating

pFAS and Adaptive Socialisation – Teacher (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2015 (6-7yrs; VABS - Classroom Ed.)	92.3	14.43	19	104.5	15.4	186	100.0%	-0.79 [-1.27, -0.32]	●
Total (95% CI)			19			186	100.0%	-0.79 [-1.27, -0.32]	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.25 (P = 0.001)

Risk of bias legend
(A) Overall ROB Rating

Adaptive: Daily Living Skills – Caregiver: VABS

FASD and Adaptive Daily Living – Caregiver (8 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kerns et al 2016 (8-14yrs; VABS-II)	81.5	13.7	22	106.3	15.4	22	11.7%	-1.67 [-2.37, -0.98]	?
Crawford et al 2020 (8-12yrs; VABS-II)	77.83	8.3	36	112.66	16.87	29	11.8%	-2.68 [-3.36, -2.00]	●
Fagerlund et al 2012 (8-20yrs; VABS)	73.69	19.5	73	99.9	12.79	40	13.3%	-1.49 [-1.93, -1.06]	●
May et al 2020a (6-7yrs; VABS-II)	104.3	16.4	35	108.5	14.4	194	13.6%	-0.28 [-0.65, 0.08]	●
May et al 2020b (6-7yrs; VABS-II)	99.3	21.6	24	106	16.9	150	13.3%	-0.38 [-0.81, 0.05]	●
May et al 2020c (6-7yrs; VABS)	99.6	16	32	103.5	11.5	298	13.6%	-0.32 [-0.69, 0.04]	●
May et al 2021 (6-7yrs; VABS-II)	83.5	15.5	4	106.3	14.8	50	9.4%	-1.51 [-2.57, -0.45]	●
Quattlebaum et al 2013 (6-12yrs; VABS)	62.47	16.51	97	84.54	16.43	28	13.2%	-1.33 [-1.78, -0.88]	●
Total (95% CI)			323			811	100.0%	-1.16 [-1.71, -0.62]	

Heterogeneity: Tau² = 0.54; Chi² = 69.09, df = 7 (P < 0.00001); I² = 90%
Test for overall effect: Z = 4.17 (P < 0.0001)

Risk of bias legend
(A) Overall ROB Rating

FAS and Adaptive Daily Living – Caregiver (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; VABS)	107	13.6	5	100.7	10.6	761	100.0%	0.59 [-0.29, 1.47]	●
Total (95% CI)			5			761	100.0%	0.59 [-0.29, 1.47]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.32 (P = 0.19)

Risk of bias legend
(A) Overall ROB Rating

pFAS and Adaptive Daily Living – Caregiver (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; VABS)	95.9	10.5	44	100.7	10.6	761	62.6%	-0.45 [-0.76, -0.15]	●
Howell et al 2006 (15yrs; VABS; dysmorphic)	103.2	12.99	45	105.74	12.94	54	37.4%	-0.19 [-0.59, 0.20]	●
Total (95% CI)			89			815	100.0%	-0.36 [-0.60, -0.11]	

Heterogeneity: Tau² = 0.00; Chi² = 1.02, df = 1 (P = 0.31); I² = 2%
Test for overall effect: Z = 2.85 (P = 0.004)

Risk of bias legend
(A) Overall ROB Rating

ARND/Others and Adaptive Daily Living – Caregiver (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; VABS; ARND)	97.8	11.3	44	100.7	10.6	761	56.9%	-0.27 [-0.58, 0.03]	●
Howell et al 2006 (15yrs; VABS; HE)	103.62	16.19	76	105.74	12.94	54	43.1%	-0.14 [-0.49, 0.21]	●
Total (95% CI)			120			815	100.0%	-0.22 [-0.45, 0.01]	

Heterogeneity: Tau² = 0.00; Chi² = 0.31, df = 1 (P = 0.58); I² = 0%
Test for overall effect: Z = 1.84 (P = 0.07)

Risk of bias legend
(A) Overall ROB Rating

Adaptive: Daily Living Skills – Teacher: VABS

FASD and Adaptive Daily Living – Teacher (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
May et al 2020a (6-7yrs; VABS-II)	95.2	20.7	38	104.9	16.6	273	32.2%	-0.56 [-0.91, -0.22]
May et al 2020b (6-7yrs; VABS-II)	93	14.8	43	100.3	14.3	342	36.0%	-0.51 [-0.83, -0.19]
May et al 2020c (6-7yrs; VABS)	96.6	14.4	35	99.3	13.2	437	31.8%	-0.20 [-0.55, 0.14]
Total (95% CI)			116			1052	100.0%	**-0.43 [-0.64, -0.21]**

Heterogeneity: Tau² = 0.01; Chi² = 2.49, df = 2 (P = 0.29); I² = 20%
Test for overall effect: Z = 3.90 (P < 0.0001)

Risk of bias legend
(A) Overall ROB Rating

FAS and Adaptive Daily Living – Teacher (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
May et al 2015 (6-7yrs; VABS - Classroom Ed.)	99.4	11.79	7	107.6	16.39	186	100.0%	-0.50 [-1.26, 0.25]
Total (95% CI)			7			186	100.0%	**-0.50 [-1.26, 0.25]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.30 (P = 0.19)

Risk of bias legend
(A) Overall ROB Rating

pFAS and Adaptive Daily Living – Teacher (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
May et al 2015 (6-7yrs; VABS - Classroom Ed.)	90.8	18.25	19	107.6	16.39	186	100.0%	-1.01 [-1.49, -0.53]
Total (95% CI)			19			186	100.0%	**-1.01 [-1.49, -0.53]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.11 (P < 0.0001)

Risk of bias legend
(A) Overall ROB Rating

Adaptive: Communication – Caregiver: VABS

FASD and Adaptive Communication – Caregiver (9 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Kerns et al 2016 (8-14yrs; VABS-II)	76.5	6.8	22	108.9	13.7	22	9.7%	-2.94 [-3.82, -2.07]
Crawford et al 2020 (8-12yrs; VABS-II)	70.22	5.2	36	98.76	14.52	29	10.7%	-2.70 [-3.39, -2.02]
Fagerlund et al 2012 (8-20yrs; VABS)	74.89	21.42	73	107.1	11.19	40	11.8%	-1.73 [-2.18, -1.28]
May et al 2020a (6-7yrs; VABS-II)	99.8	17	35	113.8	25.6	194	12.1%	-0.57 [-0.93, -0.21]
May et al 2020b (6-7yrs; VABS-II)	90.9	16	24	105.1	17.5	150	11.8%	-0.82 [-1.26, -0.38]
May et al 2020c (6-7yrs; VABS)	98	14.1	32	106.2	12.7	292	12.0%	-0.64 [-1.01, -0.27]
May et al 2021 (6-7yrs; VABS-II)	85.5	7.7	4	103.7	16.1	50	8.9%	-1.14 [-2.18, -0.10]
Quattlebaum et al 2013 (6-12yrs; VABS)	74.8	15.21	97	95.5	14.82	28	11.7%	-1.36 [-1.81, -0.91]
Rockhold et al 2021 (11-12yrs; VABS)	77.41	11.32	49	105.91	9.68	46	11.3%	-2.68 [-3.24, -2.12]
Total (95% CI)			372			851	100.0%	**-1.58 [-2.15, -1.02]**

Heterogeneity: Tau² = 0.66; Chi² = 89.14, df = 8 (P < 0.00001); I² = 91%
Test for overall effect: Z = 5.48 (P < 0.00001)

Risk of bias legend
(A) Overall ROB Rating

FAS and Adaptive Communication – Caregiver (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Chambers et al 2019 (6-7yrs; VABS)	105.8	25.7	5	101.1	13.2	761	100.0%	0.35 [-0.53, 1.23]
Total (95% CI)			5			761	100.0%	**0.35 [-0.53, 1.23]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)

Risk of bias legend
(A) Overall ROB Rating

pFAS and Adaptive Communication – Caregiver (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Chambers et al 2019 (6-7yrs; VABS)	97.5	14.1	44	101.1	13.2	761	59.4%	-3.60 [-7.87, 0.67]
Howell et al 2006 (15yrs; VABS; dysmorphic)	93.02	13.86	45	99.31	12.01	54	40.6%	-6.29 [-11.45, -1.13]
Total (95% CI)			89			815	100.0%	-4.69 [-7.98, -1.40]

Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 1 (P = 0.43); I² = 0%
Test for overall effect: Z = 2.79 (P = 0.005)

Risk of bias legend
(A) Overall ROB Rating

ARND/Others and Adaptive Communication – Caregiver (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Chambers et al 2019 (6-7yrs; VABS; ARND)	92.8	12.5	44	101.1	13.2	761	55.4%	-8.30 [-12.11, -4.49]
Howell et al 2006 (15yrs; VABS; HE)	95.81	16.55	76	99.31	12.01	54	44.6%	-3.50 [-8.41, 1.41]
Total (95% CI)			120			815	100.0%	-6.16 [-10.84, -1.48]

Heterogeneity: Tau² = 6.49; Chi² = 2.29, df = 1 (P = 0.13); I² = 56%
Test for overall effect: Z = 2.58 (P = 0.010)

Risk of bias legend
(A) Overall ROB Rating

Adaptive: Communication – Teacher: VABS

FASD and Adaptive Communication – Teacher (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
May et al 2020a (6-7yrs; VABS-II)	94.4	18.8	38	103.5	14.1	273	31.9%	-0.62 [-0.96, -0.27]
May et al 2020b (6-7yrs; VABS-II)	91.5	14.9	43	99.7	14.6	342	36.6%	-0.56 [-0.88, -0.24]
May et al 2020c (6-7yrs; VABS)	94.3	16.2	35	98.1	13	437	31.5%	-0.29 [-0.63, 0.06]
Total (95% CI)			116			1052	100.0%	-0.49 [-0.69, -0.30]

Heterogeneity: Tau² = 0.00; Chi² = 2.04, df = 2 (P = 0.36); I² = 2%
Test for overall effect: Z = 4.93 (P < 0.00001)

Risk of bias legend
(A) Overall ROB Rating

FAS and Adaptive Communication – Teacher (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
May et al 2015 (6-7yrs; VABS - Classroom Ed.)	94.7	9.27	7	106.1	16.42	186	100.0%	-0.70 [-1.46, 0.06]
Total (95% CI)			7			186	100.0%	-0.70 [-1.46, 0.06]

Heterogeneity: Not applicable
Test for overall effect: Z = 1.81 (P = 0.07)

Risk of bias legend
(A) Overall ROB Rating

pFAS and Adaptive Communication – Teacher (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
May et al 2015 (6-7yrs; VABS - Classroom Ed.)	85.3	14.23	19	106.1	16.42	186	100.0%	-1.28 [-1.76, -0.79]
Total (95% CI)			19			186	100.0%	-1.28 [-1.76, -0.79]

Heterogeneity: Not applicable
Test for overall effect: Z = 5.12 (P < 0.00001)

Risk of bias legend
(A) Overall ROB Rating

Summary of available outcomes for **behaviour** (i.e., externalising, internalising)

Behaviour			
Study type	**Outcomes**	**Data**	**# studies**
Exposure Studies	**Total Behaviour – Caregiver Report**: CBCL	T-score	**5 studies:** 4 confirmed unquantifiable, 1 Any PAE
	Total Behaviour – Caregiver Report: CBCL	Frequency/OR	**4 studies:** 1 light, 3 moderate and 1 heavy
	Total Behaviour – Caregiver Report: SDQ	mean difference	**1 study:** 1 light
	Total Behaviour – Teacher Report: SDQ	Frequency/OR	**1 study:** 1 moderate
	Total Behaviour – Self Report: SDQ	Frequency/OR	**1 study:** 1 confirmed unquantifiable
	Total Externalising Behaviour – Caregiver Report: CBCL	T-score	**4 studies:** 1 very heavy, 1 Any PAE and 2 confirmed unquantifiable
	Total Externalising Behaviour – Caregiver Report: CBCL	Frequency/OR	**2 studies:** 1 light, 1 moderate, 1 heavy
	Total Externalising Behaviour – Caregiver Report: IBQ	mean/SD	**1 study:** 1 moderate PAE
	Total Externalising Behaviour – Teacher Report	N/A	**N/A**
	Total Externalising Behaviour – Self Report	N/A	**N/A**
	Total Internalising Behaviour – Caregiver Report: CBCL	T-score	**4 studies:** 1 very heavy, 1 Any PAE and 2 confirmed unquantifiable
	Total Internalising Behaviour – Caregiver Report: CBCL	Frequency/OR	**2 studies:** 1 light, 1 moderate, 1 heavy PAE
	Total Internalising Behaviour – Teacher Report	N/A	**N/A**
	Total Internalising Behaviour – Self Report	N/A	**N/A**
	Ext: Conduct Problems – Caregiver Report: SDQ/CBCL	Mean Dif; T-score	**2 studies:** 1 light, 1 confirmed unquantifiable
	Ext: Conduct Problems – Caregiver Report: CBCL, SDQ	Frequency/OR	**1 studies:** 1 light
	Ext: Conduct Problems – Self Report: SDQ	Frequency/OR	**1 studies:** 1 confirmed unquantifiable
	Ext: Conduct Problems – Caregiver Report: SDQ	Mean difference	**1 study:** 1 light
	Ext: Conduct Problems – Teacher Report: SDQ	OR/Frequency	**1 study:** 1 light
	Ext: Oppositional Defiant – Caregiver Report	N/A	**N/A**
	Ext: Oppositional Defiant – Teacher Report	N/A	**N/A**
	Ext: Aggression – Caregiver Report: CBCL	T-score	**4 studies:** 1 very heavy, 1 Any PAE and 2 confirmed unquantifiable
	Ext: Aggression – Caregiver Report: CBCL	Frequency/OR	**2 studies:** 1 light, 1 moderate, 1 heavy
	Ext: Aggression – Teacher Report	N/A	**N/A**
	Ext: Aggression – Self Report	N/A	**N/A**
	Ext: Rule-Breaking Behaviour – Caregiver Report: CBCL	T-score	**3 studies:** 2 confirmed unquantifiable, 1 any PAE
	Ext: Rule-Breaking Behaviour – Caregiver Report: CBCL	Frequency/OR	**2 studies:** 1 light, 1 moderate, 1 heavy
	Ext: Rule-Breaking Behaviour – Teacher Report	N/A	**N/A**
	Ext: Rule-Breaking Behaviour – Self Report	N/A	**N/A**

	Ext: Hyperactivity – Caregiver Report: CBCL	T-score	**1 study:** 1 very heavy
	Ext: Hyperactivity – Caregiver Report: SDQ	mean/SD (MD)	**1 study:** 1 light
	Ext: Hyperactivity – Caregiver Report: SDQ	OR/Frequency	**3 studies:** 1 light, 1 moderate, 1 heavy, 1 confirmed unquantifiable
	Ext: Hyperactivity – Self Report: SDQ	OR/Frequency	**1 studies:** 1 confirmed unquantifiable
	Ext: Hyperactivity – Teacher Report: SDQ	OR/Frequency	**1 study:** 1 light
	Ext: Attention/ Hyperactivity – Caregiver Report	N/A	
	Int: Anxious/ Depressed – Caregiver Report: CBCL	T-score	**3 studies:** 1 Any PAE, 2 confirmed unquantifiable
	Int: Anxious/ Depressed – Caregiver Report: CBCL	OR/Frequency	**1 study:** 1 moderate
	Int: Anxious/ Depressed – Teacher Report	N/A	
	Int: Anxious/Depressed – Self-report: SDQ	OR/Frequency	**1 study:** 1 confirmed unquantifiable
	Int: Anxious/ Depressed – Self Report: CBCL	T-score	**1 study:** 1 light, 1 moderate
	Int: Anxiety – Caregiver Report: CBCL	T-score	**1 study:** 1 very heavy
	Int: Anxiety – Caregiver Report: CBCL	OR/Frequency	**1 study:** 1 light, 1 heavy
	Int: Anxiety – Teacher Report	N/A	
	Int: Withdrawn/ Depressed – Caregiver Report: CBCL	T-score	**3 studies:** 1 Any PAE and 2 confirmed/unquantifiable
	Int: Withdrawn/ Depressed – Caregiver Report: CBCL	OR/Frequency	**2 studies:** 1 light, 1 moderate, 1 heavy
	Int: Withdrawn/ Depressed – Teacher Report	N/A	
	Int: Withdrawn/ Depressed – Self Report	N/A	
	Int: Somatic Complaints – Caregiver Reports: CBCL	T-score	**3 studies:** 1 Any PAE and 2 confirmed/unquantifiable
	Int: Somatic Complaints – Caregiver Report: CBCL	OR/Frequency	**2 studies:** 1 light, 1 moderate, 1 heavy
	Int: Somatic Complaints – Self Report	N/A	
	Int: Thought Problems – Caregiver Report: CBCL	T-score	**3 studies:** 1 Any PAE and 2 confirmed unquantifiable
	Int: Thought Problems – Caregiver Report: CBCL	OR/Frequency	**1 study:** 1 light, 1 heavy
	Int: Thought Problems – Self Report	N/A	
	Int: Affective Problems – Caregiver Report	N/A	
	Int: Affective Problems – Teacher Report	N/A	
	Brief Infant-Toddler Social and Emotional Assessment	aOR	**1 study:** 1 moderate
	Infant Behaviour Questionnaire – Caregiver Report	mean/SD	**1 study:** 1 moderate
Diagnosed Studies	Total Behaviour – Caregiver Report: CBCL	Frequency/OR	**1 study:** 1 FASD
	Total Behaviour – Caregiver Report: CBCL, PBCL-36	T-score	**12 studies:** 9 FASD, 3 FAS, 2 pFAS
	Total Behaviour – Teacher Report: TRF, PBCL-36	T-score	**4 studies:** 2 FASD, 2 FAS, 2 pFAS, 2 ARND/Others
	Total Behaviour – Caregiver Report: SSRS	mean/SD	**1 study:** 1 FASD
	Total Behaviour – Teacher Report: SSRS	mean/SD	**2 studies:** 2 FASD
	Total Behaviour – Self Report: ASR	T-score	**1 study**: 1 pFAS, 1 ARND/Others

Total Externalising Behaviour – Caregiver Report: CBCL	T-score	**12 studies:** 9 FASD, 2 FAS, 2 pFAS, 3 ARND/Others	
Total Externalising Behaviour – Caregiver Report: SIB-R/CBCL	Frequency/OR	**2 studies:** 2 FASD	
Total Externalising Behaviour – Caregiver Report: SSRS	mean/SD	**1 study:** 1 FASD	
Total Externalising Behaviour – Teacher Report: TRF	T-score	**6 studies:** 5 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Total Externalising Behaviour – Teacher Report: SSRS	mean/SD	**1 study:** FASD	
Total Externalising Behaviour – Self Report: ASR	T-score	**1 study:** 1 pFAS, 1 ARND/Others	
Total Internalising Behaviour – Caregiver Report: CBCL	T-score	**13 studies:** 10 FASD, 3 FAS, 2 pFAS, 3 ARND/Others	
Total Internalising Behaviour – Caregiver Report: SIB-R/CBCL	Frequency/OR	**2 studies:** 2 FASD	
Total Internalising Behaviour – Caregiver Report: SSRS	mean/SD	**1 study:** 1 FASD	
Total Internalising Behaviour – Teacher Report: TRF/CBCL	T-score	**6 studies:** 5 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Total Internalising Behaviour – Teacher Report: SSRS	mean/SD	**1 study:** 1 FASD	
Total Internalising Behaviour – Self Report: ASR	T-score	**1 study:** 1 pFAS, 1 ARND/Others	
Ext: Conduct Problems – Caregiver Report: CBCL	T-score	**5 studies:** 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Ext: Conduct Problems – Teacher Report: TRF	T-score	**5 studies:** 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Ext: Oppositional Defiant – Caregiver Report: CBCL	T-score	**5 studies:** 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Ext: Oppositional Defiant – Caregiver Report: Vanderblit-C	mean/SD	**1 study:** 1 FASD	
Ext: Oppositional Defiant – Teacher Report: TRF/CBCL	T-score	**5 studies:** 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Ext: Aggression – Caregiver Report: CBCL	T-score	**6 studies:** 5 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Ext: Aggression – Teacher Report: TRF/CBCL	T-score	**5 studies:** 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Ext: Aggression – Self Report: ASR	T-score	**1 study:** 1 pFAS, 1 ARND/Others	
Ext: Rule-Breaking Behaviour – Caregiver Report: CBCL	T-score	**7 studies:** 5 FASD, 2 FAS, 1 pFAS, 2 ARND/Others	
Ext: Rule-Breaking Behaviour – Caregiver Report: CBCL, SIB-R	Frequency/OR	**2 studies:** 2 FASD	
Ext: Rule-Breaking Behaviour – Teacher Report: TRF/CBCL	T-score	**4 studies:** 3 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Ext: Rule-Breaking Behaviour – Self Report: ASR	T-score	**1 study:** 1 pFAS, 1 ARND/Others	
Ext: Hyperactivity – Caregiver Report: CBRS	T-score	**1 study:** 1 FASD	
Ext: Hyperactivity – Caregiver Report: CBCL	OR/Frequency	**1 study:** 1 FASD	
Ext: Hyperactivity – Caregiver Report: DBD, SSRS	mean/SD	**3 studies:** 1 FASD, 2 pFAS	
Ext: Hyperactivity – Teacher Report: DBD, SSRS, CBRS	mean/SD	**3 studies:** 1 FASD, 2 pFAS	
Ext: Attention / Hyperactivity – Caregiver Report: CBCL	T-score	**5 studies:** 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	

Ext: Attention/ Hyperactivity – Teacher Report: CBCL/TRF	T-score	**4 study:** 3 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Int: Anxious/ Depressed – Caregiver Report: CBCL, CBRS	T-score	**8 studies:** 7 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Int: Anxious/ Depressed – Caregiver Report: Vanderblit-C	mean/SD	**1 study:** 1 FASD	
Int: Anxious/ Depressed – Teacher Report: TRF	T-score	**4 studies:** 3 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Int: Anxious/ Depressed – Self Report: CBCL	T-score	**1 study:** 1 pFAS, 1 ARND/Others	
Int: Anxiety – Caregiver Report: CBCL	T-score	**6 studies:** 5 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Int: Anxiety – Teacher Report: TRF	T-score	**4 studies:** 3 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Int: Withdrawn/ Depressed – Caregiver Report: CBCL	T-score	**7 studies:** 6 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Int: Withdrawn/ Depressed – Teacher Report: TRF	T-score	**4 studies:** 3 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Int: Withdrawn/ Depressed – Self Report: TRF	T-score	**1 study:** 1 pFAS, 1 ARND/Others	
Int: Somatic Complaints – Caregiver Report: CBCL, CBRS	T-score	**3 studies:** 3 FASD	
Int: Somatic Complaints – Self Report: CBCL	T-score	**1 study:** 1 pFAS, 1 ARND/Others	
Int: Thought Problems – Caregiver Report: CBCL, CBRS	T-score	**2 studies:** 2 FASD	
Int: Thought Problems – Self Report: CBCL	T-score	**1 study:** 1 pFAS, 1 ARND/Others	
Int: Affective Problems – Caregiver Report: CBCL	T-score	**5 studies:** 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	
Int: Affective Problems – Teacher Report: TRF	T-score	**4 studies:** 3 FASD, 1 FAS, 1 pFAS, 1 ARND/Others	

GRADE ratings for behaviour

Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	Certainty
Certainty assessment						**Nº of patients**		**Effect**		**Certainty**
EXPOSURE STUDIES										
CBCL Total Behaviour Caregiver Report (T-score)										
Any PAE										
1	serious[a]	not serious	not serious	not serious	none	2518	7201	-	**SMD 0.20 higher** (0.15 higher to 0.24 higher)	⊕⊕⊕◯ Moderate
Confirmed unquantifiable										
4	serious[a]	serious[b]	not serious	serious[e,f]	none	348	393	-	**SMD 2.29 higher** (1.40 higher to 3.18 higher)	⊕◯◯◯ Very Low
0 studies for light, moderate, heavy or very heavy										
CBCL/SDQ Total Behaviour Caregiver Report (Frequency/OR) (Odds of scoring in 'clinical range'/'abnormal' scores/score >60 of CBCL)										
Light										
1	not serious	not serious	not serious	serious[d,f]	none	208	690	**OR 1.17** (0.74 to 1.85)	-	⊕⊕⊕◯ Moderate
Moderate										
3	not serious	not serious	not serious	serious[f]	none	688	1,060	**OR 1.69** (1.17 to 2.43)	-	⊕⊕⊕◯ Moderate
Heavy										
1	not serious	not serious	not serious	serious[d,f]	none	57	690	**OR 1.62** (0.85 to 3.11)	-	⊕⊕⊕◯ Moderate
0 studies for any, confirmed unquantifiable or very heavy										
SDQ Total Behaviour Caregiver Report (adjusted Mean Difference)										
Light										
1	not serious	not serious	not serious	serious[d]	none	1963	5547		**aMD 0.04 higher** (0.33 lower to 0.42 higher)	⊕⊕⊕◯ Moderate
SDQ Total Behaviour Teacher Report (Frequency/OR) (Odds of 'Abnormal/Borderline' score)										
Moderate										
1	not serious	not serious	not serious	very serious[d,e,f]	none	195	758	**aOR 1.1** (0.6 to 2.1)		⊕⊕◯◯ Low
SDQ Total Behaviour Self Report (adjusted Frequency/OR) (Cut-offs unclear)										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	serious[d]	none	57	690	**aOR 1.25** (0.99 to 1.58		⊕⊕◯◯ Low
0 studies for any, light, moderate, heavy or very heavy										
CBCL Externalising Behaviour Caregiver Report (T-score)										
Very heavy										
1	serious[a]	not serious	not serious	serious[e,f]	none	20	19	-	**SMD 1.35 higher** (0.65 higher to 2.05 higher)	⊕⊕◯◯ Low
Any PAE										
1	serious[a]	not serious	not serious	not serious	none	2518	7201	-	**SMD 0.16 higher**	⊕⊕⊕◯ Moderate

									(0.11 higher to 0.20 higher)	
Confirmed unquantifiable										
2	serious[a]	serious[b]	not serious	serious[e,f]	none	160	168	-	**SMD 1.78 higher** (0.52 higher to 3.03 higher)	⊕◯◯◯ Very low
0 studies for light, moderate or heavy										
CBCL Total Externalising Behaviour Caregiver Report (Frequency/OR) (Odds of scoring in 'clinical range'/'abnormal' scores)										
Light										
1	not serious	not serious	not serious	serious[d]	none	208	690	**OR 1.10** (0.73 to 1.66)		⊕⊕⊕◯ Moderate
Moderate										
1	serious[a]	not serious	not serious	serious[d]	none	389	117	**OR 1.79** (1.00 to 3.20)		⊕⊕◯◯ Low
Heavy										
1	not serious	not serious	not serious	serious[d]	none	57	690	**OR 1.00** (0.53 to 1.89)		⊕⊕⊕◯ Moderate
0 studies for any confirmed unquantifiable or very heavy										
CBCL Total Externalising Behaviour Caregiver Report – IBQ (mean/SD)										
Moderate										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	39	54	-	**SMD 0.37 higher** (0.04 lower to 0.79 higher)	⊕◯◯◯ Very low
0 studies for light, heavy, very heavy										
CBCL Total Internalising Behaviour Caregiver Report (T-score)										
Very heavy										
1	serious[a]	not serious	not serious	serious[e,f]	none	20	19	-	**SMD 0.71 higher** (0.06 higher to 1.36 higher)	⊕⊕◯◯ Low
Any PAE										
1	serious[a]	not serious	not serious	not serious	none	2518	7201	-	**SMD 0.14 higher** (0.10 higher to 0.19 higher)	⊕⊕⊕◯ Moderate
Confirmed unquantifiable										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	160	168	-	**SMD 1.01** (0.08 lower to 2.11 higher)	⊕◯◯◯ Very low
0 studies for light, moderate & heavy										
CBCL Total Internalising Behaviour Caregiver Report (Frequency/OR) (Odds of scoring in 'clinical range'/'abnormal' scores)										
Light										
1	not serious	not serious	not serious	serious[d]	none	208	690	**OR 1.14** (0.67 to 1.94)	1 fewer per 1,000 (from 2 fewer to 1 fewer)	⊕⊕⊕◯ Moderate
Moderate										
1	serious[a]	not serious	not serious	Serious[d,e]	none	389	117	**OR 1.67** (0.90 to 3.10)	2 fewer per 1,000 (from 3 fewer to 1 fewer)	⊕⊕◯◯ Low
Heavy										

№	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	n1	n2	Relative	Absolute	Certainty
1	serious[a]	not serious	not serious	serious[e]	none	57	690	OR 2.64 (1.36 to 5.14)	3 fewer per 1,000 (from 5 fewer to 1 fewer)	⊕⊕◯◯ Low

CBCL/SDQ Conduct Problems Caregiver Report (mean diff/T-score)

Light

1	not serious	not serious	not serious	serious[d]	none	1967	5547	-	aMD 0.04 higher (0.07 lower to 0.15 higher)	⊕⊕⊕◯ Moderate

Confirmed unquantifiable

1	serious[a]	not serious	not serious	serious[e,f]	none	61	55	-	SMD 0.88 higher (0.50 higher to 1.27 higher)	⊕⊕◯◯ Low

0 studies for any, moderate, heavy or very heavy

CBCL Conduct Problems Caregiver Report (Frequency/OR) (Cut-offs not clear)

Light

1	not serious	not serious	not serious	serious[d]	none	150	348	OR 1.20 (0.95 to 1.52)		⊕⊕⊕◯ Moderate

SDQ Conduct Problems Self Report (adjusted Frequency/OR) (Cut-offs not clear)

Confirmed unquantifiable

1	serious[a]	not serious	not serious	serious[d]	none	850	5299	aOR 1.24 (0.99 to 1.56)		⊕⊕◯◯ Low

0 studies for any, moderate, heavy or very heavy

SDQ Conduct Problems Teacher Report (Frequency/OR) (Odds of 'Abnormal/Borderline' score)

Light

1	not serious	not serious	not serious	very serious[d,e,f]	none	70	126	OR 1.37 (0.9 to 2.07)		⊕⊕◯◯ Low

CBCL Aggression Caregiver Report (T-score)

Very Heavy

1	serious[a]	not serious	not serious	serious[e,f]	none	20	19	-	SMD 0.92 higher (0.26 higher to 1.59 higher)	⊕⊕◯◯ Low

Any PAE

1	serious[a]	not serious	not serious	not serious	none	2518	7201	-	SMD 0.11 higher (0.07 higher to 0.16 higher)	⊕⊕⊕◯ Moderate

Confirmed unquantifiable

2	serious[a]	serious[b]	not serious	serious[e,f]	none	140	188	-	SMD 1.64 higher (0.72 higher to 2.57 higher)	⊕◯◯◯ Very low

0 studies for light, moderate or heavy

CBCL Aggression Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range')

Light

1	not serious	not serious	not serious	serious[d]	none	208	690	OR 1.06 (0.49 to 2.28)		⊕⊕⊕◯ Moderate

Moderate

1	serious[a]	not serious	not serious	serious[d]	none	389	117	OR 1.30 (0.70 to 2.40)		⊕⊕◯◯ Low

Heavy

1	not serious	not serious	not serious	Serious[d,e]	none	57	690	OR 1.93 (0.74 to 5.01)		⊕⊕⊕◯ Moderate

0 studies for any, confirmed unquantifiable or very heavy

CBCL Rule-Breaking Behaviour Caregiver Report (T-score)

Any PAE

1	serious[a]	not serious	not serious	not serious	none	2518	7201	-	SMD 0.09 higher (0.04 higher to 0.13 higher)	⊕⊕⊕◯ Moderate

Confirmed unquantifiable

2	serious[a]	not serious	not serious	serious[e,f]	none	107	188	-	SMD 1.16 higher (0.89 higher to 1.42 higher)	⊕⊕◯◯ Low

0 studies for light, moderate or heavy

CBCL Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range')

Light

1	not serious	not serious	not serious	Serious[d,e]	none	208	690	OR 1.60 (0.78 to 3.28)		⊕⊕⊕◯ Moderate

Moderate

1	serious[a]	not serious	not serious	serious[e]	none	389	117	OR 3.20 (1.35 to 7.60)		⊕⊕⊕◯ Moderate

Heavy

1	serious[a]	not serious	not serious	serious[d]	none	57	690	OR 0.28 (0.04 to 1.95)		⊕⊕◯◯ Low

0 studies for any, confirmed unquantifiable or very heavy

CBCL Hyperactivity Caregiver Report (T-score)

Very heavy

1	serious[a]	not serious	not serious	very serious[d,e,f]	none	18	21	-	SMD 0.26 higher (0.38 lower to 0.89 higher)	⊕◯◯◯ Very Low

0 studies for any PAE, confirmed unquantifiable, light, moderate or heavy PAE

SDQ Hyperactivity Caregiver Report (adjusted mean difference)

Light

1	serious[a]	not serious	not serious	serious[d,e]	none	1963	5547	-	aMD 0.11 higher (0.06 lower to 0.28 higher)	⊕⊕◯◯ Low

0 studies for any, confirmed unquantifiable moderate, heavy or very heavy PAE

SDQ Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')

Light

1	not serious	not serious	not serious	serious[d]	none	158	355	OR 1.25 (0.99 to 1.59)		⊕⊕⊕◯ Moderate

Moderate

1	serious[a]	not serious	not serious	serious[d]	none	657	9088	OR 1.05 (0.82 to1.34)		⊕⊕◯◯ Low

Heavy

1	serious[a]	not serious	not serious	serious[d]	none	258	9088	OR 0.90 (0.61 to 1.32)		⊕⊕◯◯ Low

SDQ Hyperactivity Self-report (adjusted OR) (Cut-offs unclear)										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	not serious	none	850	5229	**aOR 1.39** (1.15 to 1.69)		⊕⊕⊕◯ Moderate
0 studies for any or very heavy										
SDQ Hyperactivity Teacher Report (Frequency/OR) (Cut-offs unclear)										
Light										
1	not serious	not serious	not serious	serious[d,e,f]	none	107	272	**OR 0.93** (0.67 to 1.29)	-	⊕⊕◯◯ Low
CBCL Anxious/Depressed Caregiver Report (T-score)										
Any PAE										
1	serious[a]	not serious	not serious	not serious	none	2518	7201	-	**SMD 0.08 higher** (0.04 higher to 0.13 higher)	⊕⊕⊕◯ Moderate
Confirmed unquantifiable										
2	serious[a]	not serious	not serious	serious[f]	none	107	188	-	**SMD 0.73 higher** (0.48 higher to 0.98 higher)	⊕⊕◯◯ Low
0 studies for light, moderate, heavy or very heavy										
CBCL Anxious/Depressed Caregiver Reports (Frequency/OR) (Odds of scoring in 'clinical range')										
Moderate										
1	serious[a]	not serious	not serious	serious[d,e]	none	389	117	**OR 2.42** (0.70 to 8.40)		⊕⊕◯◯ Low
0 studies for light, heavy or very heavy										
SDQ Anxious/Depressed Self-Report (mean/SD) (Cut-offs not clear)										
Confirmed Unquantifiable										
1	serious[a]	not serious	not serious	serious[d]	none	850	5299	**aOR 1.16** (0.93 to 1.45)	-	⊕⊕◯◯ Low
CBCL Anxious/Depressed Self-Report (T-score)										
Light										
1	serious[a]	not serious	not serious	not serious	none	2536	2530	-	**SMD 0.07 higher** (0.01 higher to 0.12 higher)	⊕⊕⊕◯ Moderate
Moderate										
1	serious[a]	not serious	not serious	serious[d]	none	66	2530	-	**SMD 0.05 lower** (0.29 lower to 0.20 higher)	⊕⊕◯◯ Low
0 studies for any, confirmed unquantifiable, heavy or very heavy										
CBCL Anxiety Caregiver Report (T-score)										
Very Heavy										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	20	19	-	**SMD 0.20 higher** (0.43 lower to 0.83 higher)	⊕◯◯◯ Very Low
0 studies for any, confirmed unquantifiable, light, moderate or heavy										
CBCL Anxiety Caregiver Report (Frequency/OR) (Odds of scoring in 'clinical range')										
Light										
1	not serious	not serious	not serious	serious[e]	none	208	690	**OR 2.24**		⊕⊕⊕◯ Moderate

								(1.16 to 4.34)		

Heavy

1	not serious	not serious	not serious	serious[e]	none	57	690	**OR 2.82** (1.07 to 7.43)		⊕⊕⊕◯ Moderate

0 studies for any, confirmed unquantifiable, moderate or very heavy

CBCL Withdrawn/Depressed Caregiver Report (T-score)

Any PAE

1	serious[a]	not serious	not serious	not serious	none	2518	7201	-	**SMD 0.07 higher** (0.03 higher to 0.12 higher)	⊕⊕⊕◯ Moderate

Confirmed unquantifiable

2	serious[a]	not serious	not serious	serious[f]	none	107	188	-	**SMD 0.80 higher** (0.55 higher to 1.05 higher)	⊕⊕◯◯ Low

0 studies for light, moderate, heavy or very heavy

CBCL Withdrawn/Depressed Caregiver Report (OR) (Odds of scoring in 'clinical range')

Light

1	not serious	not serious	not serious	serious[d]	none	208	690	**OR 0.56** (0.27 to 1.15)		⊕⊕⊕◯ Moderate

Moderate

1	serious[a]	not serious	not serious	Serious[d,e]	none	389	117	**OR 1.30** (0.50 to 3.40)		⊕⊕◯◯ Low

Heavy

1	not serious	not serious	not serious	Serious[d,e]	none	57	690	**OR 1.26** (0.48 to 3.30)		⊕⊕⊕◯ Moderate

0 studies for any, confirmed unquantifiable or very heavy

CBCL Somatic Complaints Caregiver Report (T-score)

Any PAE

1	serious[a]	not serious	not serious	not serious	none	2518	7201	-	**SMD 0.12 higher** (0.07 higher to 0.16 higher)	⊕⊕⊕◯ Moderate

Confirmed unquantified

2	serious[a]	not serious	not serious	serious[e,f]	none	107	188	-	**SMD 0.63 higher** (0.08 higher to 1.19 higher)	⊕⊕◯◯ Low

0 studies for light, moderate, heavy or very heavy

CBCL Somatic Complaints Caregiver Report (Frequency/OR) (Odds of scoring in 'clinical range')

Light

1	not serious	not serious	not serious	serious[d]	none	208	690	**OR 1.07** (0.61 to 1.88)	**1 fewer per 1,000** (from 2 fewer to 1 fewer)	⊕⊕⊕◯ Moderate

Moderate

1	serious[a]	not serious	not serious	Serious[d,e]	none	389	117	**OR 1.41** (0.60 to 3.30)	**1 fewer per 1,000** (from 3 fewer to 1 fewer)	⊕⊕◯◯ Low

Heavy

No. of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	n	n	Effect (relative)	Effect (absolute)	Certainty
1	not serious	not serious	not serious	serious[e]	none	57	690	OR 2.74 (1.47 to 5.12)	3 fewer per 1,000 (from 5 fewer to 1 fewer)	⊕⊕⊕◯ Moderate

0 studies for any, confirmed unquantifiable or very heavy

CBCL Thought Problems Caregiver Report (T-score)

Any PAE

1	serious[a]	not serious	not serious	not serious	none	2518	7201	-	SMD 0.14 higher (0.09 higher to 0.18 higher)	⊕⊕⊕◯ Moderate

Confirmed unquantified

2	serious[a]	not serious	not serious	serious[e,f]	none	107	188	-	SMD 0.92 higher (0.66 higher to 1.17 higher)	⊕⊕◯◯ Low

0 studies for light, moderate, heavy or very heavy

CBCL Thought Problems Caregiver Report (Frequency/OR) (Odds of scoring in 'clinical range')

Light

1	not serious	not serious	not serious	serious[d]	none	208	690	OR 1.12 (0.51 to 2.47)		⊕⊕⊕◯ Moderate

Heavy

1	not serious	not serious	not serious	serious[d,e]	none	57	690	OR 0.84 (0.15 to 4.69)		⊕⊕⊕◯ Moderate

0 studies for any, confirmed unquantifiable, moderate or very heavy PAE

BITSEA – Maternal Report (adjusted odds of scoring <1SD below the mean): Possible Problem

Moderate PAE

1	not serious	not serious	not serious	serious[d,f]	none	74	126	aOR 0.59 (0.23 to 1.53)	-	⊕⊕⊕◯ Moderate

BITSEA – Maternal Report (adjusted odds of scoring <1SD below the mean): Possible Competence Deficit

Moderate PAE

1	not serious	not serious	not serious	serious[d,f]	none	74	126	aOR 1.17 (0.47 to 2.90)	-	⊕⊕⊕◯ Moderate

Infant Behaviour Questionnaire Caregiver Report: Negative Effect

Moderate PAE

1	serious[a]	not serious	not serious	serious[e,f]	none	74	126	-	SMD 0.55 higher (0.13 higher to 0.97 higher)	⊕⊕◯◯ Low

Infant Behaviour Questionnaire Caregiver Report: Effortful Control

Moderate PAE

1	serious[a]	not serious	not serious	serious[e,f]	none	74	126	-	SMD 0.08 higher (0.33 lower to 0.50 higher)	⊕⊕◯◯ Low

DIAGNOSED STUDIES

CBCL Total Behaviour Caregiver Report (Frequency/OR) (Odds of scoring in 'clinical range' >63 T-score)

FASD

1	serious[a]	not serious	not serious	serious[e,f]	none	73	40	OR 25.09 (1.47 to 429.38)	-	⊕⊕◯◯ Low

CBCL Total Behaviour Caregiver Report (T-score)

FASD

9	serious[a]	serious[b]	not serious	not serious	none	390	322	-	**SMD 1.52 higher** (1.14 higher to 1.91 higher)	⊕⊕◯◯ Low

FAS

3	serious[a]	not serious	not serious	not serious	none	73	386	-	**SMD 0.62 higher** (0.35 higher to 0.89 higher)	⊕⊕⊕◯ Moderate

pFAS

2	serious[a]	serious[b]	not serious	serious[e,f]	none	37	319	-	**SMD 1.10 higher** (0.39 higher to 1.81 higher)	⊕◯◯◯ Very low

0 studies for ARND/Others

TRF Total Behaviour Teacher Report (T-score)

FASD

2	serious[a]	not serious	not serious	serious[f]	none	155	75	-	**SMD 0.88 higher** (0.58 higher to 1.17 higher)	⊕⊕◯◯ Low

FAS

2	serious[a]	not serious	serious[c]	not serious	none	135	293	-	**SMD 0.53 higher** (0.31 higher to 0.74 higher)	⊕⊕◯◯ Low

pFAS

2	serious[a]	not serious	serious[c]	not serious	none	139	293	-	**SMD 0.54 higher** (0.33 higher to 0.74 higher)	⊕⊕◯◯ Low

ARND/Others

2	serious[a]	not serious	serious[c]	serious[f]	none	74	293	-	**SMD 0.91 higher** (0.65 higher to 1.18 higher)	⊕◯◯◯ Very low

SSRS Total Behaviour Caregiver Report (m/SD)

FASD

1	serious[a]	not serious	not serious	serious[f]	none	30	30	-	**SMD 1.63 higher** (1.04 higher to 2.22 higher)	⊕⊕◯◯ Low

SSRS Total Behaviour Teacher Report (m/SD)

FASD

2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	42	42	-	**SMD 2.22 higher** (0.22 lower to 4.66 higher)	⊕◯◯◯ Very low

ASR Total Behaviour Self Report (T-score)

pFAS

1	serious[a]	not serious	not serious	serious[e,f]	none	47	58	-	**SMD 2.61 higher** (2.08 higher to 3.14 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	serious[e,f]	none	34	58	-	**SMD 4.59 higher** (3.79 higher to 5.39 higher)	⊕⊕◯◯ Low

0 studies for FASD or FAS

CBCL Total Externalising Behaviour Caregiver Report (T-score)

FASD

9	serious[a]	serious[b]	not serious	serious[e]	none	318	990	-	**SMD 0.93 higher** (0.59 higher to 1.26 higher)	⊕◯◯◯ Very Low
FAS										
2	serious[a]	not serious	not serious	very serious[d,e,f]	none	30	80	-	**SMD 0.29 higher** (0.22 lower to 0.81 higher)	⊕◯◯◯ Very Low
pFAS										
2	serious[a]	serious[b]	not serious	serious[e,f]	none	64	787	-	**SMD 0.97 higher** (0.34 lower to 2.27 higher)	⊕◯◯◯ Very low
ARND/Others										
3	serious[a]	serious[b]	not serious	serious[e]	none	95	822	-	**SMD 0.95 higher** (0.29 higher to 1.62 higher)	⊕◯◯◯ Very low
CBCL/SIB-R Total Externalising Behaviour Caregiver Report (Odds of 'marginally serious' and 'moderate to serious' score, odds of scoring in 'clinical range' >63 CBCL T-score)										
FASD										
2	serious[a]	not serious	not serious	serious[e,f]	none	96	63	OR 15.54 (2.76 to 87.50)		⊕⊕◯◯ Low
0 studies for FAS, pFAS or ARND/Others										
SSRS Total Externalising Behaviour Caregiver Report (m/sd)										
FASD										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	23	37	-	**SMD 0.02 lower** (0.54 lower to 0.51 higher)	⊕◯◯◯ Very Low
0 studies for FAS, pFAS or ARND/Others										
TRF Total Externalising Behaviour Teacher Report (T-score)										
FASD										
5	serious[a]	not serious	not serious	not serious	none	254	1132	-	**SMD 0.78 higher** (0.52 higher to 1.05 higher)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	771	-	**SMD 0.64 higher** (0.24 lower to 1.52 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	771	-	**SMD 0.07 lower** (0.37 lower to 0.24 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e,f]	none	44	71	-	**SMD 0.82 higher** (0.51 higher to 1.12 higher)	⊕⊕◯◯ Low
SSRS Total Externalising Behaviour Teacher Report (m/sd)										
FASD										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	23	37	-	**SMD 0.24 lower** (0.77 lower to 0.28 higher)	⊕◯◯◯ Very Low
0 studies for FAS, pFAS or ARND/Others										
ASR Total Externalising Behaviour Self Report (T-score)										
pFAS										

1	serious[a]	not serious	not serious	serious[e,f]	none	47	58	-	**SMD 2.00 higher** (1.53 higher to 2.47 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	serious[e,f]	none	34	58	-	**SMD 4.08 higher** (3.34 higher to 4.82 higher)	⊕⊕◯◯ Low

0 studies for FASD or FAS

CBCL Total Internalising Behaviour Caregiver Report (T-score)

FASD

10	serious[a]	serious[b]	not serious	not serious	none	440	1278	-	**SMD 0.64 higher** (0.41 higher to 0.87 higher)	⊕⊕◯◯ Low

FAS

2	serious[a]	not serious	not serious	serious[d,e]	none	30	806	-	**SMD 0.15 lower** (0.59 lower to 0.30 higher)	⊕⊕◯◯ Low

pFAS

2	serious[a]	serious[b]	not serious	serious[d,e]	none	68	787	-	**SMD 1.19 higher** (0.53 lower to 2.90 higher)	⊕◯◯◯ Very low

ARND/Others

3	serious[a]	serious[b]	not serious	serious[d,e]	none	95	822	-	**SMD 0.69 higher** (0.06 lower to 1.44 higher)	⊕◯◯◯ Very low

CBCL/SIB-R Total Internalising Behaviour Caregiver Report (Odds of 'marginally serious' and 'moderate to serious' score, odds of scoring in 'clinical range' >63 CBCL T-score))

FASD

2	serious[a]	not serious	not serious	serious[e,f]	none	96	63	OR 15.47 (2.86 to 83.81)	-	⊕⊕◯◯ Low

0 studies for FAS, pFAS and ARND/Others

SSRS Total Internalising Behaviour Caregiver Report (m/sd)

FASD

1	serious[a]	not serious	not serious	very serious[d,e,f]	none	37	23	-	**SMD 0.37 higher** (0.16 lower to 0.89 higher)	⊕◯◯◯ Very Low

0 studies for FAS, pFAS and ARND/Others

TRF/CBCL Total Internalising Behaviour Teacher Report (T-score)

FASD

5	serious[a]	not serious	not serious	not serious	none	251	1097	-	**SMD 0.68 higher** (0.51 higher to 0.85 higher)	⊕⊕⊕◯ Moderate

FAS

1	serious[a]	not serious	not serious	serious[d,e]	none	5	771	-	**SMD 0.30 higher** (0.58 lower to 1.18 higher)	⊕⊕◯◯ Low

pFAS

1	serious[a]	not serious	not serious	serious[d,e]	none	44	771	-	**SMD 0.09 higher** (0.21 lower to 0.40 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	serious[e]	none	44	771	-	**SMD 0.48 higher** (0.18 higher to 0.79 higher)	⊕⊕◯◯ Low

SSRS Total Internalising Behaviour Teacher Report (T-score)

FASD

1	serious[a]	not serious	not serious	very serious[d,e,f]	none	37	23	-	**SMD 0.22 higher** (0.30 lower to 0.74 higher)	⊕◯◯◯ Very Low

0 studies for FAS, pFAS or ARND/Others

ASR Total Internalising Behaviour Adult Report (T-score)

pFAS

1	serious[a]	not serious	not serious	serious[e,f]	none	47	58	-	**SMD 3.56 higher** (2.94 higher to 4.19 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	serious[e,f]	none	34	58	-	**SMD 3.91 higher** (3.20 higher to 4.63 higher)	⊕⊕◯◯ Low

0 studies for FASD or FAS

CBCL Conduct Problems Caregiver Report (T-score)

FASD

4	serious[a]	not serious	not serious	not serious	none	143	1087	-	**SMD 0.52 higher** (0.35 higher to 0.70 higher)	⊕⊕⊕◯ Moderate

FAS

1	serious[a]	not serious	not serious	not serious	none	5	761	-	**SMD 0.19 higher** (0.69 lower to 1.07 higher)	⊕⊕⊕◯ Moderate

pFAS

1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.13 higher** (0.17 lower to 0.44 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 1.06 higher** (0.75 higher to 1.37 higher)	⊕⊕◯◯ Low

TRF Conduct Problems Teacher Report (T-score)

FASD

4	serious[a]	not serious	not serious	not serious	none	128	1098	-	**SMD 0.59 higher** (0.32 higher to 0.86 higher)	⊕⊕⊕◯ Moderate

FAS

1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.03 higher** (0.85 lower to 0.91 higher)	⊕⊕◯◯ Low

pFAS

1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.02 higher** (0.29 lower to 0.32 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[b]	not serious	not serious	serious[e]	none	44	761	-	**SMD 0.82 higher** (0.52 higher to 1.13 higher)	⊕⊕◯◯ Low

CBCL Oppositional Defiant Caregiver Report (T-score)										
FASD										
4	serious[a]	not serious	not serious	not serious	none	143	1087	-	**SMD 0.46 higher** (0.20 higher to 0.72 higher)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[d]	none	5	761	-	**SMD 0.25 higher** (0.63 lower to 1.13 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 0.37 higher** (0.06 higher to 0.67 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 1.29 higher** (0.98 higher to 1.60 higher)	⊕⊕◯◯ Low
Vanderbilt-C Oppositional Defiant Disorder Caregiver Report (m/sd)										
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	16	21	-	**SMD 1.67 higher** (0.91 higher to 2.44 higher)	⊕⊕◯◯ Low
0 studies for FAS, pFAS and ARND/Others										
TRF Oppositional Defiant Disorder Teacher Report (T-score)										
FASD										
4	serious[a]	not serious	not serious	not serious	none	128	1098	-	**SMD 0.42 higher** (0.17 higher to 0.66 higher)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[e]	none	5	761	-	**SMD 0.92 higher** (0.04 higher to 1.81 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.11 higher** (0.19 lower to 0.41 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 0.76 higher** (0.46 higher to 1.07 higher)	⊕⊕◯◯ Low
CBCL Aggression Caregiver Report (T-score)										
FASD										
5	serious[a]	serious[b]	not serious	serious[e]	none	176	1120	-	**SMD 0.69 higher** (0.36 higher to 1.03 higher)	⊕◯◯◯ Very low
FAS										
1	serious[a]	not serious	not serious	serious[d]	none	5	761	-	**SMD 0.18 higher** (0.70 lower to 1.06 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 0.35 higher** (0.05 higher to 0.66 higher)	⊕⊕◯◯ Low

ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 1.26 higher** (0.95 higher to 1.57 higher)	⊕⊕◯◯ Low
TRF Aggression Teacher Report (T-score)										
FASD										
4	serious[a]	not serious	not serious	not serious	none	128	1098	-	**SMD 0.52 higher** (0.25 higher to 0.79 higher)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.64 higher** (0.24 lower to 1.52 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.12 higher** (0.18 lower to 0.43 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 0.79 higher** (0.48 higher to 1.09 higher)	⊕⊕◯◯ Low
ASR Aggression Self Report (T-score)										
pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	47	58	-	**SMD 2.48 higher** (1.96 higher to 2.99 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e,f]	none	34	58	-	**SMD 4.39 higher** (3.62 higher to 5.17 higher)	⊕⊕◯◯ Low
0 studies for FASD and FAS										
CBCL Rule-Breaking Behaviour Caregiver Report (T-score)										
FASD										
5	serious[a]	serious[b]	not serious	serious[e]	none	176	1120	-	**SMD 0.48 higher** (0.19 higher to 0.77 higher)	⊕◯◯◯ Very Low
FAS										
2	serious[a]	not serious	not serious	serious[d,e]	none	30	796	-	**SMD 0.45 higher** (0.06 lower to 0.96 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d]	none	44	761	-	**SMD 0.19 higher** (0.02 lower to 0.49 higher)	⊕⊕◯◯ Low
ARND/Others										
2	serious[a]	serious[b]	not serious	serious[e]	none	106	796	-	**SMD 0.76 higher** (0.20 higher to 1.31 higher)	⊕◯◯◯ Very low
CBCL/SIB-R Rule-Breaking Behaviour Caregiver Report (Frequency of 'marginally serious' and 'moderate to serious' score/cut-off unclear)										
FASD										
2	serious[a]	serious[b]	not serious	serious[e,f]	none	37	49	**OR 5.31** (1.93 to 14.60	-	⊕◯◯◯ Very low

0 studies for FAS, pFAS and ARND/Others										
TRF/CBCL Rule-Breaking Behaviour Teacher Report (T-score)										
FASD										
3	serious[a]	not serious	not serious	not serious	none	124	1048	-	**SMD 0.60 higher** (0.41 higher to 0.79 higher)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.00** (0.88 lower to 0.88 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.02 higher** (0.29 lower to 0.32 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 0.80 higher** (0.49 higher to 1.10 higher)	⊕⊕◯◯ Low
ASR Rule-Breaking Behaviour Self Report (T-score)										
pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	47	58	-	**SMD 1.25 higher** (0.82 higher to 1.67 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e,f]	none	34	58	-	**SMD 1.26 higher** (0.79 higher to 1.72 higher)	⊕⊕◯◯ Low
0 studies for FASD or FAS										
CBRS Hyperactivity Caregiver Report (T-score)										
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	25	13	-	**SMD 2.10 higher** (1.26 higher to 2.94 higher)	⊕⊕◯◯ Low
0 studies for FAS, pFAS and ARND/Others										
CBCL Hyperactivity Caregiver Report (Frequency/OR) (Cut-off unclear)										
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	16/17 (94.1%)	10/26 (38.5%)	**OR 25.60** (2.93 to 224.05)	**557 more per 1000** (from 262 more to 608 more)	⊕⊕◯◯ Low
0 studies for FAS, pFAS and ARND/Others										
DBD/SSRS Hyperactivity Caregiver Report (m/SD)										
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	37	23	-	**SMD 0.76 higher** (0.22 higher to 1.30 higher)	⊕⊕◯◯ Low
pFAS										
2	serious[a]	serious[b]	not serious	serious[e,f]	none	45	117	-	**SMD 0.41 higher** (0.30 lower to 1.13 higher)	⊕◯◯◯ Very low
0 studies for FAS and ARND/Others										
DBD/SSRS Hyperactivity Teacher Report (m/SD)										

FASD										
1	serious[a]	not serious	not serious	very serious[d,e,f]	none	37	23	-	**SMD 0.28 lower** (0.81 lower to 0.24 higher)	⊕◯◯◯ Very low
pFAS										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	45	117	-	**SMD 0.39 higher** (0.19 lower to 0.97 higher)	⊕◯◯◯ Very low
0 studies for FAS, pFAS and ARND/Others										
CBCL Attention/Hyperactivity Caregiver Report (T-score)										
FASD										
4	serious[a]	not serious	not serious	not serious	none	143	1087	-	**SMD 0.48 higher** (0.30 higher to 0.66 higher)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	761	-	**SMD 0.57 higher** (0.31 lower to 1.45 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.29 higher** (0.01 lower to 0.60 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 1.08 higher** (0.77 higher to 1.39 higher)	⊕⊕◯◯ Low
CBCL/TRF Attention/Hyperactivity Teacher Report (T-score)										
FASD										
3	serious[a]	not serious	not serious	not serious	none	124	1048	-	**SMD 0.65 higher** (0.46 higher to 0.83 higher)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[e]	none	5	761	-	**SMD 0.98 higher** (0.10 higher to 1.86 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	761	-	**SMD 0.23 higher** (0.08 lower to 0.53 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	761	-	**SMD 0.85 higher** (0.55 higher to 1.16 higher)	⊕⊕◯◯ LOw
CBCL/CBRS Anxious/Depressed Caregiver Report (T-score)										
FASD										
7	serious[a]	not serious	not serious	not serious	none	239	1171	-	**SMD 0.60 higher** (0.40 higher to 0.80 higher)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	771	-	**SMD 0.01 lower** (0.89 lower to 0.87 higher)	⊕⊕◯◯ Low
pFAS										

No of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	n	n		Effect (SMD)	Certainty
1	serious[a]	not serious	not serious	serious[d,e]	none	44	771	-	**SMD 0.18 higher** (0.12 lower to 0.49 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	771	-	**SMD 0.59 higher** (0.29 higher to 0.90 higher)	⊕⊕◯◯ Low
Vanderbilt-C Anxious/Depressed Caregiver Report (m/sd)										
FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	16	21	-	**SMD 1.09 higher** (0.38 higher to 1.79 higher)	⊕⊕◯◯ Low
0 studies for FAS, pFAS and ARND/Others										
TRF Anxious/Depressed Teacher Report (T-score)										
FASD										
3	serious[a]	not serious	not serious	not serious	none	124	1048	-	**SMD 0.67 higher** (0.43 higher to 0.91 higher)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	771	-	**SMD 0.46 higher** (0.42 lower to 1.34 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	771	-	**SMD 0.19 higher** (0.11 lower to 0.50 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	771	-	**SMD 0.36 higher** (0.05 higher to 0.66 higher)	⊕⊕◯◯ Low
CBCL Anxious/Depressed Self-Report (T-score)										
pFAS										
1	serious[a]	not serious	not serious	serious[f]	none	47	58	-	**SMD 3.62 higher** (2.99 higher to 4.25 higher)	⊕⊕◯◯ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[f]	none	34	58	-	**SMD 3.83 higher** (3.37 higher to 4.29 higher)	⊕⊕◯◯ Low
CBCL Anxiety Caregiver Report (T-score)										
FASD										
5	serious[a]	not serious	not serious	not serious	none	187	1099	-	**SMD 0.60 higher** (0.37 higher to 0.82 higher)	⊕⊕⊕◯ Moderate
FAS										
1	serious[a]	not serious	not serious	serious[d]	none	5	771	-	**SMD 0.07 higher** (0.81 lower to 0.95 higher)	⊕⊕◯◯ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	771	-	**SMD 0.31 higher** (0.00 to 0.61 higher)	⊕⊕◯◯ Low

ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	771	-	**SMD 0.54 higher** (0.24 higher to 0.85 higher)	⊕⊕◯◯ Low

TRF Anxiety Teacher Report (T-score)

FASD										
3	serious[a]	not serious	not serious	serious[e]	none	124	1048	-	**SMD 0.76 higher** (0.46 higher to 1.06 higher)	⊕⊕◯◯ Low

FAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	5	771	-	**SMD 0.70 higher** (0.18 lower to 1.58 higher)	⊕⊕◯◯ Low

pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	771	-	**SMD 0.14 higher** (0.17 lower to 0.44 higher)	⊕⊕◯◯ Low

ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	771	-	**SMD 0.42 higher** (0.12 higher to 0.73 higher)	⊕⊕◯◯ Low

CBCL Withdrawn/Depressed Caregiver Report (T-score)

FASD										
6	serious[a]	not serious	not serious	not serious	none	215	1154	-	**SMD 0.66 higher** (0.41 higher to 0.90 higher)	⊕⊕⊕◯ Moderate

FAS										
1	serious[b]	not serious	not serious	serious[d]	none	5	771	-	**SMD 0.11 lower** (0.99 lower to 0.77 higher)	⊕⊕◯◯ Low

pFAS										
1	serious[a]	not serious	not serious	serious[e]	none	44	771	-	**SMD 0.32 higher** (0.01 higher to 0.62 higher)	⊕⊕◯◯ Low

ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	771	-	**SMD 0.48 higher** (0.18 higher to 0.78 higher)	⊕⊕◯◯ Low

TRF Withdrawn/Depressed Teacher Report (T-score)

FASD										
3	serious[a]	not serious	not serious	not serious	none	124	1048	-	**SMD 0.71 higher** (0.50 higher to 0.92 higher)	⊕⊕⊕◯ Moderate

FAS										
1	serious[a]	not serious	not serious	serious[d]	none	5	771	-	**SMD 0.22 lower** (1.10 lower to 0.66 higher)	⊕⊕◯◯ Low

pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	771	-	**SMD 0.03 lower** (0.34 lower to 0.27 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	serious[e]	none	44	771	-	**SMD 0.39 higher** (0.09 higher to 0.70 higher)	⊕⊕◯◯ Low

ASR Withdrawn/Depressed Self Report (T-score)

pFAS

1	serious[a]	not serious	not serious	Serious[e,f]	none	47	58	-	**SMD 2.42 higher** (1.91 higher to 2.93 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	Serious[e,f]	none	34	58	-	**SMD 3.44 higher** (2.78 higher to 4.10 higher)	⊕⊕◯◯ Low

0 studies for FASD or FAS

CBCL/CBRS Somatic Complaints Caregiver Report (T-score)

FASD

3	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	76	89	-	**SMD 0.68 higher** (0.05 lower to 1.42 higher)	⊕◯◯◯ Very low

0 studies for FAS, pFAS or ARND/Others

CBCL Somatic Self Complaints Self Report (T-score)

pFAS

1	serious[a]	not serious	not serious	Serious[e,f]	none	47	58	-	**SMD 1.77 higher** (1.31 higher to 2.22 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	Serious[e,f]	none	34	58	-	**SMD 1.78 higher** (1.28 higher to 2.28 higher)	⊕⊕◯◯ Low

0 studies for FASD or FAS

CBCL/CBRS Thought Complaints Caregiver Report (T-score)

FASD

2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	43	58	-	**SMD 1.14 higher** (0.52 lower to 2.81 higher)	⊕◯◯◯ Very low

0 studies for FAS, pFAS or ARND/Others

CBCL Thought Complaints Self Report (T-score)

pFAS

1	serious[a]	not serious	not serious	serious[e,f]	none	47	58	-	**SMD 0.82 higher** (0.42 higher to 1.22 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	Serious[e,f]	none	34	58	-	**SMD 3.58 higher** (2.90 higher to 4.26 higher)	⊕⊕◯◯ Low

0 studies for FASD or FAS

CBCL Affective Problems Caregiver Report (T-score)

FASD

4	serious[a]	not serious	not serious	not serious	none	143	1087	-	**SMD 0.78 higher** (0.52 higher to 1.04 higher)	⊕⊕⊕◯ Moderate

FAS										
1	serious[a]	not serious	not serious	serious[d]	none	5	771	-	**SMD 0.10 higher** (0.78 lower to 0.98 higher)	⊕⊕○○ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	771	-	**SMD 0.26 higher** (0.04 lower to 0.57 higher)	⊕⊕○○ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	771	-	**SMD 0.48 higher** (0.17 higher to 0.78 higher)	⊕⊕○○ Low
TRF Affective Problems Teacher Report (T-score)										
FASD										
3	serious[a]	not serious	not serious	not serious	none	124	1048	-	**SMD 0.83 higher** (0.64 higher to 1.02 higher)	⊕⊕⊕○ Moderate
FAS										
1	serious[a]	not serious	not serious	Serious[d,e]	none	5	771	-	**SMD 0.02 lower** (0.90 lower to 0.86 higher)	⊕⊕○○ Low
pFAS										
1	serious[a]	not serious	not serious	serious[d,e]	none	44	771	-	**SMD 0.17 higher** (0.13 lower to 0.48 higher)	⊕⊕○○ Low
ARND/Others										
1	serious[a]	not serious	not serious	serious[e]	none	44	771	-	**SMD 0.65 higher** (0.34 higher to 0.95 higher)	⊕⊕○○ Low

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.
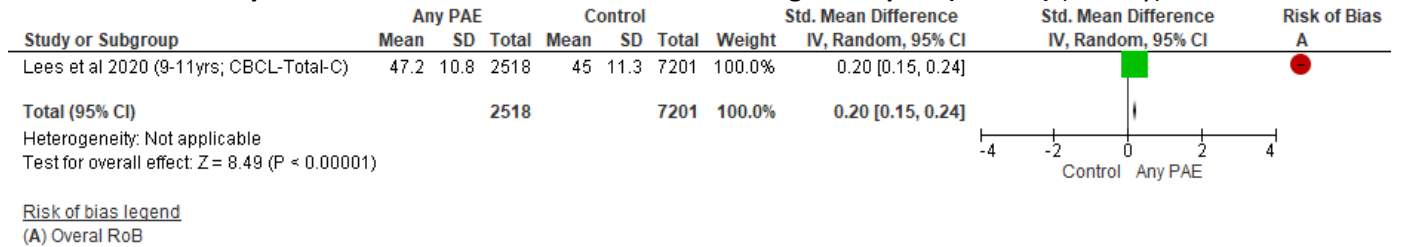
Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I^2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CI for overall estimate crossed the line of no effect; e) Wide CIs for overall estimate; f) optimal information size criteria size not met.
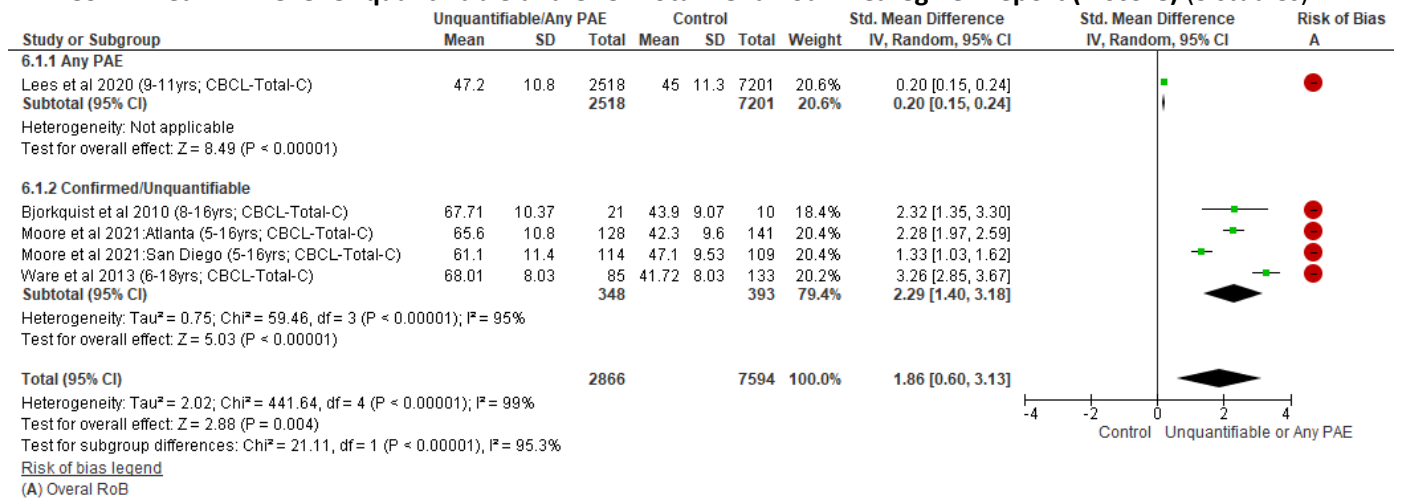
Meta-analyses for behaviour

EXPOSURE STUDIES

CBCL Total Behaviour – Caregiver Report (T-score)

Any Level PAE and CBCL Total Behaviour – Caregiver Report (T-score) (1 study)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; CBCL-Total-C)	47.2	10.8	2518	45	11.3	7201	100.0%	0.20 [0.15, 0.24]		–
Total (95% CI)			2518			7201	100.0%	**0.20 [0.15, 0.24]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 8.49 (P < 0.00001)

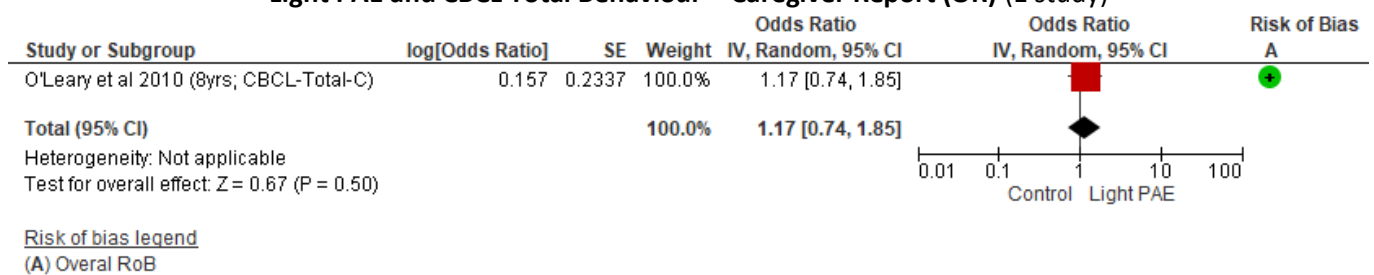Risk of bias legend
(A) Overal RoB

Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

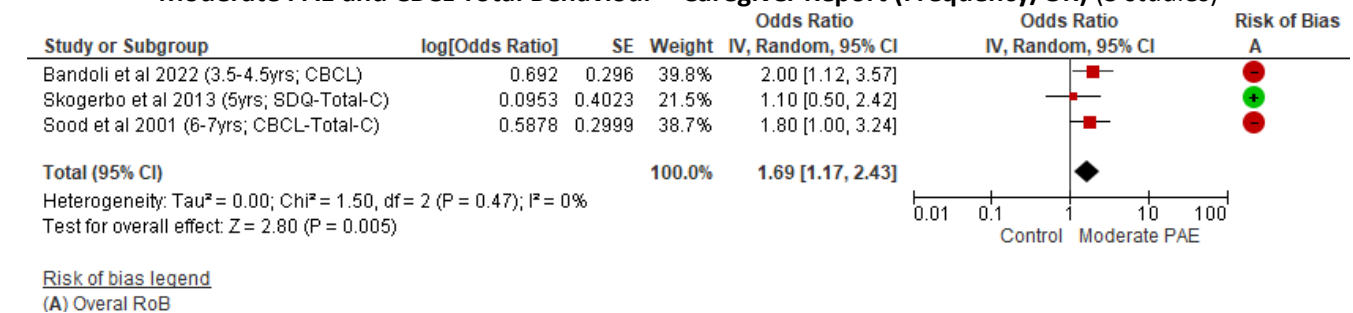**Confirmed PAE-Level Unquantifiable and CBCL Total Behaviour – Caregiver Report (T-score)** (3 studies)

Study or Subgroup	Unquantifiable/Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
6.1.1 Any PAE										
Lees et al 2020 (9-11yrs; CBCL-Total-C)	47.2	10.8	2518	45	11.3	7201	20.6%	0.20 [0.15, 0.24]		–
Subtotal (95% CI)			2518			7201	20.6%	**0.20 [0.15, 0.24]**		
Heterogeneity: Not applicable										
Test for overall effect: Z = 8.49 (P < 0.00001)										
6.1.2 Confirmed/Unquantifiable										
Bjorkquist et al 2010 (8-16yrs; CBCL-Total-C)	67.71	10.37	21	43.9	9.07	10	18.4%	2.32 [1.35, 3.30]		–
Moore et al 2021:Atlanta (5-16yrs; CBCL-Total-C)	65.6	10.8	128	42.3	9.6	141	20.4%	2.28 [1.97, 2.59]		–
Moore et al 2021:San Diego (5-16yrs; CBCL-Total-C)	61.1	11.4	114	47.1	9.53	109	20.4%	1.33 [1.03, 1.62]		–
Ware et al 2013 (6-18yrs; CBCL-Total-C)	68.01	8.03	85	41.72	8.03	133	20.2%	3.26 [2.85, 3.67]		–
Subtotal (95% CI)			348			393	79.4%	**2.29 [1.40, 3.18]**		
Heterogeneity: Tau² = 0.75; Chi² = 59.46, df = 3 (P < 0.00001); I² = 95%										
Test for overall effect: Z = 5.03 (P < 0.00001)										
Total (95% CI)			2866			7594	100.0%	**1.86 [0.60, 3.13]**		

Heterogeneity: Tau² = 2.02; Chi² = 441.64, df = 4 (P < 0.00001); I² = 99%
Test for overall effect: Z = 2.88 (P = 0.004)
Test for subgroup differences: Chi² = 21.11, df = 1 (P < 0.00001), I² = 95.3%
Risk of bias legend
(A) Overal RoB

CBCL Total Behaviour – Caregiver Report (Frequency/OR)

Light PAE and CBCL Total Behaviour – Caregiver Report (OR) (1 study)

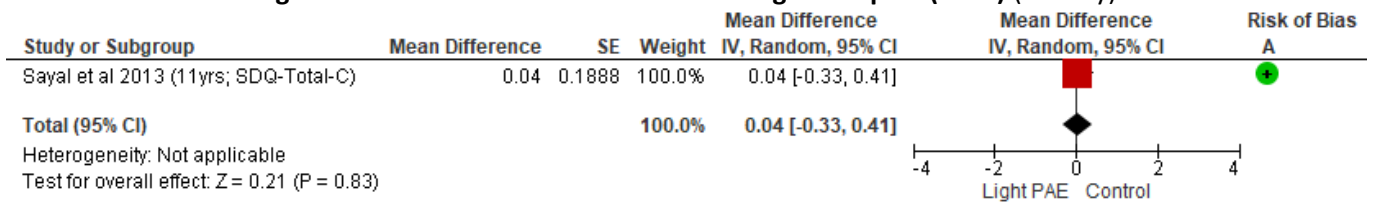| Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (8yrs; CBCL-Total-C)	0.157	0.2337	100.0%	1.17 [0.74, 1.85]		+
Total (95% CI)			100.0%	**1.17 [0.74, 1.85]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.67 (P = 0.50)

Risk of bias legend
(A) Overal RoB

Moderate PAE and CBCL Total Behaviour – Caregiver Report (Frequency/OR) (3 studies)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Bandoli et al 2022 (3.5-4.5yrs; CBCL)	0.692	0.296	39.8%	2.00 [1.12, 3.57]		–
Skogerbo et al 2013 (5yrs; SDQ-Total-C)	0.0953	0.4023	21.5%	1.10 [0.50, 2.42]		+
Sood et al 2001 (6-7yrs; CBCL-Total-C)	0.5878	0.2999	38.7%	1.80 [1.00, 3.24]		–
Total (95% CI)			100.0%	**1.69 [1.17, 2.43]**		

Heterogeneity: Tau² = 0.00; Chi² = 1.50, df = 2 (P = 0.47); I² = 0%
Test for overall effect: Z = 2.80 (P = 0.005)

Risk of bias legend
(A) Overal RoB

Heavy PAE and CBCL Total Behaviour – Caregiver Report (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI	Odds Ratio IV, Fixed, 95% CI	Risk of Bias A
O'Leary et al 2010 (8yrs; CBCL-Total-C)	0.4849	0.3309	100.0%	1.62 [0.85, 3.11]		+
Total (95% CI)			100.0%	1.62 [0.85, 3.11]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.47 (P = 0.14)

Risk of bias legend
(A) Overal RoB

Note: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, as well as CBCL results from 2yrs, 5yrs, and 8yrs. Data from participants at 8yrs and exposed in the 1st trimester was used. Sood et al 2001 also reports MD data and frequency data. Skogerbo et al 2013 reports adjusted OR.

CBCL Total Behaviour – Caregiver Report (adjusted Mean Difference)
Light PAE and CBCL Total Behaviour – Caregiver Report (aMD) (1 study)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A
Sayal et al 2013 (11yrs; SDQ-Total-C)	0.04	0.1888	100.0%	0.04 [-0.33, 0.41]		+
Total (95% CI)			100.0%	0.04 [-0.33, 0.41]		

Heterogeneity: Not applicable
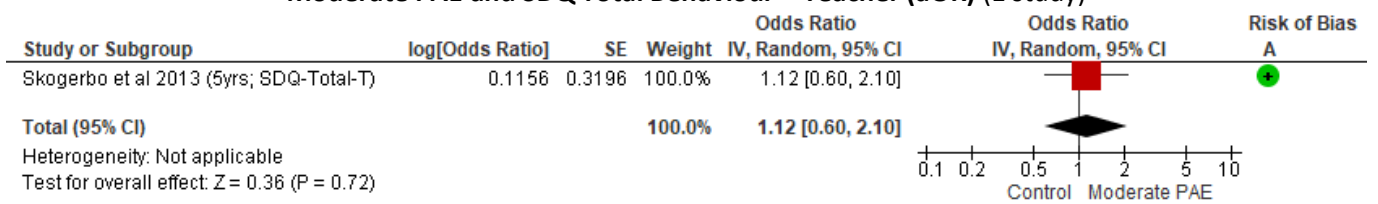Test for overall effect: Z = 0.21 (P = 0.83)

Risk of bias legend
(A) Overal RoB

SDQ Total Behaviour Teacher Report (Frequency/aOR)
Moderate PAE and SDQ Total Behaviour – Teacher (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2013 (5yrs; SDQ-Total-T)	0.1156	0.3196	100.0%	1.12 [0.60, 2.10]		+
Total (95% CI)			100.0%	1.12 [0.60, 2.10]		

Heterogeneity: Not applicable
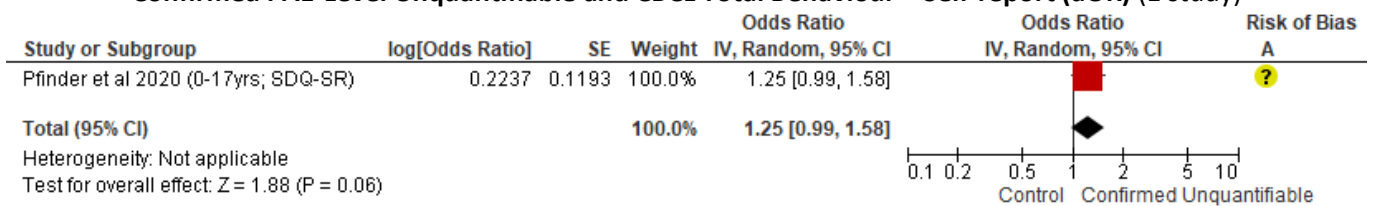Test for overall effect: Z = 0.36 (P = 0.72)

Risk of bias legend
(A) Overal RoB

Note: Upper CI and lower CI limit was entered into revman, odds ratio autogenerated by revman.

CBCL Total Behaviour Self-report (Frequency/OR)
Confirmed PAE-Level Unquantifiable and CBCL Total Behaviour – Self-report (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Pfinder et al 2020 (0-17yrs; SDQ-SR)	0.2237	0.1193	100.0%	1.25 [0.99, 1.58]		?
Total (95% CI)			100.0%	1.25 [0.99, 1.58]		

Heterogeneity: Not applicable
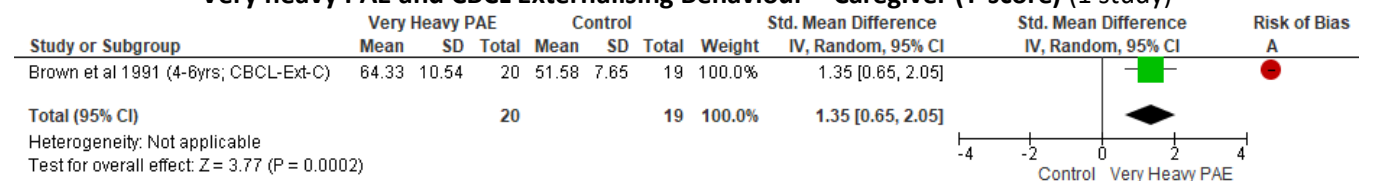Test for overall effect: Z = 1.88 (P = 0.06)

Risk of bias legend
(A) Overal RoB

CBCL Externalising Behaviour Caregiver Report (T-score)
Very heavy PAE and CBCL Externalising Behaviour – Caregiver (T-score) (1 study)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Brown et al 1991 (4-6yrs; CBCL-Ext-C)	64.33	10.54	20	51.58	7.65	19	100.0%	1.35 [0.65, 2.05]		●
Total (95% CI)			20			19	100.0%	1.35 [0.65, 2.05]		

Heterogeneity: Not applicable
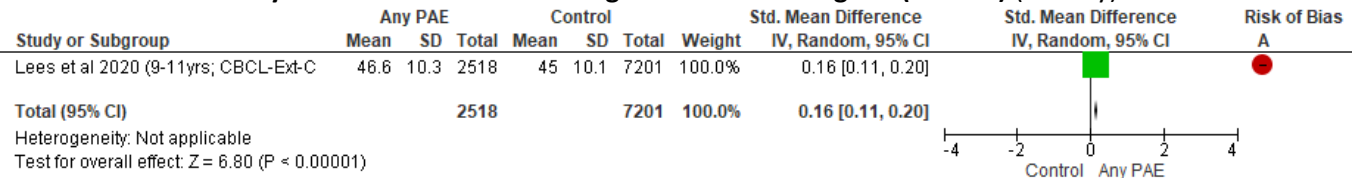Test for overall effect: Z = 3.77 (P = 0.0002)

Risk of bias legend
(A) Overall RoB

Note: Brown et al 1991 also reports a 'destructive' subdomain.

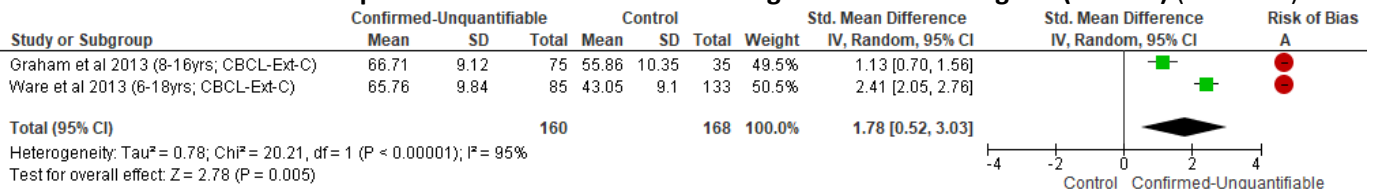## Any PAE and CBCL Externalising Behaviour – Caregiver (T-score) (1 study)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; CBCL-Ext-C)	46.6	10.3	2518	45	10.1	7201	100.0%	0.16 [0.11, 0.20]	—
Total (95% CI)			2518			7201	100.0%	0.16 [0.11, 0.20]	

Heterogeneity: Not applicable
Test for overall effect: Z = 6.80 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

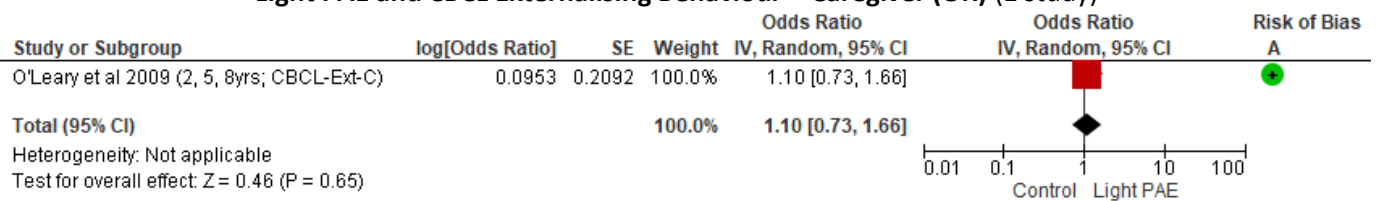## Confirmed PAE-Level Unquantifiable and CBCL Externalising Behaviour – Caregiver (T-score) (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Graham et al 2013 (8-16yrs; CBCL-Ext-C)	66.71	9.12	75	55.86	10.35	35	49.5%	1.13 [0.70, 1.56]	—
Ware et al 2013 (6-18yrs; CBCL-Ext-C)	65.76	9.84	85	43.05	9.1	133	50.5%	2.41 [2.05, 2.76]	—
Total (95% CI)			160			168	100.0%	1.78 [0.52, 3.03]	

Heterogeneity: Tau² = 0.78; Chi² = 20.21, df = 1 (P < 0.00001); I² = 95%
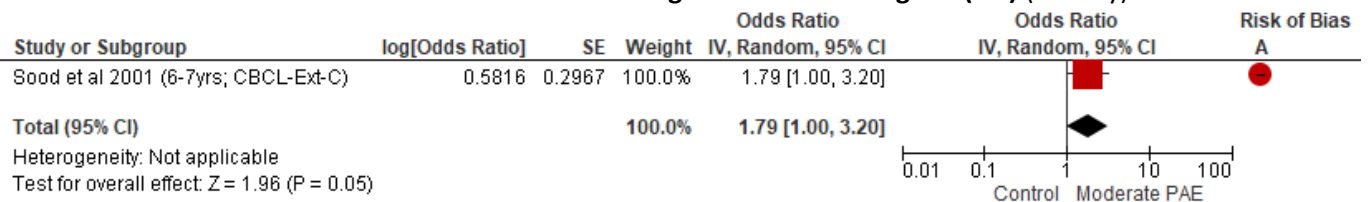Test for overall effect: Z = 2.78 (P = 0.005)

Risk of bias legend
(A) Overall RoB

CBCL Externalising Behaviour Caregiver Report (Frequency/OR)
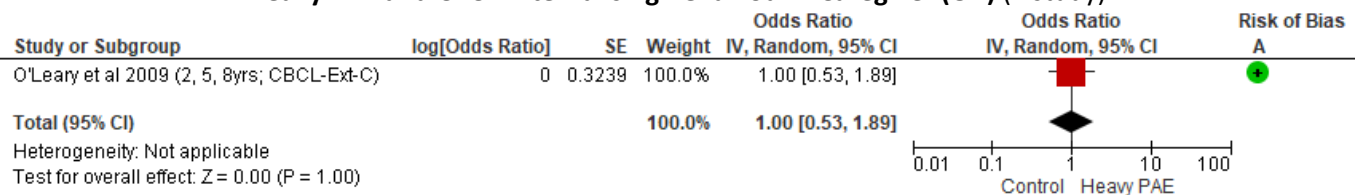## Light PAE and CBCL Externalising Behaviour – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2009 (2, 5, 8yrs; CBCL-Ext-C)	0.0953	0.2092	100.0%	1.10 [0.73, 1.66]	+
Total (95% CI)			100.0%	1.10 [0.73, 1.66]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.46 (P = 0.65)

Risk of bias legend
(A) Overall RoB

Moderate PAE and CBCL Externalising Behaviour – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sood et al 2001 (6-7yrs; CBCL-Ext-C)	0.5816	0.2967	100.0%	1.79 [1.00, 3.20]	—
Total (95% CI)			100.0%	1.79 [1.00, 3.20]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.96 (P = 0.05)

Risk of bias legend
(A) Overall RoB

Heavy PAE and CBCL Externalising Behaviour – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2009 (2, 5, 8yrs; CBCL-Ext-C)	0	0.3239	100.0%	1.00 [0.53, 1.89]	+
Total (95% CI)			100.0%	1.00 [0.53, 1.89]	

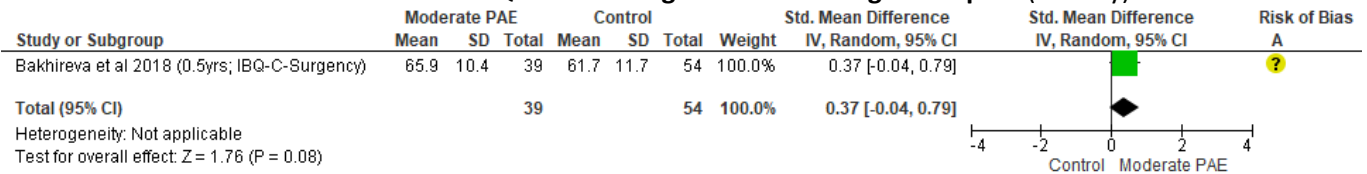Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used. O'Leary et al 2010 also reports frequency data at 2, 5, and 8yrs. Sood et al 2001 also reports MD data and frequency data.

IBQ Externalising Behaviour Caregiver Report (mean/SD)

Moderate PAE and IBQ Externalising Behaviour Caregiver Report (1 study)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bakhireva et al 2018 (0.5yrs; IBQ-C-Surgency)	65.9	10.4	39	61.7	11.7	54	100.0%	0.37 [-0.04, 0.79]		?
Total (95% CI)			39			54	100.0%	0.37 [-0.04, 0.79]		

Heterogeneity: Not applicable
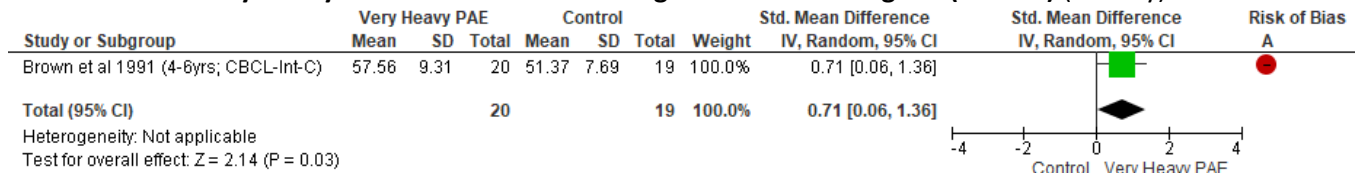Test for overall effect: Z = 1.76 (P = 0.08)

Risk of bias legend
(A) Overall RoB

CBCL Total Internalising Behaviour – Caregiver Report (T-score)

Very Heavy PAE and CBCL Internalising Behaviour – Caregiver (T-score) (1 study)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Brown et al 1991 (4-6yrs; CBCL-Int-C)	57.56	9.31	20	51.37	7.69	19	100.0%	0.71 [0.06, 1.36]		−
Total (95% CI)			20			19	100.0%	0.71 [0.06, 1.36]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.14 (P = 0.03)

Risk of bias legend
(A) Overall RoB

Any PAE and CBCL Internalising Behaviour – Caregiver (T-score) (1 study)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; CBCL-Int-C)	49.5	10.4	2518	48	10.6	7201	100.0%	0.14 [0.10, 0.19]		−
Total (95% CI)			2518			7201	100.0%	0.14 [0.10, 0.19]		

Heterogeneity: Not applicable
Test for overall effect: Z = 6.14 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

Confirmed PAE-Level Unquantifiable and CBCL Internalising Behaviour – Caregiver (T-score) (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Graham et al 2013 (8-16yrs; CBCL-Int-C)	60.48	10.19	75	55.91	10.17	35	49.3%	0.45 [0.04, 0.85]		−
Ware et al 2013 (8-16yrs; CBCL-Int-C)	60.73	10.15	85	45.52	9.39	133	50.7%	1.56 [1.25, 1.87]		−
Total (95% CI)			160			168	100.0%	1.01 [-0.08, 2.11]		

Heterogeneity: Tau² = 0.59; Chi² = 18.43, df = 1 (P < 0.0001); I² = 95%
Test for overall effect: Z = 1.81 (P = 0.07)

Risk of bias legend
(A) Overall RoB

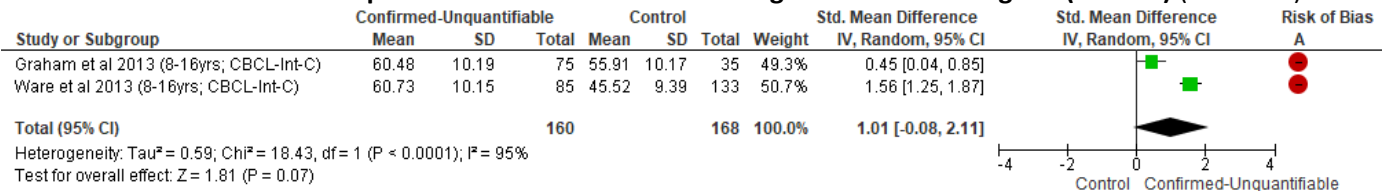## CBCL Total Internalising Behaviour Caregiver Report (Frequency/OR)

Light PAE and CBCL Internalising Behaviour – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2, 5, 8yrs; CBCL-Int-C)	0.1311	0.2712	100.0%	1.14 [0.67, 1.94]		+
Total (95% CI)			100.0%	1.14 [0.67, 1.94]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.48 (P = 0.63)

Risk of bias legend
(A) Overall RoB

Moderate PAE and CBCL Internalising Behaviour – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sood et al 2001 (6-7yrs; CBCL-Int-C)	0.513	0.3155	100.0%	1.67 [0.90, 3.10]		−
Total (95% CI)			100.0%	1.67 [0.90, 3.10]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.63 (P = 0.10)

Risk of bias legend
(A) Overall RoB

Heavy PAE and CBCL Internalising Behaviour – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2, 5, 8yrs; CBCL-Int-C)	0.9723	0.3392	100.0%	2.64 [1.36, 5.14]		+
Total (95% CI)			100.0%	2.64 [1.36, 5.14]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.87 (P = 0.004)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used. Sood et al 2001 also reports MD data and frequency data.

CBCL/SDQ Conduct Problems – Caregiver Report (MD/T-score)

Light PAE and SDQ Conduct Problems – Caregiver (aMD) (1 study)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A
Sayal et al 2013 (11yrs; SDQ-C)	0.04	0.0561	100.0%	0.04 [-0.07, 0.15]		+
Total (95% CI)			100.0%	0.04 [-0.07, 0.15]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and CBCL Conduct Problems – Caregiver (T-score) (1 study)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Gautam et al 2015 (7-16yrs; CBCL-C)	60	8	61	54	5	55	100.0%	0.88 [0.50, 1.27]		●
Total (95% CI)			61			55	100.0%	0.88 [0.50, 1.27]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.53 (P < 0.00001)
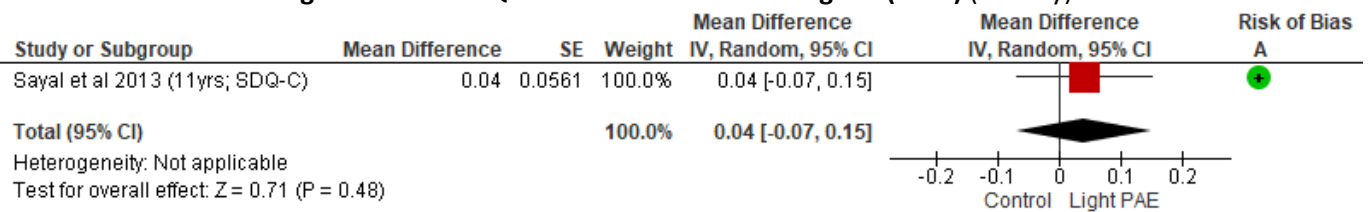
Risk of bias legend
(A) Overall RoB

CBCL/SDQ Conduct Problems Caregiver Report (Frequency/OR)

Light PAE and SDQ Conduct Problems – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sayal et al 2007 (6-7yrs; SDQ-C)	0.1837	0.1199	100.0%	1.20 [0.95, 1.52]		+
Total (95% CI)			100.0%	1.20 [0.95, 1.52]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.53 (P = 0.13)

Risk of bias legend
(A) Overall RoB

Note: Sayal et al 2007 also reports data from 3 and 6yrs.

CBCL/SDQ Conduct Problems Self Report (Frequency/OR)

Confirmed PAE-Level Unquantifiable and SDQ Conduct Problems – Self Report (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Pfinder et al 2020 (11-17yrs; SDQ)	0.2173	0.116	100.0%	1.24 [0.99, 1.56]		?
Total (95% CI)			100.0%	1.24 [0.99, 1.56]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.87 (P = 0.06)

Risk of bias legend
(A) Overall RoB

SDQ Conduct Problems Teacher Report (Frequency/OR)

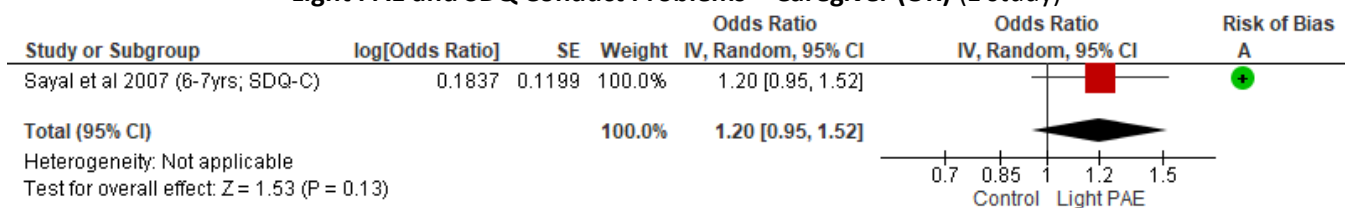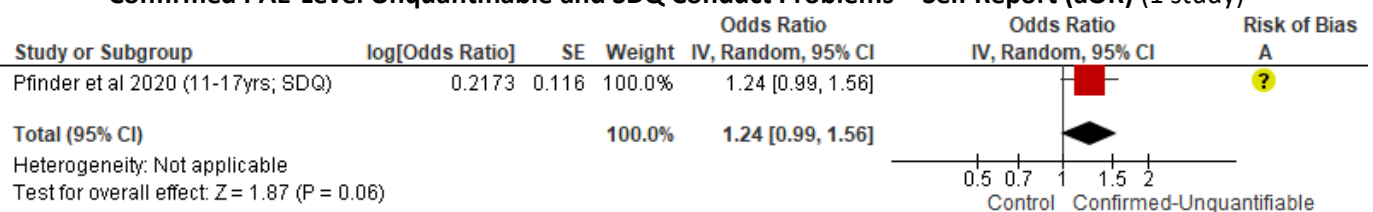### Light PAE and SDQ Conduct Problems – Teacher (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sayal et al 2007 (7-9yrs; SDQ-T)	0.3126	0.211	100.0%	1.37 [0.90, 2.07]		+
Total (95% CI)			100.0%	**1.37 [0.90, 2.07]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.48 (P = 0.14)

Risk of bias legend
(A) Overall RoB

Note: Sayal et al 2007 also reports data from 3 and 6yrs.
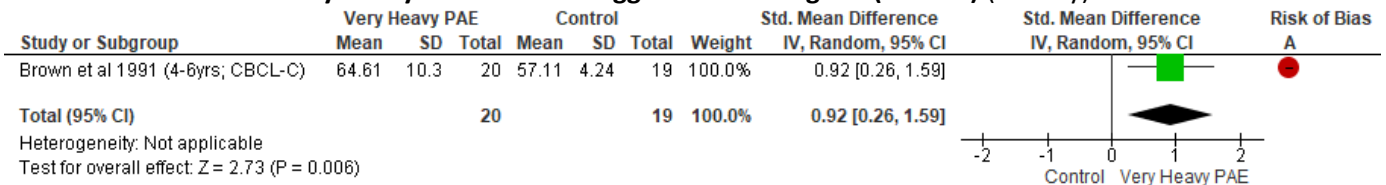
CBCL Aggression Caregiver Report (T-score)

Very heavy PAE and CBCL Aggression - Caregiver (T-score) (1 study)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Brown et al 1991 (4-6yrs; CBCL-C)	64.61	10.3	20	57.11	4.24	19	100.0%	0.92 [0.26, 1.59]		−
Total (95% CI)			20			19	100.0%	**0.92 [0.26, 1.59]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.73 (P = 0.006)

Risk of bias legend
(A) Overall RoB

Any PAE and CBCL Aggression – Caregiver (T-score) (1 study)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; CBCL-C)	53.1	5.7	2518	52.5	5.2	7201	100.0%	0.11 [0.07, 0.16]		−
Total (95% CI)			2518			7201	100.0%	**0.11 [0.07, 0.16]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.86 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

Confirmed PAE-Level Unquantifiable and CBCL Aggression – Caregiver (T-score) (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Vaurio et al 2011 (6-16yrs; CBCL-C)	67.58	11.26	55	55.18	9.85	55	49.3%	1.16 [0.76, 1.57]		−
Ware et al 2013 (6-18yrs; CBCL-C)	67.54	11.37	85	51.6	3.23	133	50.7%	2.11 [1.77, 2.45]		−
Total (95% CI)			140			188	100.0%	**1.64 [0.72, 2.57]**		

Heterogeneity: Tau² = 0.41; Chi² = 12.37, df = 1 (P = 0.0004); I² = 92%
Test for overall effect: Z = 3.47 (P = 0.0005)

Risk of bias legend
(A) Overall RoB

CBCL Aggression Caregiver Report (Frequency/OR)

Light PAE and CBCL Aggression – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2009 (2, 5, 8yrs; CBCL-C)	0.0554	0.3922	100.0%	1.06 [0.49, 2.28]		+
Total (95% CI)			100.0%	**1.06 [0.49, 2.28]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.14 (P = 0.89)

Risk of bias legend
(A) Overall RoB

Moderate PAE and CBCL Aggression – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sood et al 2001 (6-7yrs; CBCL-C)	0.2594	0.3143	100.0%	1.30 [0.70, 2.40]		🔴
Total (95% CI)			100.0%	**1.30 [0.70, 2.40]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)

Risk of bias legend
(A) Overall RoB

Heavy PAE and CBCL Aggression – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2009 (2, 5, 8yrs; CBCL-C)	0.6552	0.4879	100.0%	1.93 [0.74, 5.01]		🟢
Total (95% CI)			100.0%	**1.93 [0.74, 5.01]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.34 (P = 0.18)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used. Sood et al 2001 also reports MD data and frequency data.

CBCL Rule Breaking Behaviour (T-score)

Any PAE and CBCL Rule-Breaking Behaviour (T-score) (1 study)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; CBCL-C)	52.9	4.9	2518	52.5	4.6	7201	100.0%	0.09 [0.04, 0.13]		🔴
Total (95% CI)			2518			7201	100.0%	**0.09 [0.04, 0.13]**		

Heterogeneity: Not applicable
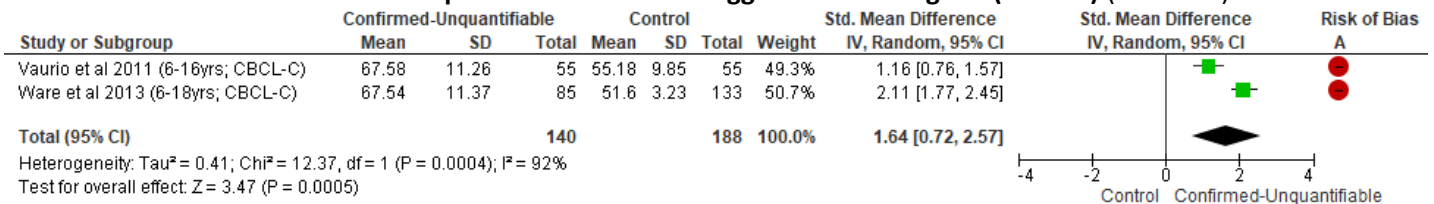Test for overall effect: Z = 3.69 (P = 0.0002)

Risk of bias legend
(A) Overall RoB

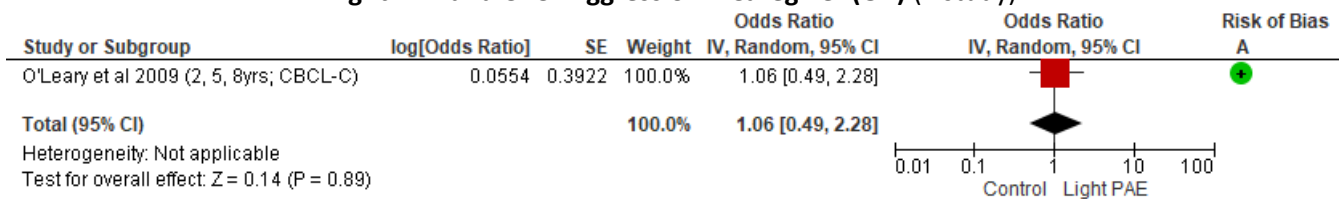Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

Confirmed PAE-Level Unquantifiable and CBCL Rule-Breaking Behaviour (T-score) (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Vaurio et al 2011 (6-16yrs; CBCL-C)	64.74	9.58	55	54.93	7.72	55	42.0%	1.12 [0.72, 1.52]		🔴
Ware et al 2013 (6-18yrs; CBCL-C)	58.06	7.12	52	52.06	3.98	133	58.0%	1.18 [0.84, 1.52]		🔴
Total (95% CI)			107			188	100.0%	**1.16 [0.89, 1.42]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = 0.82); I² = 0%
Test for overall effect: Z = 8.68 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

CBCL Rule Breaking Behaviour (Frequency/OR)

Light PAE and CBCL Rule-Breaking Behaviour (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2009 (2, 5, 8yrs; CBCL-C)	0.4697	0.3664	100.0%	1.60 [0.78, 3.28]		🟢
Total (95% CI)			100.0%	**1.60 [0.78, 3.28]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.28 (P = 0.20)

Risk of bias legend
(A) Overall RoB

Moderate PAE and CBCL Rule-Breaking Behaviour (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sood et al 2001 (6-7yrs; CBCL-C)	1.1632	0.4413	100.0%	3.20 [1.35, 7.60]		⊖
Total (95% CI)			100.0%	3.20 [1.35, 7.60]		
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.64 (P = 0.008)						

0.01 0.1 1 10 100
Control   Moderate PAE

Risk of bias legend
(A) Overall RoB

Heavy PAE and CBCL Rule-Breaking Behaviour (OR) (1 study)

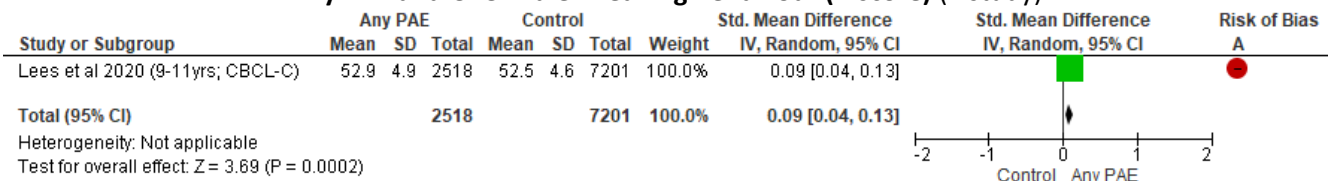| Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2009 (2, 5, 8yrs; CBCL-C)	-1.2755	0.9915	100.0%	0.28 [0.04, 1.95]		⊕
Total (95% CI)			100.0%	0.28 [0.04, 1.95]		
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.29 (P = 0.20)						

0.01 0.1 1 10 100
Control   Heavy PAE

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used. Sood et al 2001 also reports MD data and frequency data.

CBCL Hyperactivity Caregiver Report (T-score)
Very Heavy PAE and CBCL Hyperactivity – Caregiver (T-score) (1 study)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Brown et al 1991 (4-6yrs; CBCL-C)	63.89	7.16	18	61.71	9.26	21	100.0%	0.26 [-0.38, 0.89]		⊖
Total (95% CI)			18			21	100.0%	0.26 [-0.38, 0.89]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.79 (P = 0.43)										

-4 -2 0 2 4
Control   Very Heavy PAE

Risk of bias legend
(A) Overall RoB

SDQ Hyperactivity Caregiver Report (Mean Difference)
Light PAE and SDQ Hyperactivity – Caregiver (aMD) (1 study)

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias A
Sayal et al 2013 (11yrs; SDQ-C)	0.11	0.0867	100.0%	0.11 [-0.06, 0.28]		⊕
Total (95% CI)			100.0%	0.11 [-0.06, 0.28]		
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.27 (P = 0.20)						

-0.5 -0.25 0 0.25 0.5
Control   Light PAE

Risk of bias legend
(A) Overall RoB

SDQ Hyperactivity Caregiver Report (Frequency/OR)
Light PAE and SDQ Hyperactivity – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sayal et al 2007 (6-7yrs; SDQ-C)	0.2268	0.1209	100.0%	1.25 [0.99, 1.59]		⊕
Total (95% CI)			100.0%	1.25 [0.99, 1.59]		
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.88 (P = 0.06)						

0.1 0.2 0.5 1 2 5 10
Control   Light PAE

Risk of bias legend
(A) Overall RoB

Note: Sayal et al 2007 also reports data from 3 and 6yrs.

Moderate PAE and SDQ Hyperactivity – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Mitchell et al 2020 (5-15yrs; SDQ)	0.0488	0.1261	100.0%	1.05 [0.82, 1.34]		?
Total (95% CI)			100.0%	1.05 [0.82, 1.34]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.39 (P = 0.70)

Risk of bias legend
(A) Overall RoB

Heavy PAE and SDQ Hyperactivity – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Mitchell et al 2020 (5-15yrs; SDQ)	-0.1054	0.1954	100.0%	0.90 [0.61, 1.32]		?
Total (95% CI)			100.0%	0.90 [0.61, 1.32]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)

Risk of bias legend
(A) Overall RoB

SDQ Hyperactivity Self Report (Frequency/OR)

Confirmed PAE-Level Unquantifiable and SDQ Hyperactivity – Self Report (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Pfinder et al 2020 (11-17yrs; SDQ)	0.3322	0.0982	100.0%	1.39 [1.15, 1.69]		?
Total (95% CI)			100.0%	1.39 [1.15, 1.69]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.38 (P = 0.0007)

Risk of bias legend
(A) Overall RoB

SDQ Hyperactivity Teacher Report (Frequency/OR)

Light PAE and SDQ Hyperactivity – Teacher (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sayal et al 2007 (7-9yrs; SDQ-T)	-0.0726	0.1673	100.0%	0.93 [0.67, 1.29]		+
Total (95% CI)			100.0%	0.93 [0.67, 1.29]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.43 (P = 0.66)

Risk of bias legend
(A) Overall RoB

Note: Sayal et al 2007 also reports data from 3 and 6yrs.

CBCL Anxious/Depressed Caregiver Report (T-score)

Any PAE and CBCL Anxious/Depressed – Caregiver (T-score) (1 study)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; CBCL-C)	53.8	6	2518	53.3	5.9	7201	100.0%	0.08 [0.04, 0.13]		●
Total (95% CI)			2518			7201	100.0%	0.08 [0.04, 0.13]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.64 (P = 0.0003)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

Confirmed PAE-Level Unquantifiable and CBCL Anxious/Depressed – Caregiver (T-score) (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Vaurio et al 2011 (6-16yrs; CBCL-C)	55.86	7.11	52	52.17	4.28	133	58.2%	0.70 [0.37, 1.03]		🔴
Ware et al 2013 (8-16yrs; CBCL-C)	63.08	10.33	55	55.8	8.45	55	41.8%	0.77 [0.38, 1.15]		🔴
Total (95% CI)			107			188	100.0%	0.73 [0.48, 0.98]		

Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.81); I² = 0%
Test for overall effect: Z = 5.70 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

CBCL Anxious/Depressed Caregiver Report (Frequency/OR)
Moderate PAE (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sood et al 2001 (6-7yrs; CBCL-C)	0.8858	0.6339	100.0%	2.42 [0.70, 8.40]		🔴
Total (95% CI)			100.0%	2.42 [0.70, 8.40]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.40 (P = 0.16)

Risk of bias legend
(A) Overall RoB

Note: Sood et al 2001 also reports MD data and frequency data.

SDQ Anxious/Depressed Self Report (aOR)
Confirmed PAE-Level Unquantifiable and SDQ Anxious/Depressed – Self-report (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Pfinder et al 2020 (11-17yrs; SDQ)	0.1484	0.1128	100.0%	1.16 [0.93, 1.45]		🟡
Total (95% CI)			100.0%	1.16 [0.93, 1.45]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.32 (P = 0.19)

Risk of bias legend
(A) Overall RoB

Note: Pfinder et al 2020 reports SDQ emotional problems.

CBCL Anxious/Depressed Self-Report (T-score)
Light PAE and CBCL Anxious/Depressed Self-Report (T-score) (1 study)

Study or Subgroup	Light PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Alati et al 2009 (14yrs; YSR)	7.2	4.6	2536	6.9	4.4	2530	100.0%	0.07 [0.01, 0.12]		🔴
Total (95% CI)			2536			2530	100.0%	0.07 [0.01, 0.12]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.37 (P = 0.02)

Risk of bias legend
(A) Overall RoB

Moderate PAE and CBCL Anxious/Depressed Self-Report (T-score) (1 study)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Alati et al 2009 (14yrs; YSR)	6.7	4.6	66	6.9	4.4	2530	100.0%	-0.05 [-0.29, 0.20]		🔴
Total (95% CI)			66			2530	100.0%	-0.05 [-0.29, 0.20]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.36 (P = 0.72)

Risk of bias legend
(A) Overall RoB

CBCL Anxiety Caregiver Report (T-score)

Very Heavy PAE and CBCL Anxiety – Caregiver (T-score) (1 study)

Study or Subgroup	Very Heavy PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Brown et al 1991 (8-16yrs; CBCL-C)	57.78	4.71	20	56.74	5.28	19	100.0%	0.20 [-0.43, 0.83]		⊖
Total (95% CI)			20			19	100.0%	0.20 [-0.43, 0.83]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)

Risk of bias legend
(A) Overall RoB

CBCL Anxiety Caregiver Report (Frequency/OR)

Light PAE and CBCL Anxiety – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2 5, 8yrs; CBCL-C)	0.8081	0.3366	100.0%	2.24 [1.16, 4.34]		⊕
Total (95% CI)			100.0%	2.24 [1.16, 4.34]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.40 (P = 0.02)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used.

Heavy PAE and CBCL Anxiety – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2 5, 8yrs; CBCL-C)	1.0366	0.4944	100.0%	2.82 [1.07, 7.43]		⊕
Total (95% CI)			100.0%	2.82 [1.07, 7.43]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.10 (P = 0.04)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used.

CBCL Withdrawn/Depressed Caregiver Report (T-score)

Any PAE and CBCL Withdrawn/Depressed – Caregiver (T-score) (1 study)

Study or Subgroup	Any PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Lees et al 2020 (9-11yrs; CBCL-C)	53.7	5.9	2518	53.3	5.6	7201	100.0%	0.07 [0.03, 0.12]		⊖
Total (95% CI)			2518			7201	100.0%	0.07 [0.03, 0.12]		

Heterogeneity: Not applicable
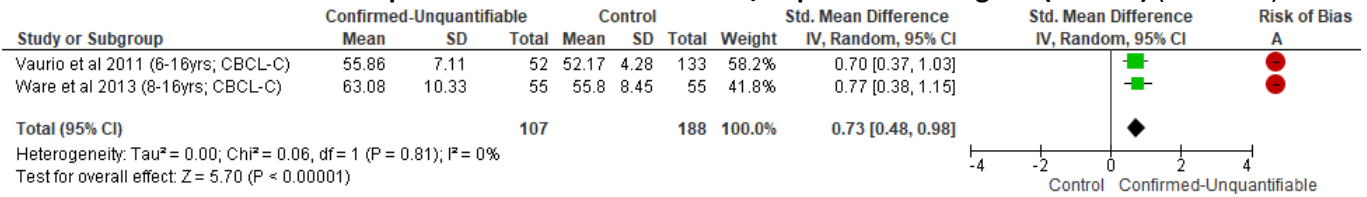Test for overall effect: Z = 3.04 (P = 0.002)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

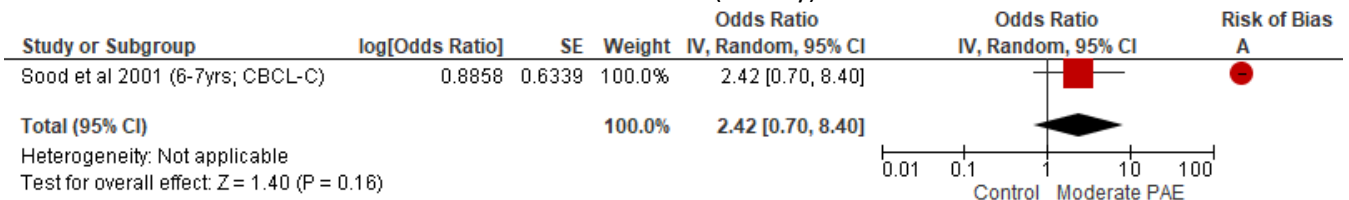### Confirmed PAE-Level Unquantifiable and CBCL Withdrawn/Depressed – Caregiver (T-score) (2 studies)

Study or Subgroup	Confirmed-Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Vaurio et al 2011 (6-16yrs; CBCL-C)	61.84	10.75	55	55.16	8.95	55	43.0%	0.67 [0.29, 1.06]		⊖
Ware et al 2013 (8-16yrs; CBCL-C)	57.02	7.52	52	52.36	3.86	133	57.0%	0.90 [0.57, 1.24]		⊖
Total (95% CI)			107			188	100.0%	0.80 [0.55, 1.05]		

Heterogeneity: Tau² = 0.00; Chi² = 0.79, df = 1 (P = 0.37); I² = 0%
Test for overall effect: Z = 6.24 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

CBCL Withdrawn/Depressed Caregiver Report (Frequency/OR)

Light PAE and Withdrawn/Depressed – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2 5, 8yrs; CBCL-C)	-0.5848	0.3697	100.0%	0.56 [0.27, 1.15]		+
Total (95% CI)			100.0%	**0.56 [0.27, 1.15]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.58 (P = 0.11)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used.

Moderate PAE and Withdrawn/Depressed – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sood et al 2001 (6-7yrs; CBCL-C)	0.2653	0.489	100.0%	1.30 [0.50, 3.40]		−
Total (95% CI)			100.0%	**1.30 [0.50, 3.40]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.54 (P = 0.59)

Risk of bias legend
(A) Overall RoB

Note: Sood et al 2001 also reports MD data and frequency data.

Heavy PAE and Withdrawn/Depressed – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2 5, 8yrs; CBCL-C)	0.23	0.4918	100.0%	1.26 [0.48, 3.30]		+
Total (95% CI)			100.0%	**1.26 [0.48, 3.30]**		

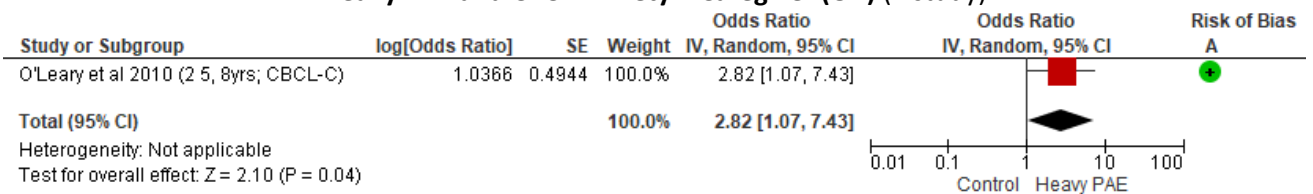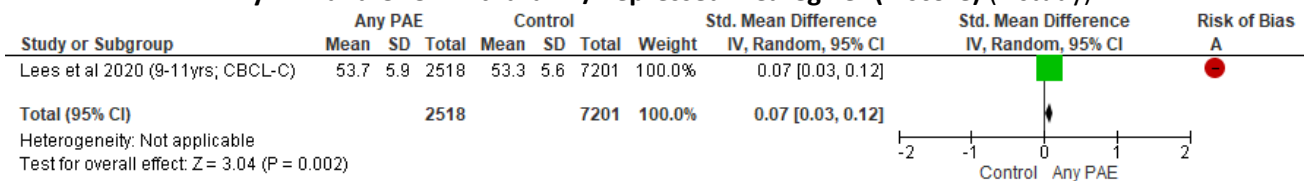Heterogeneity: Not applicable
Test for overall effect: Z = 0.47 (P = 0.64)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used.

CBCL Somatic Complaints Caregiver Report (T-Score)

Any PAE and CBCL Somatic Complaints (T-score) (1 study)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; CBCL-C)	55.4	6.2	2518	54.7	6	7201	100.0%	0.12 [0.07, 0.16]		−
Total (95% CI)			2518			7201	100.0%	**0.12 [0.07, 0.16]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.99 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

Confirmed PAE-Level Unquantifiable and CBCL Somatic Complaints (T-score) (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Vaurio et al 2011 (6-16yrs; CBCL-C)	60.7	9.57	55	57.4	9.57	55	48.8%	0.34 [-0.03, 0.72]		−
Ware et al 2013 (8-16yrs; CBCL-C)	59.51	9.1	52	53.45	5.36	133	51.2%	0.91 [0.58, 1.25]		−
Total (95% CI)			107			188	100.0%	**0.63 [0.08, 1.19]**		

Heterogeneity: Tau² = 0.13; Chi² = 4.92, df = 1 (P = 0.03); I² = 80%
Test for overall effect: Z = 2.23 (P = 0.03)

Risk of bias legend
(A) Overall RoB

CBCL Somatic Complaints Caregiver Report (Frequency/OR)

Light PAE and CBCL Somatic Complaints – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2 5, 8yrs; CBCL-C)	0.0685	0.2871	100.0%	1.07 [0.61, 1.88]		+
Total (95% CI)			100.0%	1.07 [0.61, 1.88]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.24 (P = 0.81)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used.

Moderate PAE and CBCL Somatic Complaints – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Sood et al 2001 (6-7yrs; CBCL-C)	0.3415	0.4349	100.0%	1.41 [0.60, 3.30]		−
Total (95% CI)			100.0%	1.41 [0.60, 3.30]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)

Risk of bias legend
(A) Overall RoB

Heavy PAE and CBCL Somatic Complaints – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2 5, 8yrs; CBCL-C)	1.0092	0.3183	100.0%	2.74 [1.47, 5.12]		+
Total (95% CI)			100.0%	2.74 [1.47, 5.12]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.17 (P = 0.002)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used. Sood et al 2001 also reports MD data and frequency data.

CBCL Thought Complaints Caregiver Report (T-score)

Any PAE and CBCL Thought Complaints – Caregiver (T-score) (1 study)

Study or Subgroup	Any PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lees et al 2020 (9-11yrs; CBCL-C)	54.3	6.1	2518	53.5	5.7	7201	100.0%	0.14 [0.09, 0.18]		−
Total (95% CI)			2518			7201	100.0%	0.14 [0.09, 0.18]		

Heterogeneity: Not applicable
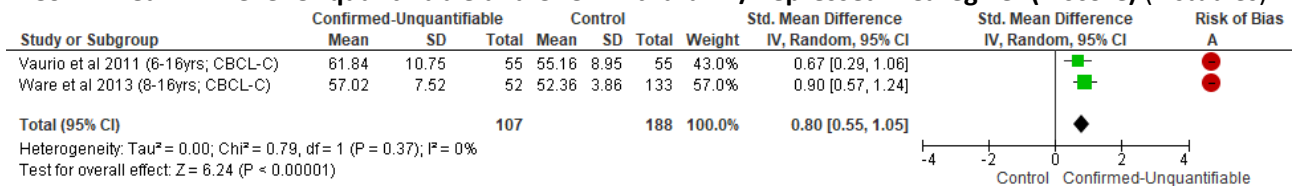Test for overall effect: Z = 5.95 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

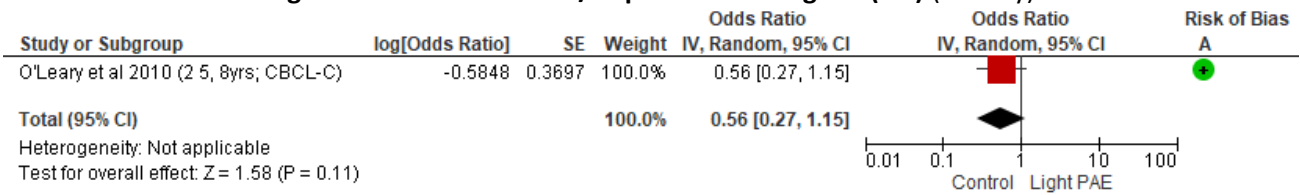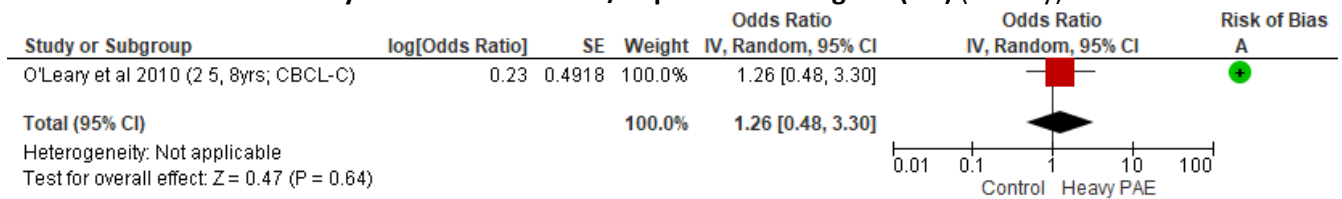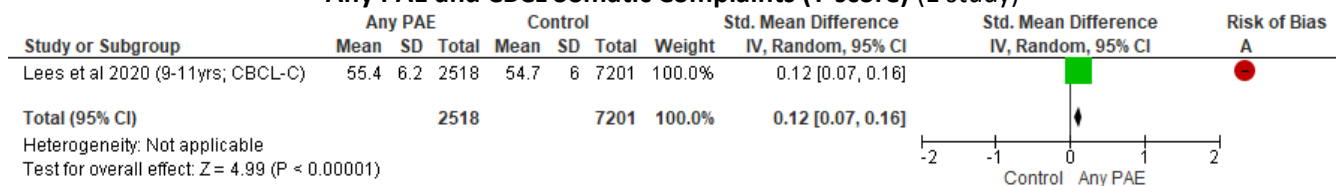### Confirmed PAE-Level Unquantifiable and CBCL Thought Complaints – Caregiver (T-score) (2 studies)

Study or Subgroup	Confirmed-Unquantifiable Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Vaurio et al 2011 (6-16yrs; CBCL-C)	65.14	11.62	55	56.27	8.28	55	42.2%	0.87 [0.48, 1.26]		−
Ware et al 2013 (8-16yrs; CBCL-C)	57.55	8.45	52	52.33	3.76	133	57.8%	0.95 [0.61, 1.28]		−
Total (95% CI)			107			188	100.0%	0.92 [0.66, 1.17]		

Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
Test for overall effect: Z = 7.05 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

CBCL Thought Complaints Caregiver Report (Frequency/OR)
Light PAE and CBCL Thought Complaints – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI	Odds Ratio IV, Fixed, 95% CI	Risk of Bias A
O'Leary et al 2010 (2 5, 8yrs; CBCL-C)	0.1154	0.4024	100.0%	1.12 [0.51, 2.47]		+
Total (95% CI)			**100.0%**	**1.12 [0.51, 2.47]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.29 (P = 0.77)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used.

Heavy PAE and CBCL Thought Complaints – Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2 5, 8yrs; CBCL-C)	-0.1758	0.8782	100.0%	0.84 [0.15, 4.69]		+
Total (95% CI)			**100.0%**	**0.84 [0.15, 4.69]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.20 (P = 0.84)

Risk of bias legend
(A) Overall RoB

Notes: O'Leary et al 2010 reports 1st trimester and 3rd trimester exposure, data from the 1st trimester was used.

BITSEA Maternal Report - Possible Problem (adjusted OR)
Moderate PAE and BITSEA Maternal Report – Possible Problem (1 study)
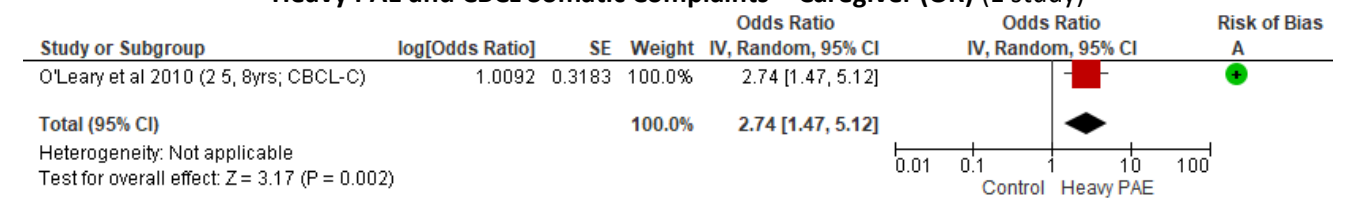
Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Halliday et al 2017 (2yrs; BITSEA)	-0.5222	0.4834	100.0%	0.59 [0.23, 1.53]		+
Total (95% CI)			**100.0%**	**0.59 [0.23, 1.53]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.08 (P = 0.28)

Risk of bias legend
(A) Overal RoB

BITSEA Maternal Report - Possible Competence Deficit (adjusted OR)
Moderate PAE and BITSEA Maternal Report – Possible Competence Deficit (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Halliday et al 2017 (2yrs; BITSEA)	0.1548	0.4642	100.0%	1.17 [0.47, 2.90]		+
Total (95% CI)			**100.0%**	**1.17 [0.47, 2.90]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)

Risk of bias legend
(A) Overal RoB

IBQ Caregiver Report – Negative Effect (mean/SD)
Moderate PAE and IBQ Caregiver Report Negative Effect (1 study)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bakhireva et al 2018 (0.5yrs; IBQ-C)	50.8	11.9	39	43.5	13.9	54	100.0%	0.55 [0.13, 0.97]		?
Total (95% CI)			**39**			**54**	**100.0%**	**0.55 [0.13, 0.97]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.58 (P = 0.010)

Risk of bias legend
(A) Overall RoB

IBQ Caregiver – Effortful Control (mean/SD)

Moderate PAE and IBQ Caregiver Report Effortful Control (1 study)

Study or Subgroup	Moderate PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Bakhireva et al 2018 (0.5yrs; IBQ-C)	65.9	8.6	39	65.1	9.9	54	100.0%	0.08 [-0.33, 0.50]	?
Total (95% CI)			39			54	100.0%	0.08 [-0.33, 0.50]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.40 (P = 0.69)

Control — Moderate PAE

Risk of bias legend
(A) Overal RoB

DIAGNOSED STUDIES

CBCL Total Behaviour Caregiver Report (Frequency/OR)

FASD and CBCL Total Behaviour – Caregiver (Frequency/OR) (1 study)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Fagerlund et al 2011 (8-21yrs; CBCL-C)	17	73	0	40	100.0%	25.09 [1.47, 429.38]	?
Total (95% CI)		73		40	100.0%	25.09 [1.47, 429.38]	
Total events	17		0				

Heterogeneity: Not applicable
Test for overall effect: Z = 2.22 (P = 0.03)

FASD — Control

Risk of bias legend
(A) Overal RoB

CBCL Total Behaviour Caregiver Report (T-score)

FASD and CBCL/PBCL Total Behaviour – Caregiver (T-score) (9 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kern et al 2016 (8-14yrs; CBCL-Total-C)	64.4	9.6	22	45.3	8.9	22	9.5%	2.03 [1.29, 2.77]	?
Kodituwakku et al 2006b (6-8yrs; PBCL-36-Total-C)	9.14	5.72	22	3.92	3.7	60	11.5%	1.20 [0.67, 1.72]	?
Kalberg et al 2013 (6-7yrs; PBCL-36-Total-C)	14.2	8.1	61	6.7	6.4	52	12.7%	1.01 [0.62, 1.40]	⚫
Fagerlund et al 2011 (8-21yrs; CBCL-C)	56.59	8.89	73	42.1	8.76	40	12.3%	1.63 [1.19, 2.07]	?
Mattson & Riley 2000 (4-16yrs; CBCL-Total-C)	67.9	10.61	33	53.3	12.79	33	11.4%	1.23 [0.70, 1.76]	⚫
Quattlebaum and O'Connor 2013 (6-12yrs; PBCL-36-C)	21.33	7.59	97	7.5	6.32	28	11.9%	1.88 [1.39, 2.36]	⚫
Stevens et al 2015 (8-12yrs; CBCL-Total-C)	72.51	6.4	37	46.3	10.4	21	8.9%	3.21 [2.40, 4.02]	⚫
Nayak et al 2012 (4-16yrs; CBCL-C)	22.96	11.16	26	11	8.02	27	10.9%	1.22 [0.63, 1.81]	⚫
Popova et al 2019 (7-9yrs; CBCL-Total-C)	56.2	9.1	19	48.85	9.1	39	11.1%	0.80 [0.23, 1.37]	⚫
Total (95% CI)			390			322	100.0%	1.52 [1.14, 1.91]	

Heterogeneity: Tau² = 0.26; Chi² = 36.11, df = 8 (P < 0.0001); I² = 78%
Test for overall effect: Z = 7.82 (P < 0.00001)

Control — FASD

Risk of bias legend
(A) Overal RoB

Note: Nayak et al 2012 also reports data from 0-4yrs.

FAS and CBCL/PBCL-36 Total Behaviour – Caregiver (T-score) (3 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2006 (6-7yrs; PBCL-36-Total-C)	5.3	3.8	11	3.9	3.7	67	17.7%	0.37 [-0.27, 1.01]	⚫
May et al 2007 (4-8yrs; PBCL-36-Total-C)	12.6	8.82	55	6.5	7.91	133	69.5%	0.74 [0.42, 1.07]	⚫
May et al 2015 (6-7yrs; PBCL-36-Total-C)	7.9	6.57	7	6	5.94	186	12.7%	0.32 [-0.44, 1.07]	⚫
Total (95% CI)			73			386	100.0%	0.62 [0.35, 0.89]	

Heterogeneity: Tau² = 0.00; Chi² = 1.74, df = 2 (P = 0.42); I² = 0%
Test for overall effect: Z = 4.53 (P < 0.00001)

Control — FAS

Risk of bias legend
(A) Overal RoB

pFAS and CBCL/PBCL-36 Total Behaviour – Caregiver (T-score) (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2007 (4-8yrs; PBCL-36-Total-C)	12.2	6.16	18	6.5	7.91	133	49.8%	0.73 [0.23, 1.23]		➖
May et al 2015 (6-7yrs; PBCL-36-Total-C)	15.3	9.55	19	6	5.94	186	50.2%	1.46 [0.97, 1.95]		🔴
Total (95% CI)			37			319	100.0%	1.10 [0.39, 1.81]		

Heterogeneity: Tau² = 0.20; Chi² = 4.12, df = 1 (P = 0.04); I² = 76%
Test for overall effect: Z = 3.02 (P = 0.003)

Risk of bias legend
(A) Overal RoB

TRF/PBCL-36 Total Behaviour Teacher Report (T-score)

FASD and PBCL-36 Total Behaviour – Teacher (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kalberg et al 2013 (6-7yrs; PBCL-36-Total-T)	12.3	7.5	61	6.3	5.9	52	59.5%	0.87 [0.49, 1.26]		🔴
Quattlebaum and O'Connor 2013 (6-12yrs; PBCL-36-T)	11.12	7.2	94	4.98	5.85	23	40.5%	0.88 [0.41, 1.35]		🔴
Total (95% CI)			155			75	100.0%	0.88 [0.58, 1.17]		

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%
Test for overall effect: Z = 5.74 (P < 0.00001)

Risk of bias legend
(A) Overal RoB

FAS and TRF Total Behaviour – Teacher (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2013a (6-7yrs; TRF-Total)	50.2	42.6	66	29.1	29.1	87	41.5%	0.59 [0.26, 0.92]		➖
May et al 2016 (6-7yrs; TRF-Total)	35.9	34.7	69	22.9	24	206	58.5%	0.48 [0.20, 0.75]		➖
Total (95% CI)			135			293	100.0%	0.53 [0.31, 0.74]		

Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 4.89 (P < 0.00001)

Risk of bias legend
(A) Overal RoB

pFAS and TRF Total Behaviour – Teacher (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2013a (6-7yrs; TRF-Total)	45.1	42.2	51	29.1	29.1	87	34.5%	0.46 [0.11, 0.81]		🔴
May et al 2016 (6-7yrs; TRF-Total)	39.6	38.2	88	22.9	24	206	65.5%	0.58 [0.32, 0.83]		🔴
Total (95% CI)			139			293	100.0%	0.54 [0.33, 0.74]		

Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 5.11 (P < 0.00001)

Risk of bias legend
(A) Overal RoB

ARND/Others and TRF Total Behaviour – Teacher (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2013a (6-7yrs; TRF-Total; ARND)	58.3	33.7	35	29.1	29.1	87	42.3%	0.95 [0.54, 1.36]		➖
May et al 2016 (6-7yrs; TRF-Total; ARND)	46.6	37.8	39	22.9	24	206	57.7%	0.89 [0.54, 1.24]		🔴
Total (95% CI)			74			293	100.0%	0.91 [0.65, 1.18]		

Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.81); I² = 0%
Test for overall effect: Z = 6.71 (P < 0.00001)

Risk of bias legend
(A) Overal RoB

SSRS Total Behaviour Caregiver Report (mean/SD)

FASD and SSRS Total Behaviour Caregiver Report (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Greenbaum et al 2009 (6-13yrs; SSRS-Total)	129	29.577	30	89.8	15.884	30	100.0%	1.63 [1.04, 2.22]		🔴
Total (95% CI)			30			30	100.0%	1.63 [1.04, 2.22]		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.42 (P < 0.00001)

Risk of bias legend
(A) Overal RoB

SSRS Total Behaviour Teacher Report (mean/SD)

FASD and SSRS Total Behaviour Teacher Report (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Greenbaum et al 2009 (6-13yrs; SSRS-Total)	122.4	31.5951	30	95.3	16.9098	30	53.2%	1.06 [0.51, 1.60]		🔴
Olswang et al 2010 (9yrs; SSRS-Total)	122.8	7.4	12	92.5	9	12	46.8%	3.55 [2.19, 4.91]		🔴
Total (95% CI)			42			42	100.0%	2.22 [-0.22, 4.66]		

Heterogeneity: Tau² = 2.83; Chi² = 11.17, df = 1 (P = 0.0008); I² = 91%
Test for overall effect: Z = 1.78 (P = 0.07)

Risk of bias legend
(A) Overal RoB

Note: Greenbaum et al 2009 reported mean values adjusted for SES, tobacco exposure, abuse, adoption / foster home history.

ASR Total Behaviour Self-Report (T-score)

pFAS and ASR Total Behaviour – Self-report (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR-Total)	53.14	1.44	47	49.51	1.33	58	100.0%	2.61 [2.08, 3.14]		🔴
Total (95% CI)			47			58	100.0%	2.61 [2.08, 3.14]		

Heterogeneity: Not applicable
Test for overall effect: Z = 9.71 (P < 0.00001)

Risk of bias legend
(A) Overal RoB

ARND/Others and ASR Total Behaviour – Self-report (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR-Total; non-syndromal)	56.95	2	34	49.51	1.33	58	100.0%	4.59 [3.79, 5.39]		🔴
Total (95% CI)			34			58	100.0%	4.59 [3.79, 5.39]		

Heterogeneity: Not applicable
Test for overall effect: Z = 11.25 (P < 0.00001)

Risk of bias legend
(A) Overal RoB

Note: Lynch et al 2017 also reports other minor CBCL subdomains. pFAS was exposed, dysmorphic and ARND/other was exposed, cognitively affected.

CBCL Total Externalising Behaviour Caregiver Report (T-score)

FASD and CBCL Externalising Behaviour – Caregiver (T-score) (9 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kerns et al 2016 (8-14yrs; CBCL-Ext-C)	63.1	9.6	22	45.6	8.3	22	8.5%	1.92 [1.19, 2.64]		🟡
Fagerlund et al 2011 (8-21yrs; CBCL-Ext-C)	53.59	10.7	73	43.75	8.66	40	11.8%	0.97 [0.57, 1.38]		🟡
Greenbaum et al 2009 (6-13yrs; CBCL-Ext-C)	67.6	22.9783	33	47.3	12.245	34	10.7%	1.09 [0.58, 1.61]		🔴
Mattson & Riley 2000 (4-16yrs; CBCL-Ext-C)	66.5	13.97	33	53.6	12.22	33	10.7%	0.97 [0.46, 1.48]		🔴
May et al 2020a (6-7yrs; CBCL-Ext-C)	53.1	14	35	47.4	8.9	195	12.2%	0.58 [0.21, 0.94]		🔴
May et al 2020b (6-7yrs; CBCL-Ext-C)	54.2	10.8	43	48	8.4	232	12.5%	0.70 [0.37, 1.03]		🔴
May et al 2020c (6-7yrs; CBCL-Ext-C)	53.5	10.6	32	49.4	9.5	298	12.2%	0.43 [0.06, 0.79]		🔴
Popova et al 2019 (7-9yrs; CBCL-Ext-C)	51.6	19.73	19	48.85	17.53	39	10.3%	0.15 [-0.40, 0.70]		🔴
Quattlebaum & O'Connor 2013 (6-12yrs; CBCL-Ext-C)	68.66	8.86	28	47.71	12.1	97	11.0%	1.82 [1.34, 2.29]		🔴
Total (95% CI)			318			990	100.0%	0.93 [0.59, 1.26]		

Heterogeneity: Tau² = 0.20; Chi² = 39.71, df = 8 (P < 0.00001); I² = 80%
Test for overall effect: Z = 5.46 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Externalising Behaviour – Caregiver (T-score) (2 studies)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-Ext-C)	51.6	15.3	5	52.7	10.3	771	30.0%	-0.11 [-0.99, 0.77]		🔴
Coles et al 1997 (7-8yrs; CBCL-Ext-C)	59.89	11.32	25	54.77	10.52	35	70.0%	0.47 [-0.06, 0.99]		🔴
Total (95% CI)			30			806	100.0%	0.29 [-0.22, 0.81]		

Heterogeneity: Tau² = 0.03; Chi² = 1.20, df = 1 (P = 0.27); I² = 17%
Test for overall effect: Z = 1.12 (P = 0.26)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Externalising Behaviour – Caregiver (T-score) (2 studies)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; CBCL-Ext-C; FAS/pFAS)	65.2	10.6	20	47.1	10.4	16	46.3%	1.68 [0.91, 2.46]		🔴
Chambers et al 2019 (6-7yrs; CBCL-Ext-C)	56.3	9.9	44	52.7	10.3	771	53.7%	0.35 [0.05, 0.65]		🔴
Total (95% CI)			64			787	100.0%	0.97 [-0.34, 2.27]		

Heterogeneity: Tau² = 0.80; Chi² = 9.84, df = 1 (P = 0.002); I² = 90%
Test for overall effect: Z = 1.45 (P = 0.15)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Externalising Behaviour – Caregiver (T-score) (3 studies)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; CBCL-Ext-C; SE)	64.4	11.8	24	47.1	10.4	16	28.0%	1.50 [0.78, 2.23]		🔴
Chambers et al 2019 (6-7yrs; CBCL-Ext-C; ARND)	64.5	8.8	44	52.7	10.3	771	38.3%	1.15 [0.84, 1.46]		🔴
Coles et al 1997 (7-8yrs; CBCL-Ext-C; NCNS/AE)	57.9	12.79	27	54.77	10.52	35	33.7%	0.27 [-0.24, 0.77]		🔴
Total (95% CI)			95			822	100.0%	0.95 [0.29, 1.62]		

Heterogeneity: Tau² = 0.27; Chi² = 10.90, df = 2 (P = 0.004); I² = 82%
Test for overall effect: Z = 2.81 (P = 0.005)

Risk of bias legend
(A) Overall RoB

Note: Astley et al 2009 also reports CBCL total competency sum. Greenbaum et al 2009 reported mean values adjusted for SES, tobacco exposure, abuse, adoption ⁄ foster home history.
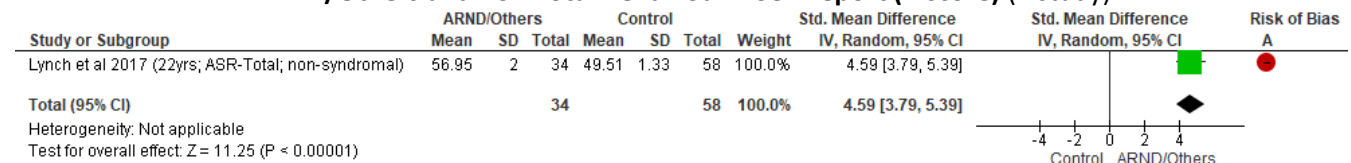
CBCL/SIB-R Total Externalising Behaviour Caregiver Report (Frequency/OR)

FASD and CBCL/SIB-R Externalising Behaviour – Caregiver (OR) (2 studies)

Study or Subgroup	FASD Events	FASD Total	Control Events	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Fagerlund et al 2011 (8-21yrs; CBCL-Ext-C)	10	73	0	40	36.4%	13.39 [0.76, 234.88]		🟡
Jirikowic et al 2008b (5-8yrs; SIB-R-Ext-C)	10	23	1	23	63.6%	16.92 [1.94, 147.77]		🔴
Total (95% CI)		96		63	100.0%	15.54 [2.76, 87.50]		
Total events	20		1					

Heterogeneity: Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0%
Test for overall effect: Z = 3.11 (P = 0.002)

Risk of bias legend
(A) Overall RoB

Note: Jirikowic et al 2008b also reports other minor CBCL subdomains.

SSRS Total Externalising Behaviour Caregiver Report (m/sd)

FASD and SSRS Externalising Behaviour – Caregiver (mean/SD) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Rasmussen et al 2011a (3-8yrs; SSRS-Ext-C)	8.57	2.63	23	8.61	2.61	37	100.0%	-0.02 [-0.54, 0.51]		🔴
Total (95% CI)			23			37	100.0%	-0.02 [-0.54, 0.51]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.06 (P = 0.95)

Risk of bias legend
(A) Overall RoB

TRF Total Externalising Behaviour Teacher Report (T-score)

FASD and CBCL/TRF Externalising Behaviour – Teacher (T-score) (5 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Greenbaum et al 2009 (6-13yrs; TRF-Ext-T)	69.8	20.106	33	48.3	10.4957	34	14.7%	1.33 [0.80, 1.86]		🔴
May et al 2020a (6-7yrs; CBCL-Ext-T)	56	11.9	38	50.2	8.8	269	22.8%	0.63 [0.28, 0.97]		🔴
May et al 2020b (6-7yrs; CBCL-Ext-T)	53.8	11	47	48.9	8.4	370	24.8%	0.56 [0.25, 0.87]		🔴
May et al 2020c (6-7yrs; TRF-Ext-T)	53.5	9.6	42	48.5	7.8	444	24.1%	0.63 [0.31, 0.95]		🔴
Quattlebaum & O'Connor 2013 (6-12yrs; CBCL-Ext-T)	61.47	9.92	94	50.2	8.31	15	13.6%	1.15 [0.58, 1.72]		🔴
Total (95% CI)			**254**			**1132**	**100.0%**	**0.78 [0.52, 1.05]**		

Heterogeneity: Tau² = 0.05; Chi² = 8.94, df = 4 (P = 0.06); I² = 55%
Test for overall effect: Z = 5.88 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and TRF Externalising Behaviour – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-Ext-T)	54.8	9	5	49	9	771	100.0%	0.64 [-0.24, 1.52]		🔴
Total (95% CI)			**5**			**771**	**100.0%**	**0.64 [-0.24, 1.52]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.43 (P = 0.15)

Risk of bias legend
(A) Overall RoB

pFAS and TRF Externalising Behaviour – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-Ext-T)	48.4	9.6	44	49	9	771	100.0%	-0.07 [-0.37, 0.24]		🔴
Total (95% CI)			**44**			**771**	**100.0%**	**-0.07 [-0.37, 0.24]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.43 (P = 0.67)

Risk of bias legend
(A) Overall RoB

ARND/Others and TRF Externalising Behaviour – Teacher (T-score) (1 study)

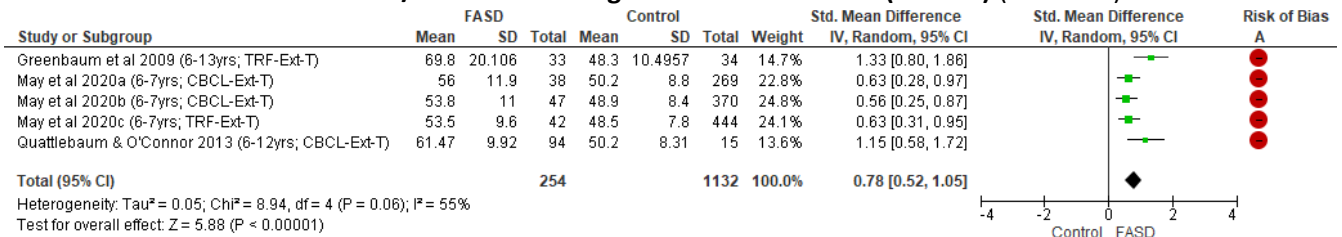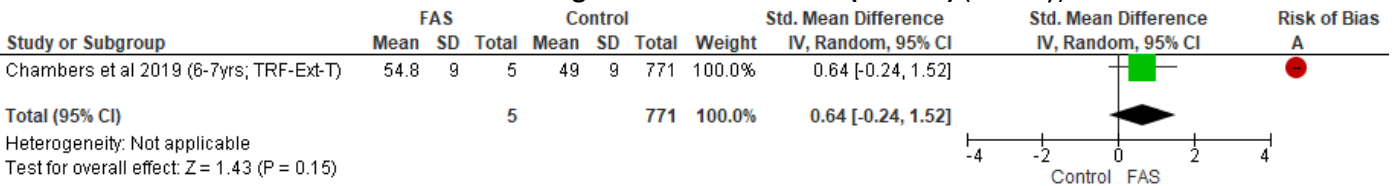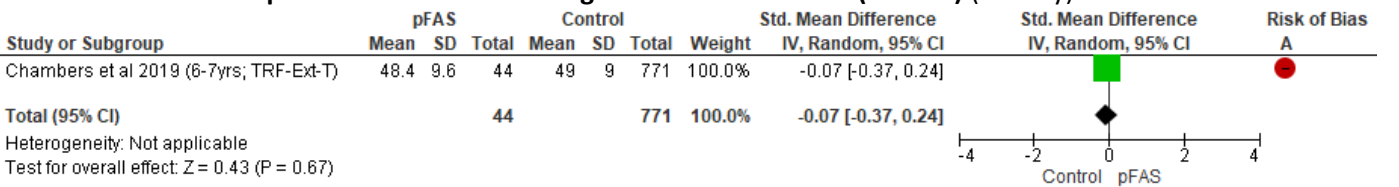| Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-Ext-T; ARND)	56.4	9.7	44	49	9	771	100.0%	0.82 [0.51, 1.12]		🔴
Total (95% CI)			**44**			**771**	**100.0%**	**0.82 [0.51, 1.12]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.23 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Greenbaum et al 2009 reported mean values adjusted for SES, tobacco exposure, abuse, adoption / foster home history.

SSRS Total Externalising Behaviour Teacher Report (m/sd)

FASD and SSRS Externalising Behaviour – Teacher (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Rasmussen et al 2011a (3-8yrs; SSRS-Ext-T)	4.06	3.39	23	5	4.05	37	100.0%	-0.24 [-0.77, 0.28]		🔴
Total (95% CI)			**23**			**37**	**100.0%**	**-0.24 [-0.77, 0.28]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.91 (P = 0.36)

Risk of bias legend
(A) Overall RoB

ASR Total Externalising Behaviour Self Report (T-score)

pFAS and ASR Externalising Behaviour – Self-report (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR-Ext)	54.66	1.41	47	51.94	1.3	58	100.0%	2.00 [1.53, 2.47]		🔴
Total (95% CI)			**47**			**58**	**100.0%**	**2.00 [1.53, 2.47]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 8.28 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and ASR Externalising Behaviour – Self-report (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR-Ext; Cogn Affected)	58.42	1.96	34	51.94	1.3	58	100.0%	4.08 [3.34, 4.82]		🔴
Total (95% CI)			34			58	100.0%	4.08 [3.34, 4.82]		

Heterogeneity: Not applicable
Test for overall effect: Z = 10.86 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lynch et al 2017 also reports other minor CBCL subdomains.

CBCL Total Internalising Behaviour Caregiver Report (T-score)
FASD and CBCL Internalising Behaviour – Caregiver (T-score) (10 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Kerns et al 2016 (8-14yrs; CBCL-Int-C)	56.6	14.2	22	47.1	9.6	22	7.4%	0.77 [0.16, 1.38]		🟡
Fagerlund et al 2011 (8-21yrs; CBCL-Int-C)	53.92	10.22	73	44.8	8.08	40	10.6%	0.95 [0.55, 1.36]		🟡
Greenbaum et al 2009 (6-13yrs; CBCL-Int-C)	50.6	22.4038	33	53.4	11.6619	34	9.4%	-0.16 [-0.64, 0.32]		🔴
Krueger et al 2020 (8-16yrs; CBCL-Int-C)	63.08	11.78	39	50.29	11.1	34	9.1%	1.10 [0.61, 1.60]		🔴
Mattson & Riley 2000 (4-16yrs; CBCL-Int-C)	58.9	12.56	33	51.1	12.74	33	9.1%	0.61 [0.12, 1.10]		🔴
May et al 2020a (6-7yrs; CBCL-Int-C)	53.1	13.3	38	47.5	9.3	273	11.8%	0.57 [0.22, 0.91]		🔴
May et al 2020b (6-7yrs; CBCL-Int-C)	53.7	11	49	48.5	9.7	444	12.6%	0.53 [0.23, 0.82]		🔴
May et al 2020c (6-7yrs; CBCL-Int-C)	54.3	10.6	37	48.1	8.9	331	11.8%	0.68 [0.34, 1.02]		🔴
Popova et al 2019 (7-9yrs; CBCL-Int-C)	53.97	19.27	19	51.23	18.36	39	8.3%	0.14 [-0.40, 0.69]		🔴
Quattlebaum & O'Connor 2013 (6-12yrs; CBCL-Int-C)	63.58	10.11	97	50.61	14.48	28	9.9%	1.15 [0.70, 1.59]		🔴
Total (95% CI)			440			1278	100.0%	0.64 [0.41, 0.87]		

Heterogeneity: Tau² = 0.08; Chi² = 25.32, df = 9 (P = 0.003); I² = 64%
Test for overall effect: Z = 5.52 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Krueger et al 2020 also reports other minor CBCL subdomains. Greenbaum et al 2009 reported mean values adjusted for SES, tobacco exposure, abuse, adoption / foster home history.
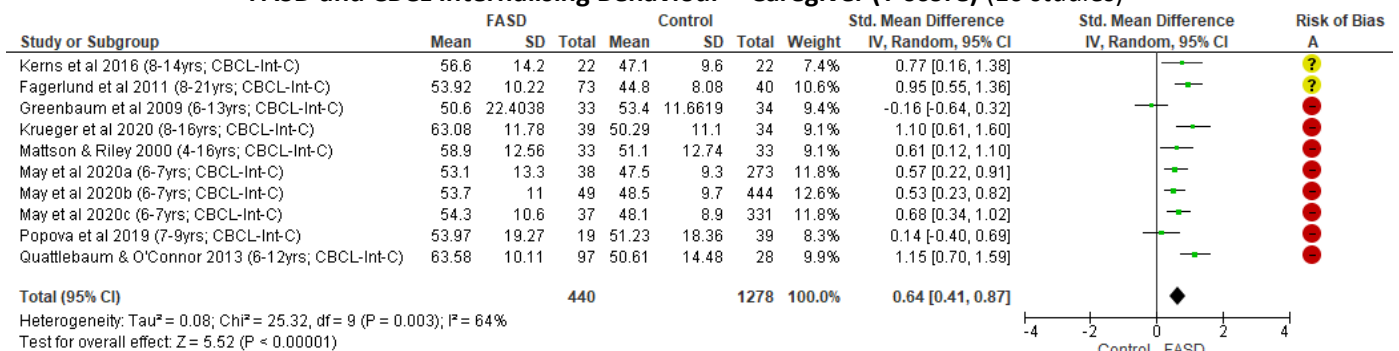
Funnel Plot: FASD diagnosis and CBCL Internalising Behaviour.

FAS and CBCL Internalising Behaviour – Caregiver (T-score) (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-Int-C)	50	14.3	5	53.1	9.6	771	25.4%	-0.32 [-1.20, 0.56]		🔴
Coles et al 1997 (7-8yrs; CBCL-Int-C)	52.79	6.15	25	53.63	10.99	35	74.6%	-0.09 [-0.60, 0.42]		🔴
Total (95% CI)			30			806	100.0%	-0.15 [-0.59, 0.30]		

Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 0.66 (P = 0.51)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Internalising Behaviour – Caregiver (T-score) (2 studies)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; CBCL-Int-C; FAS/pFAS)	63.9	9.9	20	44.6	7.6	16	47.4%	2.11 [1.27, 2.94]	−
Chambers et al 2019 (6-7yrs; CBCL-Int-C)	56.5	8.3	44	53.1	9.6	771	52.6%	0.36 [0.05, 0.66]	−
Total (95% CI)			64			787	100.0%	1.19 [-0.53, 2.90]	

Heterogeneity: Tau² = 1.43; Chi² = 14.89, df = 1 (P = 0.0001); I² = 93%
Test for overall effect: Z = 1.36 (P = 0.17)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Internalising Behaviour – Caregiver (T-score) (3 studies)

Study or Subgroup	ARND/Other Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; CBCL-Int-C; SE/AE)	60.6	10.1	24	44.6	7.6	16	28.6%	1.71 [0.96, 2.45]	−
Chambers et al 2019 (6-7yrs; CBCL-Int-C; ARND)	58.2	10.6	44	53.1	9.6	771	37.5%	0.53 [0.22, 0.83]	−
Coles et al 1997 (7-8yrs; CBCL-Int-C; NCNS)	53.73	8.49	27	53.63	10.99	35	33.9%	0.01 [-0.49, 0.51]	−
Total (95% CI)			95			822	100.0%	0.69 [-0.06, 1.44]	

Heterogeneity: Tau² = 0.36; Chi² = 13.69, df = 2 (P = 0.001); I² = 85%
Test for overall effect: Z = 1.81 (P = 0.07)

Risk of bias legend
(A) Overall RoB

CBCL/SIB-R Total Internalising Behaviour Caregiver Report (Frequency/OR)

FASD and CBCL/SIB-R Internalising Behaviour – Caregiver (OR) (2 studies)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Fagerlund et al 2011 (8-21yrs; CBCL-Int-C)	13	73	1	40	66.4%	8.45 [1.06, 67.20]	?
Jirikowic et al 2008b (5-8yrs; SIB-R-Int-C)	12	23	0	23	33.6%	51.09 [2.77, 940.96]	−
Total (95% CI)		96		63	100.0%	15.47 [2.86, 83.81]	
Total events	25		1				

Heterogeneity: Tau² = 0.00; Chi² = 0.97, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 3.18 (P = 0.001)
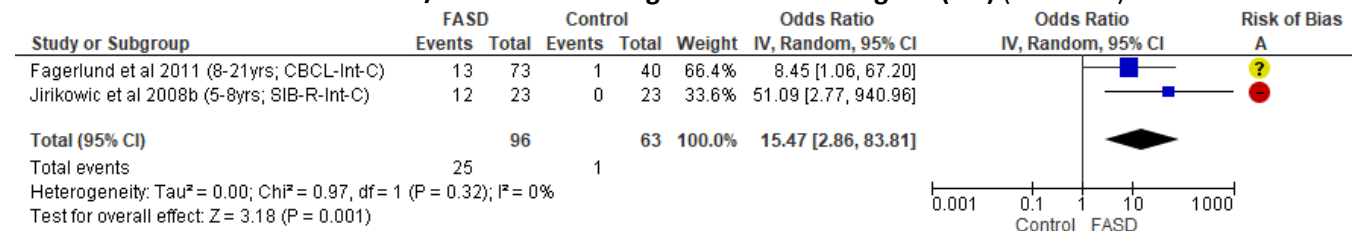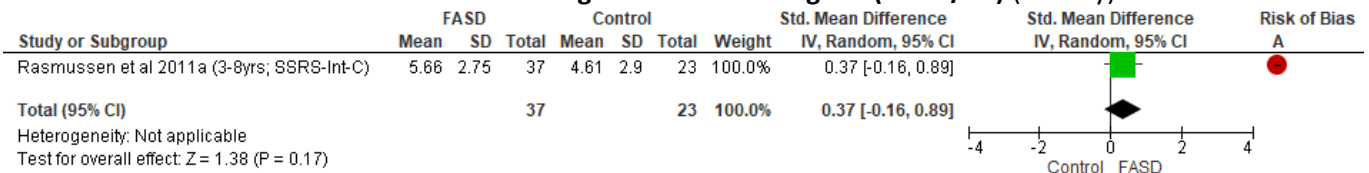
Risk of bias legend
(A) Overall RoB

Note: Jirikowic et al 2008b also reports other minor CBCL subdomains.

SSRS Total Internalising Behaviour Caregiver Report (m/SD)

FASD and SSRS Internalising Behaviour – Caregiver (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Rasmussen et al 2011a (3-8yrs; SSRS-Int-C)	5.66	2.75	37	4.61	2.9	23	100.0%	0.37 [-0.16, 0.89]	−
Total (95% CI)			37			23	100.0%	0.37 [-0.16, 0.89]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.38 (P = 0.17)

Risk of bias legend
(A) Overall RoB

TRF/CBCL Total Internalising Behaviour Teacher Report (T-score)

FASD and TRF/CBCL Internalising Behaviour – Teacher (T-score) (5 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Greenbaum et al 2009 (6-13yrs; CBCL-Int-T)	57.7	22.9783	33	50	12.245	34	12.0%	0.42 [-0.07, 0.90]	−
May et al 2020a (6-7yrs; TRF-Int-T)	54.1	10.3	38	46.7	9.2	273	23.6%	0.79 [0.45, 1.14]	−
May et al 2020b (6-7yrs; TRF-Int-T)	49.7	11.4	49	44.5	8.7	444	31.7%	0.58 [0.28, 0.87]	−
May et al 2020c (6-7yrs; TRF-Int-C)	52.1	10.8	37	45	7.9	331	23.5%	0.86 [0.52, 1.21]	−
Quattlebaum & O'Connor 2013 (6-12yrs; TRF-Int-T)	56.65	9.78	94	50.4	11.73	15	9.2%	0.62 [0.07, 1.17]	−
Total (95% CI)			251			1097	100.0%	0.68 [0.51, 0.85]	

Heterogeneity: Tau² = 0.00; Chi² = 3.11, df = 4 (P = 0.54); I² = 0%
Test for overall effect: Z = 7.94 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Internalising Behaviour – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-Int-T)	49.4	11.4	5	46.5	9.7	771	100.0%	0.30 [-0.58, 1.18]		🔴
Total (95% CI)			5			771	100.0%	**0.30 [-0.58, 1.18]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Internalising Behaviour – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-Int-T)	47.4	11	44	46.5	9.7	771	100.0%	0.09 [-0.21, 0.40]		🔴
Total (95% CI)			44			771	100.0%	**0.09 [-0.21, 0.40]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.55)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Internalising Behaviour – Teacher (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-Int-T; ARND)	51.2	10.6	44	46.5	9.7	771	100.0%	0.48 [0.18, 0.79]		🔴
Total (95% CI)			44			771	100.0%	**0.48 [0.18, 0.79]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.10 (P = 0.002)

Risk of bias legend
(A) Overall RoB

Note: Greenbaum et al 2009 reported mean values adjusted for SES, tobacco exposure, abuse, adoption / foster home history.

SSRS Total Internalising Behaviour Teacher Report (m/SD)

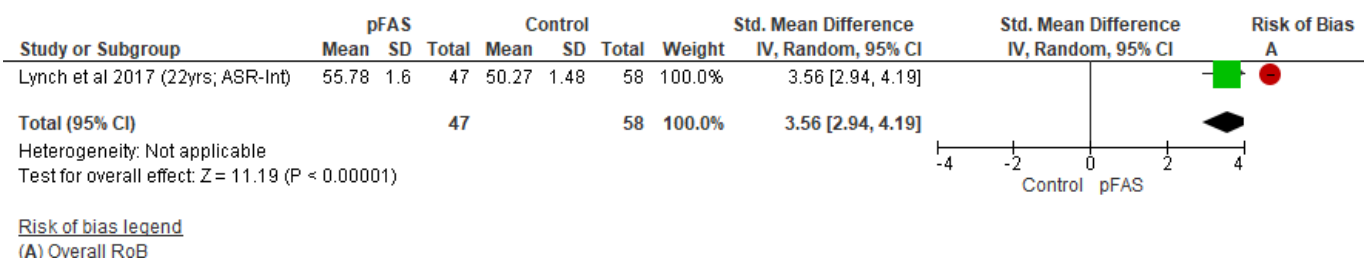## FASD and SSRS Internalising Behaviour – Teacher (mean/SD) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Rasmussen et al 2011a (3-8yrs; SSRS-Int-T)	3.13	2.89	37	2.5	2.67	23	100.0%	0.22 [-0.30, 0.74]		🔴
Total (95% CI)			37			23	100.0%	**0.22 [-0.30, 0.74]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.83 (P = 0.41)

Risk of bias legend
(A) Overall RoB

pFAS and ASR Internalising Behaviour – Self-report (T-score) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR-Int)	55.78	1.6	47	50.27	1.48	58	100.0%	3.56 [2.94, 4.19]		🔴
Total (95% CI)			47			58	100.0%	**3.56 [2.94, 4.19]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 11.19 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and ASR Internalising Behaviour – Self-report (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR-Int; Cog Affected)	57.34	2.23	34	50.27	1.48	58	100.0%	3.91 [3.20, 4.63]		🔴
Total (95% CI)			34			58	100.0%	**3.91 [3.20, 4.63]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 10.71 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lynch et al 2017 also reports other minor CBCL subdomains.

CBCL Conduct Problems Caregiver Report (T-score)

FASD and CBCL Conduct Problems – Caregiver (T-score) (4 studies)
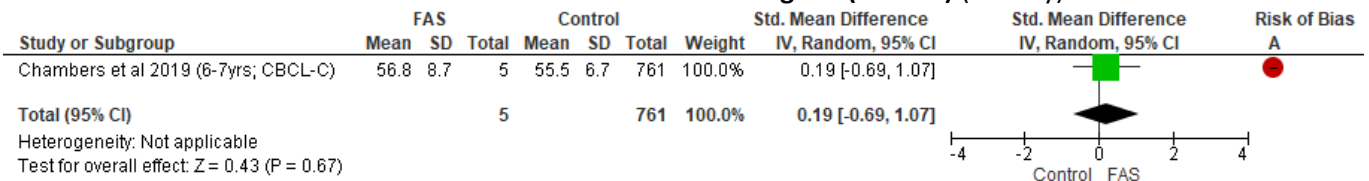
Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; CBCL-C)	57.1	8.8	38	52.9	5.2	273	26.7%	0.73 [0.38, 1.07]		🔴
May et al 2020b (6-7yrs; CBCL-C)	55.5	7.2	49	53.3	5.2	444	36.0%	0.40 [0.11, 0.70]		🔴
May et al 2020c (6-7yrs; CBCL-C)	56.9	7.1	37	53.8	5.7	331	27.0%	0.53 [0.19, 0.87]		🔴
Popova et al 2019 (7-9yrs; CBCL-C)	56.6	16.26	19	52.24	6.94	39	10.3%	0.40 [-0.16, 0.95]		🔴
Total (95% CI)			**143**			**1087**	**100.0%**	**0.52 [0.35, 0.70]**		

Heterogeneity: Tau² = 0.00; Chi² = 2.18, df = 3 (P = 0.54); I² = 0%
Test for overall effect: Z = 5.78 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Conduct Problems – Caregiver (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	56.8	8.7	5	55.5	6.7	761	100.0%	0.19 [-0.69, 1.07]		🔴
Total (95% CI)			**5**			**761**	**100.0%**	**0.19 [-0.69, 1.07]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.43 (P = 0.67)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Conduct Problems – Caregiver (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	56.4	7.3	44	55.5	6.7	761	100.0%	0.13 [-0.17, 0.44]		🔴
Total (95% CI)			**44**			**761**	**100.0%**	**0.13 [-0.17, 0.44]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.86 (P = 0.39)

ARND/Others and CBCL Conduct Problems – Caregiver (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C; ARND)	62.8	9.7	44	55.5	6.7	761	100.0%	1.06 [0.75, 1.37]		🔴
Total (95% CI)			**44**			**761**	**100.0%**	**1.06 [0.75, 1.37]**		

Heterogeneity: Not applicable
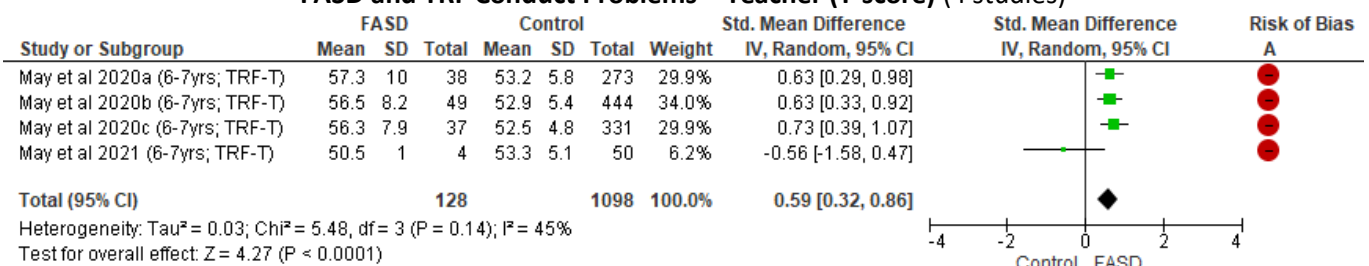Test for overall effect: Z = 6.73 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

TRF Conduct Problems Teacher Report (T-score)

FASD and TRF Conduct Problems – Teacher (T-score) (4 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; TRF-T)	57.3	10	38	53.2	5.8	273	29.9%	0.63 [0.29, 0.98]		🔴
May et al 2020b (6-7yrs; TRF-T)	56.5	8.2	49	52.9	5.4	444	34.0%	0.63 [0.33, 0.92]		🔴
May et al 2020c (6-7yrs; TRF-T)	56.3	7.9	37	52.5	4.8	331	29.9%	0.73 [0.39, 1.07]		🔴
May et al 2021 (6-7yrs; TRF-T)	50.5	1	4	53.3	5.1	50	6.2%	-0.56 [-1.58, 0.47]		🔴
Total (95% CI)			**128**			**1098**	**100.0%**	**0.59 [0.32, 0.86]**		

Heterogeneity: Tau² = 0.03; Chi² = 5.48, df = 3 (P = 0.14); I² = 45%
Test for overall effect: Z = 4.27 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

FAS and TRF Conduct Problems – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	53	4.5	5	52.8	5.9	761	100.0%	0.03 [-0.85, 0.91]		🔴
Total (95% CI)			**5**			**761**	**100.0%**	**0.03 [-0.85, 0.91]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.08 (P = 0.94)

Risk of bias legend
(A) Overall RoB

pFAS and TRF Conduct Problems – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-Ext-T)	52.9	6.1	44	52.8	5.9	761	100.0%	0.02 [-0.29, 0.32]	🔴
Total (95% CI)			44			761	100.0%	0.02 [-0.29, 0.32]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.11 (P = 0.91)

Risk of bias legend
(A) Overall RoB

ARND/Others and TRF Conduct Problems – Teacher (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	57.8	8.6	44	52.8	5.9	761	100.0%	0.82 [0.52, 1.13]	🔴
Total (95% CI)			44			761	100.0%	0.82 [0.52, 1.13]	

Heterogeneity: Not applicable
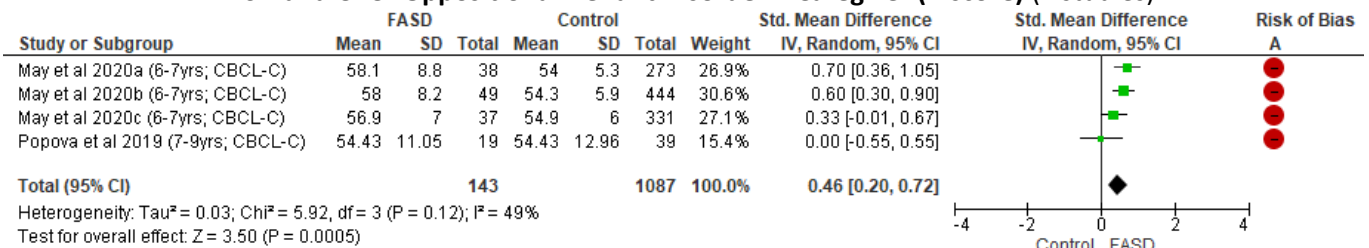Test for overall effect: Z = 5.26 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

CBCL Oppositional Defiant Disorder Caregiver Report (T-score)

FASD and CBCL Oppositional Defiant Disorder – Caregiver (T-score) (4 studies)

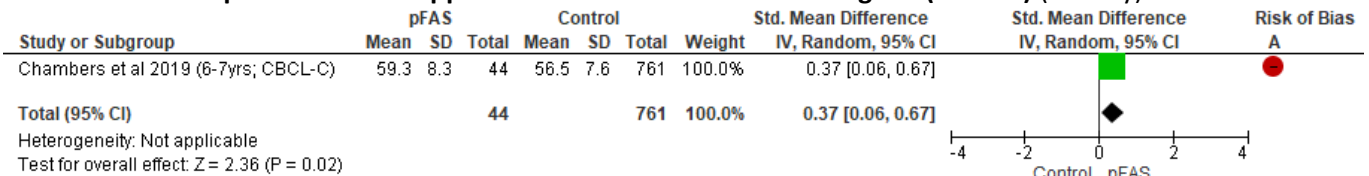| Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; CBCL-C)	58.1	8.8	38	54	5.3	273	26.9%	0.70 [0.36, 1.05]	🔴
May et al 2020b (6-7yrs; CBCL-C)	58	8.2	49	54.3	5.9	444	30.6%	0.60 [0.30, 0.90]	🔴
May et al 2020c (6-7yrs; CBCL-C)	56.9	7	37	54.9	6	331	27.1%	0.33 [-0.01, 0.67]	🔴
Popova et al 2019 (7-9yrs; CBCL-C)	54.43	11.05	19	54.43	12.96	39	15.4%	0.00 [-0.55, 0.55]	🔴
Total (95% CI)			143			1087	100.0%	0.46 [0.20, 0.72]	

Heterogeneity: Tau² = 0.03; Chi² = 5.92, df = 3 (P = 0.12); I² = 49%
Test for overall effect: Z = 3.50 (P = 0.0005)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Oppositional Defiant Disorder – Caregiver (T-score) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	58.4	8.6	5	56.5	7.6	761	100.0%	0.25 [-0.63, 1.13]	🔴
Total (95% CI)			5			761	100.0%	0.25 [-0.63, 1.13]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.56 (P = 0.58)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Oppositional Defiant Disorder – Caregiver (T-score) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	59.3	8.3	44	56.5	7.6	761	100.0%	0.37 [0.06, 0.67]	🔴
Total (95% CI)			44			761	100.0%	0.37 [0.06, 0.67]	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.36 (P = 0.02)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Oppositional Defiant Disorder – Caregiver (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C; ARND)	66.4	8.7	44	56.5	7.6	761	100.0%	1.29 [0.98, 1.60]	🔴
Total (95% CI)			44			761	100.0%	1.29 [0.98, 1.60]	

Heterogeneity: Not applicable
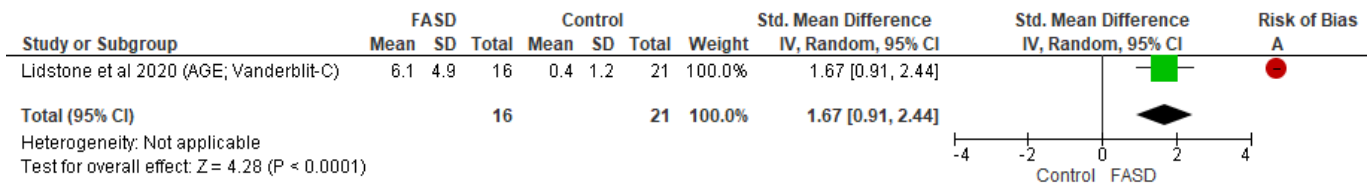Test for overall effect: Z = 8.15 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Vanderbilt-C Oppositional Defiant Disorder Caregiver Report (m/SD)

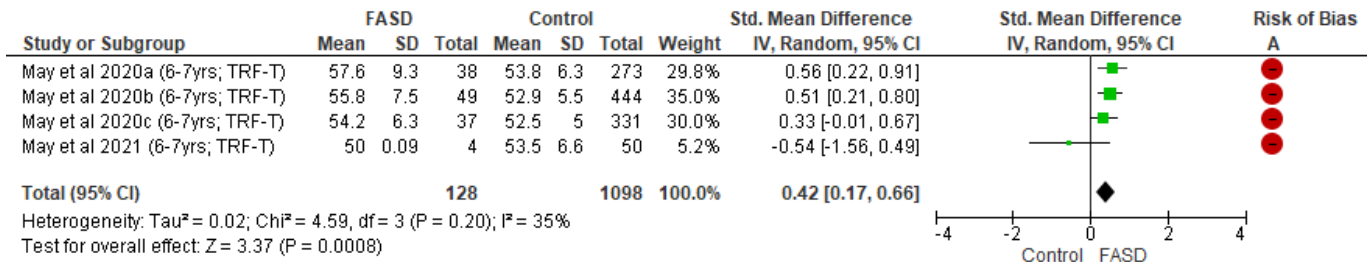### FASD and Vanderblit-C Oppositional Defiant Disorder – Caregiver (mean/SD) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lidstone et al 2020 (AGE; Vanderblit-C)	6.1	4.9	16	0.4	1.2	21	100.0%	1.67 [0.91, 2.44]	🔴
Total (95% CI)			16			21	100.0%	1.67 [0.91, 2.44]	

Heterogeneity: Not applicable
Test for overall effect: Z = 4.28 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

TRF Oppositional Defiant Disorder Teacher Report (T-score)

FASD and TRF Oppositional Defiant Disorder – Teacher (T-score) (4 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; TRF-T)	57.6	9.3	38	53.8	6.3	273	29.8%	0.56 [0.22, 0.91]	🔴
May et al 2020b (6-7yrs; TRF-T)	55.8	7.5	49	52.9	5.5	444	35.0%	0.51 [0.21, 0.80]	🔴
May et al 2020c (6-7yrs; TRF-T)	54.2	6.3	37	52.5	5	331	30.0%	0.33 [-0.01, 0.67]	🔴
May et al 2021 (6-7yrs; TRF-T)	50	0.09	4	53.5	6.6	50	5.2%	-0.54 [-1.56, 0.49]	🔴
Total (95% CI)			128			1098	100.0%	0.42 [0.17, 0.66]	

Heterogeneity: Tau² = 0.02; Chi² = 4.59, df = 3 (P = 0.20); I² = 35%
Test for overall effect: Z = 3.37 (P = 0.0008)

Risk of bias legend
(A) Overall RoB

FAS and TRF Oppositional Defiant Disorder – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	57.8	6	5	52.8	5.4	761	100.0%	0.92 [0.04, 1.81]	🔴
Total (95% CI)			5			761	100.0%	0.92 [0.04, 1.81]	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.06 (P = 0.04)

Risk of bias legend
(A) Overall RoB

pFAS and TRF Oppositional Defiant Disorder – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	53.4	5.9	44	52.8	5.4	761	100.0%	0.11 [-0.19, 0.41]	🔴
Total (95% CI)			44			761	100.0%	0.11 [-0.19, 0.41]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.71 (P = 0.48)

Risk of bias legend
(A) Overall RoB

ARND/Others and TRF Oppositional Defiant Disorder – Teacher (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	57	7.2	44	52.8	5.4	761	100.0%	0.76 [0.46, 1.07]	🔴
Total (95% CI)			44			761	100.0%	0.76 [0.46, 1.07]	

Heterogeneity: Not applicable
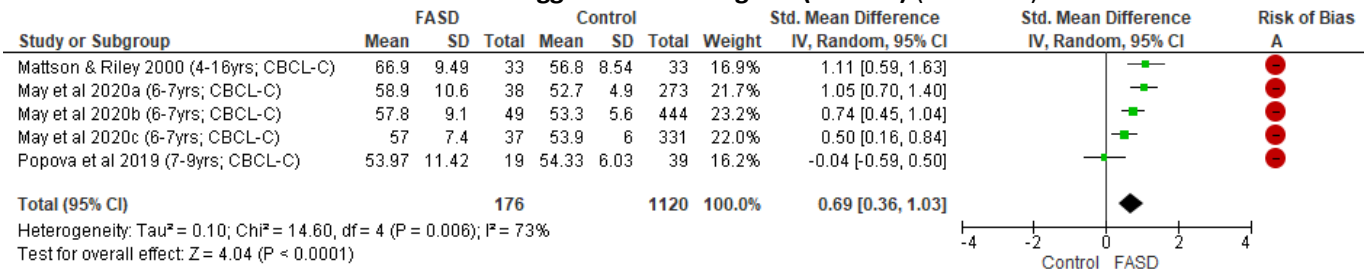Test for overall effect: Z = 4.87 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

CBCL Aggression Caregiver Report (T-score)

FASD and CBCL Aggression – Caregiver (T-score) (5 studies)

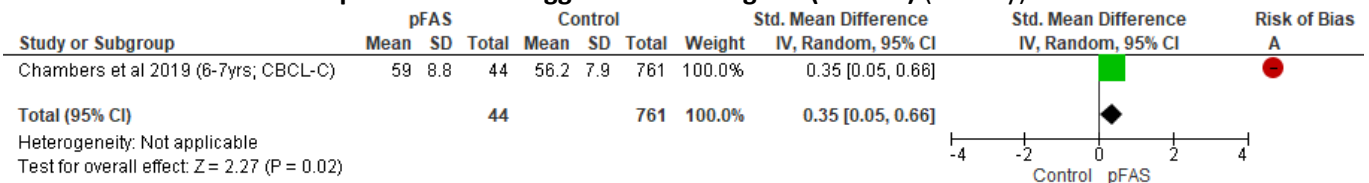| Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson & Riley 2000 (4-16yrs; CBCL-C)	66.9	9.49	33	56.8	8.54	33	16.9%	1.11 [0.59, 1.63]		🔴
May et al 2020a (6-7yrs; CBCL-C)	58.9	10.6	38	52.7	4.9	273	21.7%	1.05 [0.70, 1.40]		🔴
May et al 2020b (6-7yrs; CBCL-C)	57.8	9.1	49	53.3	5.6	444	23.2%	0.74 [0.45, 1.04]		🔴
May et al 2020c (6-7yrs; CBCL-C)	57	7.4	37	53.9	6	331	22.0%	0.50 [0.16, 0.84]		🔴
Popova et al 2019 (7-9yrs; CBCL-C)	53.97	11.42	19	54.33	6.03	39	16.2%	-0.04 [-0.59, 0.50]		🔴
Total (95% CI)			176			1120	100.0%	0.69 [0.36, 1.03]		

Heterogeneity: Tau² = 0.10; Chi² = 14.60, df = 4 (P = 0.006); I² = 73%
Test for overall effect: Z = 4.04 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Aggression – Caregiver (T-score) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	57.6	10.4	5	56.2	7.9	761	100.0%	0.18 [-0.70, 1.06]		🔴
Total (95% CI)			5			761	100.0%	0.18 [-0.70, 1.06]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.39 (P = 0.69)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Aggression – Caregiver (T-score) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	59	8.8	44	56.2	7.9	761	100.0%	0.35 [0.05, 0.66]		🔴
Total (95% CI)			44			761	100.0%	0.35 [0.05, 0.66]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.27 (P = 0.02)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Aggression – Caregiver (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C; ARND)	66.3	10	44	56.2	7.9	761	100.0%	1.26 [0.95, 1.57]		🔴
Total (95% CI)			44			761	100.0%	1.26 [0.95, 1.57]		

Heterogeneity: Not applicable
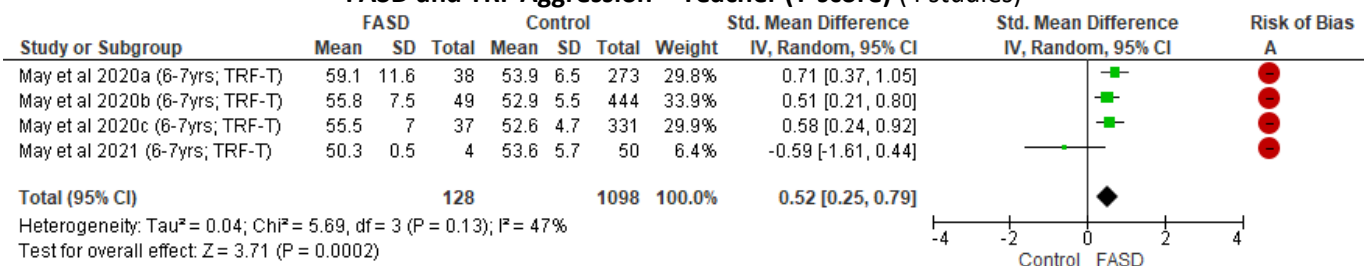Test for overall effect: Z = 7.95 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

TRF/CBCL Aggression Teacher Report (T-score)

FASD and TRF Aggression – Teacher (T-score) (4 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; TRF-T)	59.1	11.6	38	53.9	6.5	273	29.8%	0.71 [0.37, 1.05]		🔴
May et al 2020b (6-7yrs; TRF-T)	55.8	7.5	49	52.9	5.5	444	33.9%	0.51 [0.21, 0.80]		🔴
May et al 2020c (6-7yrs; TRF-T)	55.5	7	37	52.6	4.7	331	29.9%	0.58 [0.24, 0.92]		🔴
May et al 2021 (6-7yrs; TRF-T)	50.3	0.5	4	53.6	5.7	50	6.4%	-0.59 [-1.61, 0.44]		🔴
Total (95% CI)			128			1098	100.0%	0.52 [0.25, 0.79]		

Heterogeneity: Tau² = 0.04; Chi² = 5.69, df = 3 (P = 0.13); I² = 47%
Test for overall effect: Z = 3.71 (P = 0.0002)
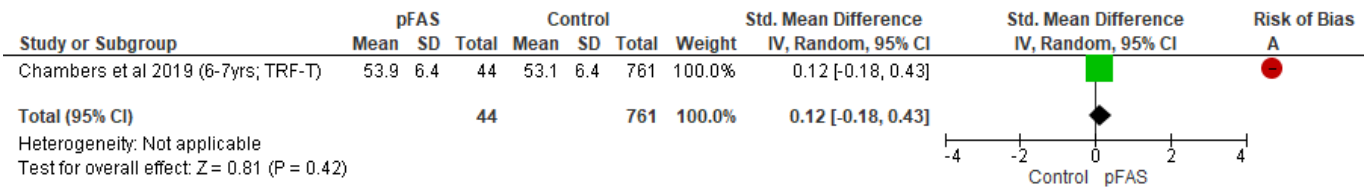
Risk of bias legend
(A) Overall RoB

FAS and TRF Aggression – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	57.2	5.9	5	53.1	6.4	761	100.0%	0.64 [-0.24, 1.52]		🔴
Total (95% CI)			5			761	100.0%	0.64 [-0.24, 1.52]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.43 (P = 0.15)

Risk of bias legend
(A) Overall RoB

pFAS and TRF Aggression – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	53.9	6.4	44	53.1	6.4	761	100.0%	0.12 [-0.18, 0.43]		−
Total (95% CI)			44			761	100.0%	0.12 [-0.18, 0.43]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.81 (P = 0.42)

Risk of bias legend
(A) Overall RoB

ARND/Others and TRF Aggression – Teacher (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	58.2	7.9	44	53.1	6.4	761	100.0%	0.79 [0.48, 1.09]		−
Total (95% CI)			44			761	100.0%	0.79 [0.48, 1.09]		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.02 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ASR Aggression Self-Report (T-score)

pFAS and ASR Aggression - Self-Report (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR)	7.63	0.75	47	5.84	0.69	58	100.0%	2.48 [1.96, 2.99]		−
Total (95% CI)			47			58	100.0%	2.48 [1.96, 2.99]		

Heterogeneity: Not applicable
Test for overall effect: Z = 9.44 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and ASR Aggression - Self-Report (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR; Cogn Affected)	9.54	1.04	34	5.84	0.69	58	100.0%	4.39 [3.62, 5.17]		−
Total (95% CI)			34			58	100.0%	4.39 [3.62, 5.17]		

Heterogeneity: Not applicable
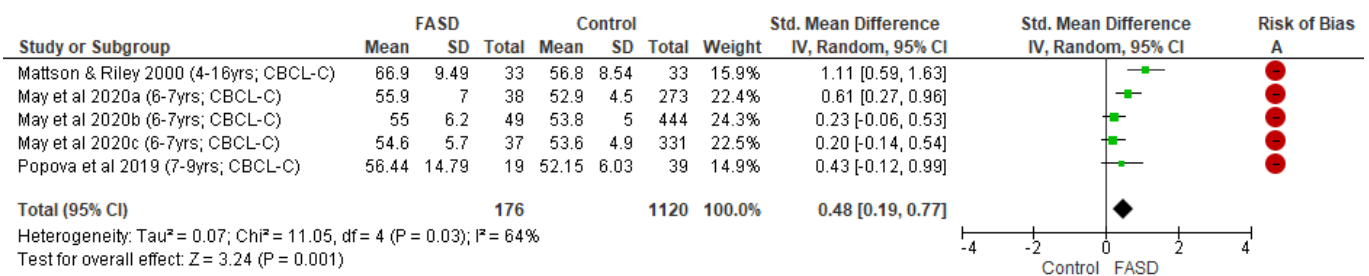Test for overall effect: Z = 11.11 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lynch et al 2017 also reports other minor CBCL subdomains.

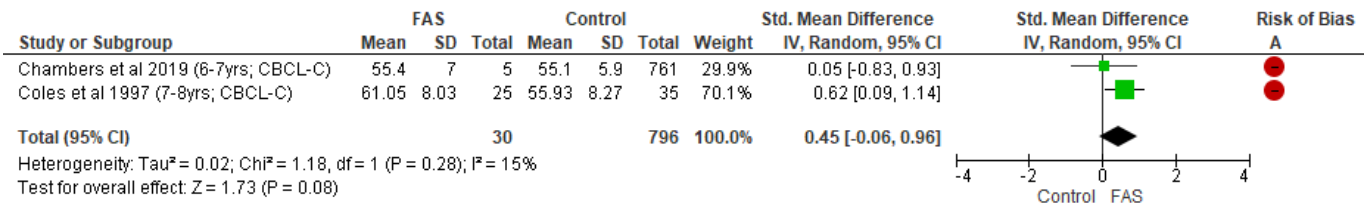## CBCL Rule-Breaking Behaviour Caregiver Report (T-score)

FASD and CBCL Rule-Breaking Behaviour – Caregiver (T-score) (5 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson & Riley 2000 (4-16yrs; CBCL-C)	66.9	9.49	33	56.8	8.54	33	15.9%	1.11 [0.59, 1.63]		−
May et al 2020a (6-7yrs; CBCL-C)	55.9	7	38	52.9	4.5	273	22.4%	0.61 [0.27, 0.96]		−
May et al 2020b (6-7yrs; CBCL-C)	55	6.2	49	53.8	5	444	24.3%	0.23 [-0.06, 0.53]		−
May et al 2020c (6-7yrs; CBCL-C)	54.6	5.7	37	53.6	4.9	331	22.5%	0.20 [-0.14, 0.54]		−
Popova et al 2019 (7-9yrs; CBCL-C)	56.44	14.79	19	52.15	6.03	39	14.9%	0.43 [-0.12, 0.99]		−
Total (95% CI)			176			1120	100.0%	0.48 [0.19, 0.77]		

Heterogeneity: Tau² = 0.07; Chi² = 11.05, df = 4 (P = 0.03); I² = 64%
Test for overall effect: Z = 3.24 (P = 0.001)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Rule-Breaking Behaviour – Caregiver (T-score) (2 studies)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	55.4	7	5	55.1	5.9	761	29.9%	0.05 [-0.83, 0.93]		🔴
Coles et al 1997 (7-8yrs; CBCL-C)	61.05	8.03	25	55.93	8.27	35	70.1%	0.62 [0.09, 1.14]		🔴
Total (95% CI)			30			796	100.0%	0.45 [-0.06, 0.96]		

Heterogeneity: Tau² = 0.02; Chi² = 1.18, df = 1 (P = 0.28); I² = 15%
Test for overall effect: Z = 1.73 (P = 0.08)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Rule-Breaking Behaviour – Caregiver (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	56.2	6.4	44	55.1	5.9	761	100.0%	0.19 [-0.12, 0.49]		🔴
Total (95% CI)			44			761	100.0%	0.19 [-0.12, 0.49]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.20 (P = 0.23)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Rule-Breaking Behaviour – Caregiver (T-score) (2 studies)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C; ARND)	61.3	8.4	44	55.1	5.9	761	53.3%	1.02 [0.71, 1.33]		🔴
Coles et al 1997 (7-8yrs; CBCL; non-syndromal)	59.78	8.47	62	55.93	8.27	35	46.7%	0.45 [0.04, 0.87]		🔴
Total (95% CI)			106			796	100.0%	0.76 [0.20, 1.31]		

Heterogeneity: Tau² = 0.13; Chi² = 4.57, df = 1 (P = 0.03); I² = 78%
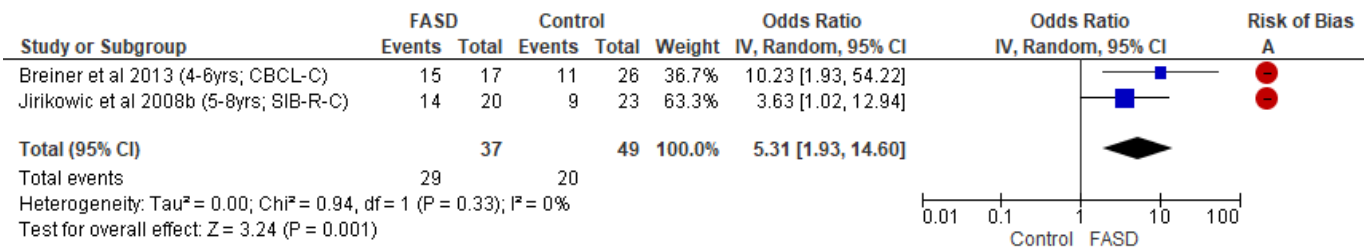Test for overall effect: Z = 2.67 (P = 0.007)

Risk of bias legend
(A) Overall RoB

CBCL/SIB-R Rule-Breaking Behaviour Caregiver Report (Frequency/OR)

FASD and CBCL/SIB-R Rule-Breaking Behaviour – Caregiver (OR) (2 studies)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Breiner et al 2013 (4-6yrs; CBCL-C)	15	17	11	26	36.7%	10.23 [1.93, 54.22]		🔴
Jirikowic et al 2008b (5-8yrs; SIB-R-C)	14	20	9	23	63.3%	3.63 [1.02, 12.94]		🔴
Total (95% CI)		37		49	100.0%	5.31 [1.93, 14.60]		
Total events	29		20					

Heterogeneity: Tau² = 0.00; Chi² = 0.94, df = 1 (P = 0.33); I² = 0%
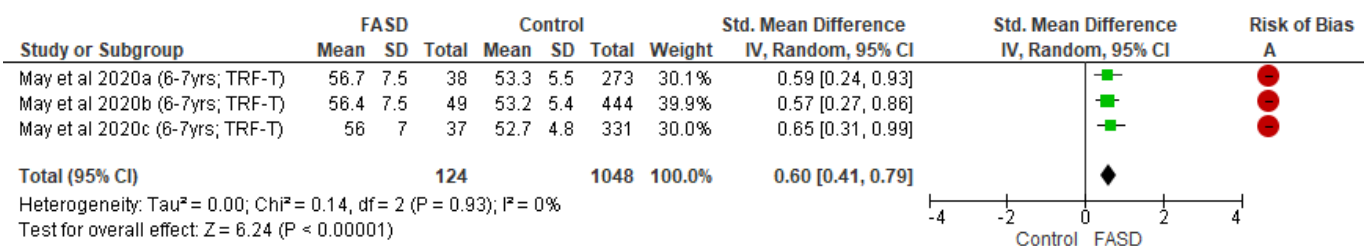Test for overall effect: Z = 3.24 (P = 0.001)

Risk of bias legend
(A) Overall RoB

Note: Briener et al 2013 also reports other minor CBCL subdomains. Jirikowic et al 2008b also reports other minor CBCL subdomains.

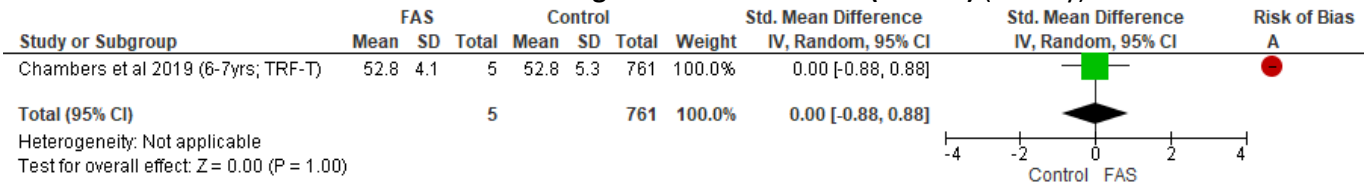## TRF/CBCL/SIB-R Rule-Breaking Behaviour Teacher Report (T-score)

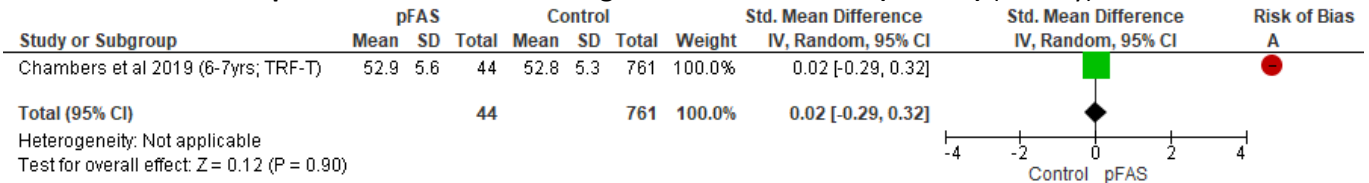## FASD and TRF Rule-Breaking Behaviour – Teacher (T-score) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; TRF-T)	56.7	7.5	38	53.3	5.5	273	30.1%	0.59 [0.24, 0.93]		🔴
May et al 2020b (6-7yrs; TRF-T)	56.4	7.5	49	53.3	5.4	444	39.9%	0.57 [0.27, 0.86]		🔴
May et al 2020c (6-7yrs; TRF-T)	56	7	37	52.7	4.8	331	30.0%	0.65 [0.31, 0.99]		🔴
Total (95% CI)			124			1048	100.0%	0.60 [0.41, 0.79]		

Heterogeneity: Tau² = 0.00; Chi² = 0.14, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 6.24 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and TRF Rule-Breaking Behaviour – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	52.8	4.1	5	52.8	5.3	761	100.0%	0.00 [-0.88, 0.88]		●
Total (95% CI)			5			761	100.0%	**0.00 [-0.88, 0.88]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

Risk of bias legend
(A) Overall RoB

pFAS and TRF Rule-Breaking Behaviour – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	52.9	5.6	44	52.8	5.3	761	100.0%	0.02 [-0.29, 0.32]		●
Total (95% CI)			44			761	100.0%	**0.02 [-0.29, 0.32]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.12 (P = 0.90)

Risk of bias legend
(A) Overall RoB

ARND/Others and TRF Rule-Breaking Behaviour – Teacher (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	57.1	6.9	44	52.8	5.3	761	100.0%	0.80 [0.49, 1.10]		●
Total (95% CI)			44			761	100.0%	**0.80 [0.49, 1.10]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.09 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ASR Rule-Breaking Behaviour Self Report (T-score)

pFAS and ASR Rule-Breaking Behaviour – Self-report (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR)	4.38	0.5	47	3.78	0.46	58	100.0%	1.25 [0.82, 1.67]		●
Total (95% CI)			47			58	100.0%	**1.25 [0.82, 1.67]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.79 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and ASR Rule-Breaking Behaviour – Self-report (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR; Cogn Affected)	4.49	0.7	34	3.78	0.46	58	100.0%	1.26 [0.79, 1.72]		●
Total (95% CI)			34			58	100.0%	**1.26 [0.79, 1.72]**		

Heterogeneity: Not applicable
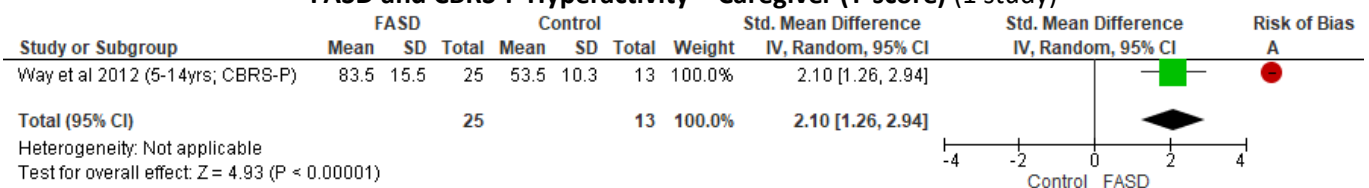Test for overall effect: Z = 5.33 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lynch et al 2017 also reports other minor CBCL subdomains.

CBRS Hyperactivity Caregiver Report (T-score)
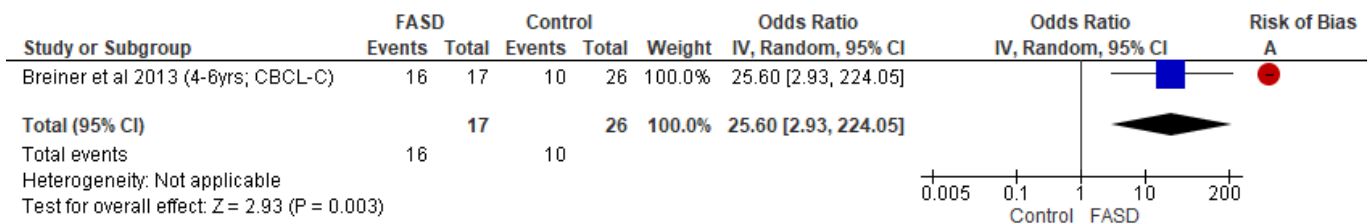
FASD and CBRS-P Hyperactivity – Caregiver (T-score) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Way et al 2012 (5-14yrs; CBRS-P)	83.5	15.5	25	53.5	10.3	13	100.0%	2.10 [1.26, 2.94]		●
Total (95% CI)			25			13	100.0%	**2.10 [1.26, 2.94]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.93 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

CBCL Hyperactivity Caregiver Report (Frequency/OR)

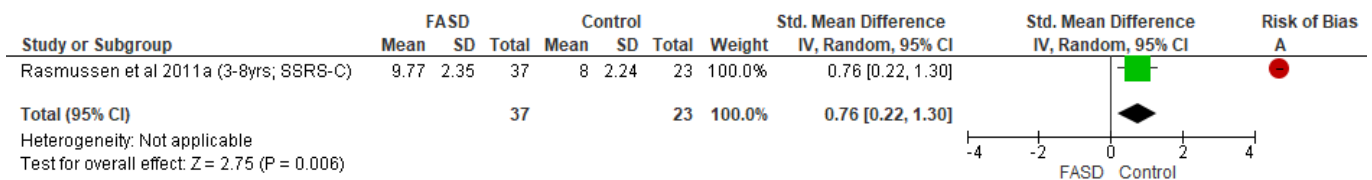### FASD and CBCL Hyperactivity – Caregiver (OR) (1 study)

Study or Subgroup	FASD Events	FASD Total	Control Events	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Breiner et al 2013 (4-6yrs; CBCL-C)	16	17	10	26	100.0%	25.60 [2.93, 224.05]		🔴
Total (95% CI)		17		26	100.0%	25.60 [2.93, 224.05]		
Total events	16		10					

Heterogeneity: Not applicable
Test for overall effect: Z = 2.93 (P = 0.003)

Risk of bias legend
(A) Overall RoB

Note: Briener et al 2013 also reports other minor CBCL subdomains.

Non-T-Score Ratings: DBD/SSRS Hyperactivity Caregiver Report (m/SD)

FASD and SSRS Hyperactivity – Caregiver (mean/SD) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Rasmussen et al 2011a (3-8yrs; SSRS-C)	9.77	2.35	37	8	2.24	23	100.0%	0.76 [0.22, 1.30]		🔴
Total (95% CI)			37			23	100.0%	0.76 [0.22, 1.30]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.75 (P = 0.006)

Risk of bias legend
(A) Overall RoB

pFAS and DBD Hyperactivity – Caregiver (mean/SD) (2 studies)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008a (6-7yrs; DBD-C; FAS/pFAS)	1	1.27	23	0.91	1.85	57	50.5%	0.05 [-0.43, 0.54]		❓
Kodituwakku et al 2006b (6-7yrs; DBD-C; FAS/pFAS)	1.59	1.74	22	0.57	1.09	60	49.5%	0.78 [0.28, 1.29]		❓
Total (95% CI)			45			117	100.0%	0.41 [-0.30, 1.13]		

Heterogeneity: Tau² = 0.20; Chi² = 4.19, df = 1 (P = 0.04); I² = 76%
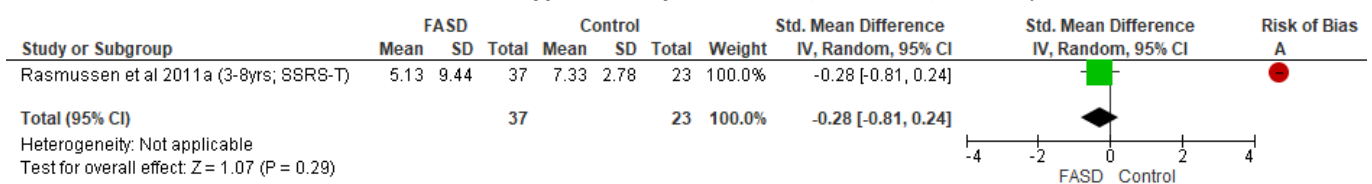Test for overall effect: Z = 1.13 (P = 0.26)

Risk of bias legend
(A) Overall RoB

Note: Kodituwakku et al 2006b includes one participant with an ARND diagnosis.

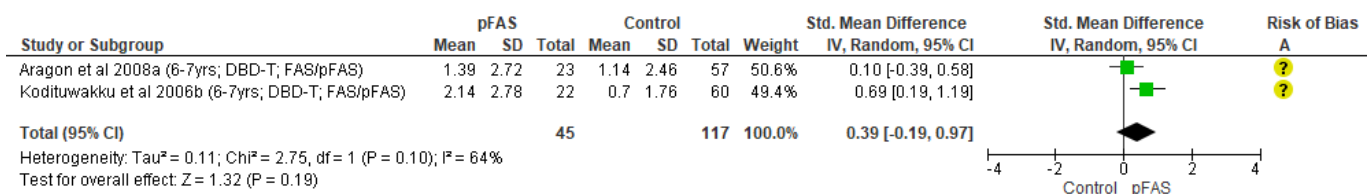## Non-T-Score Ratings: DBD/SSRS Hyperactivity Teacher Report (m/SD)

FASD and SSRS Hyperactivity – Teacher (mean/SD) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Rasmussen et al 2011a (3-8yrs; SSRS-T)	5.13	9.44	37	7.33	2.78	23	100.0%	-0.28 [-0.81, 0.24]		🔴
Total (95% CI)			37			23	100.0%	-0.28 [-0.81, 0.24]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.07 (P = 0.29)

Risk of bias legend
(A) Overall RoB

pFAS and DBD Hyperactivity – Teacher (mean/SD) (2 studies)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Aragon et al 2008a (6-7yrs; DBD-T; FAS/pFAS)	1.39	2.72	23	1.14	2.46	57	50.6%	0.10 [-0.39, 0.58]		❓
Kodituwakku et al 2006b (6-7yrs; DBD-T; FAS/pFAS)	2.14	2.78	22	0.7	1.76	60	49.4%	0.69 [0.19, 1.19]		❓
Total (95% CI)			45			117	100.0%	0.39 [-0.19, 0.97]		

Heterogeneity: Tau² = 0.11; Chi² = 2.75, df = 1 (P = 0.10); I² = 64%
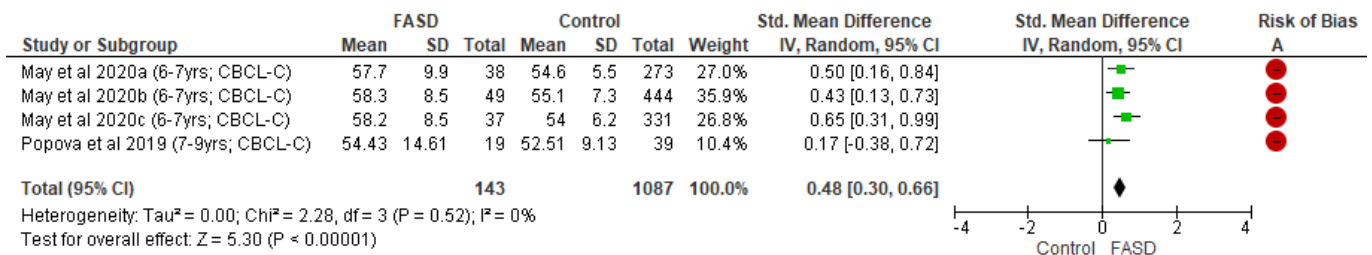Test for overall effect: Z = 1.32 (P = 0.19)

Risk of bias legend
(A) Overall RoB

Note: Kodituwakku et al 2006b includes one participant with an ARND diagnosis.

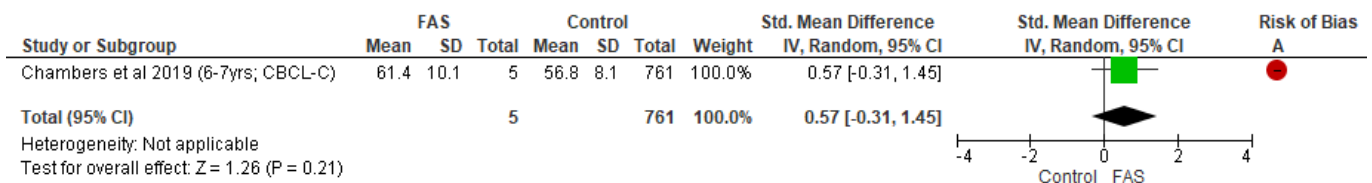## CBCL Attention/Hyperactivity Caregiver Report (T-score)

FASD and CBCL Attention/Hyperactivity – Caregiver (T-score) (4 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; CBCL-C)	57.7	9.9	38	54.6	5.5	273	27.0%	0.50 [0.16, 0.84]	🔴
May et al 2020b (6-7yrs; CBCL-C)	58.3	8.5	49	55.1	7.3	444	35.9%	0.43 [0.13, 0.73]	🔴
May et al 2020c (6-7yrs; CBCL-C)	58.2	8.5	37	54	6.2	331	26.8%	0.65 [0.31, 0.99]	🔴
Popova et al 2019 (7-9yrs; CBCL-C)	54.43	14.61	19	52.51	9.13	39	10.4%	0.17 [-0.38, 0.72]	🔴
Total (95% CI)			**143**			**1087**	**100.0%**	**0.48 [0.30, 0.66]**	

Heterogeneity: Tau² = 0.00; Chi² = 2.28, df = 3 (P = 0.52); I² = 0%
Test for overall effect: Z = 5.30 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Attention/Hyperactivity – Caregiver (T-score) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	61.4	10.1	5	56.8	8.1	761	100.0%	0.57 [-0.31, 1.45]	🔴
Total (95% CI)			**5**			**761**	**100.0%**	**0.57 [-0.31, 1.45]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.26 (P = 0.21)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Attention/Hyperactivity – Caregiver (T-score) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	59.2	9.9	44	56.8	8.1	761	100.0%	0.29 [-0.01, 0.60]	🔴
Total (95% CI)			**44**			**761**	**100.0%**	**0.29 [-0.01, 0.60]**	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.88 (P = 0.06)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Attention/Hyperactivity – Caregiver (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C; ARND)	65.7	10.2	44	56.8	8.1	761	100.0%	1.08 [0.77, 1.39]	🔴
Total (95% CI)			**44**			**761**	**100.0%**	**1.08 [0.77, 1.39]**	

Heterogeneity: Not applicable
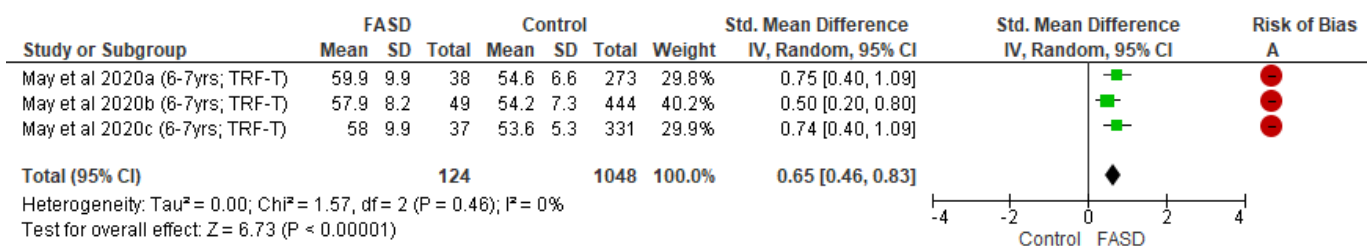Test for overall effect: Z = 6.87 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

TRF Attention/Hyperactivity Teacher Report (T-score)

FASD and TRF Attention/Hyperactivity – Teacher (T-score) (3 studies)

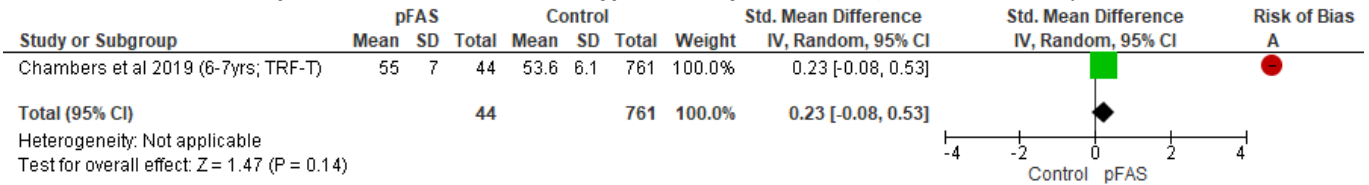| Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; TRF-T)	59.9	9.9	38	54.6	6.6	273	29.8%	0.75 [0.40, 1.09]	🔴
May et al 2020b (6-7yrs; TRF-T)	57.9	8.2	49	54.2	7.3	444	40.2%	0.50 [0.20, 0.80]	🔴
May et al 2020c (6-7yrs; TRF-T)	58	9.9	37	53.6	5.3	331	29.9%	0.74 [0.40, 1.09]	🔴
Total (95% CI)			**124**			**1048**	**100.0%**	**0.65 [0.46, 0.83]**	

Heterogeneity: Tau² = 0.00; Chi² = 1.57, df = 2 (P = 0.46); I² = 0%
Test for overall effect: Z = 6.73 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and TRF Attention/Hyperactivity – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	59.6	6.9	5	53.6	6.1	761	100.0%	0.98 [0.10, 1.86]		🔴
Total (95% CI)			**5**			**761**	**100.0%**	**0.98 [0.10, 1.86]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.19 (P = 0.03)

Risk of bias legend
(A) Overall RoB

pFAS and TRF Attention/Hyperactivity – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	55	7	44	53.6	6.1	761	100.0%	0.23 [-0.08, 0.53]		🔴
Total (95% CI)			**44**			**761**	**100.0%**	**0.23 [-0.08, 0.53]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.47 (P = 0.14)

Risk of bias legend
(A) Overall RoB

ARND/Others and TRF Attention/Hyperactivity – Teacher (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	58.9	7.7	44	53.6	6.1	761	100.0%	0.85 [0.55, 1.16]		🔴
Total (95% CI)			**44**			**761**	**100.0%**	**0.85 [0.55, 1.16]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 5.46 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

CBCL/CBRS Anxious/Depressed Caregiver Report (T-score)

FASD and CBCL/CBRS Anxious/Depressed – Caregiver (T-score) (7 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Krueger et al 2020 (8-16yrs; CBCL-C)	64.56	11.19	39	55.5	7.43	34	11.9%	0.93 [0.45, 1.42]		🔴
Mattson & Riley 2000 (4-16yrs; CBCL-C)	59.5	10.64	33	54.5	8.22	33	11.7%	0.52 [0.03, 1.01]		🔴
May et al 2020a (6-7yrs; CBCL-C)	55.9	7.6	38	52.5	4.7	273	18.7%	0.66 [0.32, 1.00]		🔴
May et al 2020b (6-7yrs; CBCL-C)	55.2	6.1	49	53.2	5.1	444	21.9%	0.38 [0.09, 0.68]		🔴
May et al 2020c (6-7yrs; CBCL-C)	56.3	7.6	37	53.1	4.8	331	18.8%	0.62 [0.28, 0.96]		🔴
Popova et al 2019 (7-9yrs; CBCL-C)	57.35	13.97	19	54.98	11.05	39	9.9%	0.19 [-0.36, 0.74]		🔴
Way et al 2012 (5-14yrs; CBRS-P)	63.6	16.6	24	47.5	5.6	17	7.0%	1.19 [0.51, 1.87]		🔴
Total (95% CI)			**239**			**1171**	**100.0%**	**0.60 [0.40, 0.80]**		

Heterogeneity: Tau² = 0.02; Chi² = 9.05, df = 6 (P = 0.17); I² = 34%
Test for overall effect: Z = 5.98 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Anxious/Depressed – Caregiver (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	56.2	8.8	5	56.3	7.1	771	100.0%	-0.01 [-0.89, 0.87]		🔴
Total (95% CI)			**5**			**771**	**100.0%**	**-0.01 [-0.89, 0.87]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.03 (P = 0.98)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Anxious/Depressed – Caregiver (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	57.6	7.2	44	56.3	7.1	771	100.0%	0.18 [-0.12, 0.49]		🔴
Total (95% CI)			**44**			**771**	**100.0%**	**0.18 [-0.12, 0.49]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.18 (P = 0.24)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Anxious/Depressed – Caregiver (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C; ARND)	60.6	9.4	44	56.3	7.1	771	100.0%	0.59 [0.29, 0.90]	🔴
Total (95% CI)			44			771	100.0%	0.59 [0.29, 0.90]	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.81 (P = 0.0001)

Risk of bias legend
(A) Overall RoB

Vanderbilt-C Anxious/Depressed Caregiver Report (m/sd)

FASD and Vanderblit-C Anxious/Depressed – Caregiver (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lidstone et al 2020 (7-17yrs; Vanderblit-C)	1.7	1.9	16	0.2	0.7	21	100.0%	1.09 [0.38, 1.79]	🔴
Total (95% CI)			16			21	100.0%	1.09 [0.38, 1.79]	

Heterogeneity: Not applicable
Test for overall effect: Z = 3.04 (P = 0.002)

Risk of bias legend
(A) Overall RoB

TRF Anxious/Depressed Teacher Report (T-score)

FASD and TRF Anxious/Depressed – Teacher (T-score) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; TRF-T)	56.5	7.2	38	52.8	4.1	273	31.2%	0.81 [0.46, 1.15]	🔴
May et al 2020b (6-7yrs; TRF-T)	54.2	7.2	49	52	4.6	444	37.5%	0.45 [0.15, 0.74]	🔴
May et al 2020c (6-7yrs; TRF-T)	55.1	6.7	37	51.9	3.6	331	31.3%	0.80 [0.45, 1.14]	🔴
Total (95% CI)			124			1048	100.0%	0.67 [0.43, 0.91]	

Heterogeneity: Tau² = 0.02; Chi² = 3.26, df = 2 (P = 0.20); I² = 39%
Test for overall effect: Z = 5.42 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and TRF Anxious/Depressed – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	55.4	6.2	5	52.8	5.6	771	100.0%	0.46 [-0.42, 1.34]	🔴
Total (95% CI)			5			771	100.0%	0.46 [-0.42, 1.34]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.03 (P = 0.30)

Risk of bias legend
(A) Overall RoB

pFAS and TRF Anxious/Depressed – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	53.9	7.2	44	52.8	5.6	771	100.0%	0.19 [-0.11, 0.50]	🔴
Total (95% CI)			44			771	100.0%	0.19 [-0.11, 0.50]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.24 (P = 0.21)

Risk of bias legend
(A) Overall RoB

ARND/Others and TRF Anxious/Depressed – Teacher (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	54.8	6.1	44	52.8	5.6	771	100.0%	0.36 [0.05, 0.66]	🔴
Total (95% CI)			44			771	100.0%	0.36 [0.05, 0.66]	

Heterogeneity: Not applicable
Test for overall effect: Z = 2.29 (P = 0.02)

Risk of bias legend
(A) Overall RoB

ASR Anxious/Depressed Self Report (T-score)

pFAS and ASR Anxious/Depressed – Self Report (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR)	8.53	0.89	47	5.42	0.82	58	100.0%	3.62 [2.99, 4.25]	⊖
Total (95% CI)			47			58	100.0%	3.62 [2.99, 4.25]	

Heterogeneity: Not applicable
Test for overall effect: Z = 11.26 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and ASR Anxious/Depressed – Self Report (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR; Cogn Affected)	9.25	1.23	34	5.42	0.82	58	100.0%	3.83 [3.37, 4.29]	⊖
Total (95% CI)			34			58	100.0%	3.83 [3.37, 4.29]	

Heterogeneity: Not applicable
Test for overall effect: Z = 16.17 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lynch et al 2017 also reports other minor CBCL subdomains.

CBCL/BASC Anxiety Caregiver Report (T-score)

FASD and CBCL/BASC Anxiety – Caregiver (T-score) (5 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Krueger et al 2020 (8-16yrs; BASC-3-C)	59.21	13.52	39	51.77	13.08	34	16.0%	0.55 [0.08, 1.02]	⊖
May et al 2020a (6-7yrs; CBCL-C)	56.6	8.1	38	52.5	4.8	273	23.4%	0.77 [0.43, 1.12]	⊖
May et al 2020b (6-7yrs; CBCL-C)	55.3	6.7	49	53.7	5.6	444	27.5%	0.28 [-0.02, 0.58]	⊖
May et al 2020c (6-7yrs; CBCL-C)	57.3	7.6	37	53.4	5.4	331	23.5%	0.69 [0.34, 1.03]	⊖
Way et al 2012 (5-14yrs; CBRS-P)	70.5	27.4	24	50.1	8.2	17	9.6%	0.92 [0.27, 1.58]	⊖
Total (95% CI)			187			1099	100.0%	0.60 [0.37, 0.82]	

Heterogeneity: Tau² = 0.03; Chi² = 6.59, df = 4 (P = 0.16); I² = 39%
Test for overall effect: Z = 5.20 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Krueger et al 2020 also reports other minor subdomains.

FAS and CBCL Anxiety – Caregiver (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	56.8	8.8	5	56.3	7.1	771	100.0%	0.07 [-0.81, 0.95]	⊖
Total (95% CI)			5			771	100.0%	0.07 [-0.81, 0.95]	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.16 (P = 0.88)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Anxiety – Caregiver (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	58.7	8	44	56.5	7.1	771	100.0%	0.31 [0.00, 0.61]	⊖
Total (95% CI)			44			771	100.0%	0.31 [0.00, 0.61]	

Heterogeneity: Not applicable
Test for overall effect: Z = 1.98 (P = 0.05)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Anxiety – Caregiver (T-score) (1 study)

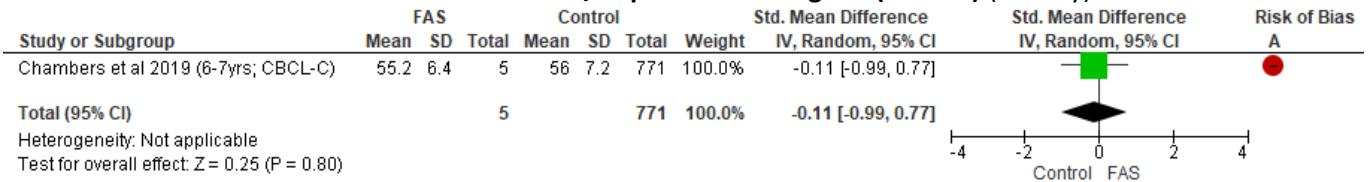| Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C; ARND)	60.4	8.5	44	56.5	7.1	771	100.0%	0.54 [0.24, 0.85]		🔴
Total (95% CI)			44			771	100.0%	**0.54 [0.24, 0.85]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.49 (P = 0.0005)

Risk of bias legend
(A) Overall RoB

TRF Anxiety Teacher Report (T-score)

FASD and TRF Anxiety – Teacher (T-score) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; TRF-T)	57.7	7.7	38	53.2	5.6	273	32.1%	0.76 [0.42, 1.11]		🔴
May et al 2020b (6-7yrs; TRF-T)	54.9	6.7	49	52.2	5	444	36.1%	0.52 [0.22, 0.82]		🔴
May et al 2020c (6-7yrs; TRF-T)	56.5	7.2	37	51.9	4	331	31.8%	1.04 [0.69, 1.39]		🔴
Total (95% CI)			124			1048	100.0%	**0.76 [0.46, 1.06]**		

Heterogeneity: Tau² = 0.04; Chi² = 4.97, df = 2 (P = 0.08); I² = 60%
Test for overall effect: Z = 4.99 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and TRF Anxiety – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	57.2	11	5	53.1	5.8	771	100.0%	0.70 [-0.18, 1.58]		🔴
Total (95% CI)			5			771	100.0%	**0.70 [-0.18, 1.58]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.56 (P = 0.12)

Risk of bias legend
(A) Overall RoB

pFAS and TRF Anxiety – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	53.9	6.4	44	53.1	5.8	771	100.0%	0.14 [-0.17, 0.44]		🔴
Total (95% CI)			44			771	100.0%	**0.14 [-0.17, 0.44]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.88 (P = 0.38)

Risk of bias legend
(A) Overall RoB

ARND/Others and TRF Anxiety – Teacher (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	55.6	7.9	44	53.1	5.8	771	100.0%	0.42 [0.12, 0.73]		🔴
Total (95% CI)			44			771	100.0%	**0.42 [0.12, 0.73]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.71 (P = 0.007)

Risk of bias legend
(A) Overall RoB

CBCL Withdrawn/Depressed Caregiver Report (T-score)

FASD and CBCL Withdrawn/Depressed – Caregiver (T-score) (6 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Krueger et al 2020 (8-16yrs; CBCL-C)	60.92	9.11	39	53.94	5.4	34	14.1%	0.91 [0.42, 1.39]		🔴
Mattson & Riley 2000 (4-16yrs; CBCL-C)	61.6	11.2	33	55.2	9.09	33	13.8%	0.62 [0.13, 1.11]		🔴
May et al 2020a (6-7yrs; CBCL-C)	57.7	9.3	38	52.6	4.1	273	19.1%	1.01 [0.67, 1.36]		🔴
May et al 2020b (6-7yrs; CBCL-C)	56.1	7.9	49	53.4	5.2	444	21.4%	0.49 [0.19, 0.78]		🔴
May et al 2020c (6-7yrs; CBCL-C)	56.9	7.5	37	53.1	5	331	19.3%	0.72 [0.37, 1.06]		🔴
Popova et al 2019 (7-9yrs; CBCL-C)	54.98	13.97	19	54.43	11.6	39	12.2%	0.04 [-0.50, 0.59]		🔴
Total (95% CI)			215			1154	100.0%	**0.66 [0.41, 0.90]**		

Heterogeneity: Tau² = 0.05; Chi² = 11.23, df = 5 (P = 0.05); I² = 55%
Test for overall effect: Z = 5.22 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Krueger et al 2020 also reports other minor subdomains.

FAS and CBCL Withdrawn/Depressed – Caregiver (T-score) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	55.2	6.4	5	56	7.2	771	100.0%	-0.11 [-0.99, 0.77]		●
Total (95% CI)			5			771	100.0%	-0.11 [-0.99, 0.77]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.25 (P = 0.80)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Withdrawn/Depressed – Caregiver (T-score) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	58.3	7.6	44	56	7.2	771	100.0%	0.32 [0.01, 0.62]		●
Total (95% CI)			44			771	100.0%	0.32 [0.01, 0.62]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.05 (P = 0.04)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Withdrawn/Depressed – Caregiver (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C; ARND)	59.5	8.7	44	56	7.2	771	100.0%	0.48 [0.18, 0.78]		●
Total (95% CI)			44			771	100.0%	0.48 [0.18, 0.78]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.09 (P = 0.002)

Risk of bias legend
(A) Overall RoB

TRF Withdrawn/Depressed Teacher Report (T-score)

FASD and TRF Withdrawn/Depressed – Teacher (T-score) (3 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; TRF-T)	55.8	5.5	38	53	5.7	273	31.0%	0.49 [0.15, 0.83]		●
May et al 2020b (6-7yrs; TRF-T)	56.1	7.7	49	52.2	4.6	444	38.5%	0.78 [0.48, 1.08]		●
May et al 2020c (6-7yrs; TRF-T)	56.2	7.8	37	52.2	4.2	331	30.5%	0.85 [0.51, 1.20]		●
Total (95% CI)			124			1048	100.0%	0.71 [0.50, 0.92]		

Heterogeneity: Tau² = 0.01; Chi² = 2.44, df = 2 (P = 0.30); I² = 18%
Test for overall effect: Z = 6.70 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and TRF Withdrawn/Depressed – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	52	3.1	5	53.3	5.8	771	100.0%	-0.22 [-1.10, 0.66]		●
Total (95% CI)			5			771	100.0%	-0.22 [-1.10, 0.66]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.50 (P = 0.62)

Risk of bias legend
(A) Overall RoB

pFAS and TRF Withdrawn/Depressed – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	53.1	4.6	44	53.3	5.8	771	100.0%	-0.03 [-0.34, 0.27]		●
Total (95% CI)			44			771	100.0%	-0.03 [-0.34, 0.27]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.22 (P = 0.82)

Risk of bias legend
(A) Overall RoB

ARND/Others and TRF Withdrawn/Depressed – Teacher (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	55.4	6.4	44	53.1	5.8	771	100.0%	0.39 [0.09, 0.70]		🔴
Total (95% CI)			44			771	100.0%	0.39 [0.09, 0.70]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.54 (P = 0.01)

Risk of bias legend
(A) Overall RoB

ASR Withdrawn/Depressed Self Report (T-score)

pFAS and ASR Withdrawn/Depressed – Self-report (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR)	4.23	0.44	47	3.21	0.4	58	100.0%	2.42 [1.91, 2.93]		🔴
Total (95% CI)			47			58	100.0%	2.42 [1.91, 2.93]		

Heterogeneity: Not applicable
Test for overall effect: Z = 9.32 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and ASR Withdrawn/Depressed – Self-report (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR; Cogn Affected)	4.9	0.61	34	3.21	0.4	58	100.0%	3.44 [2.78, 4.10]		🔴
Total (95% CI)			34			58	100.0%	3.44 [2.78, 4.10]		

Heterogeneity: Not applicable
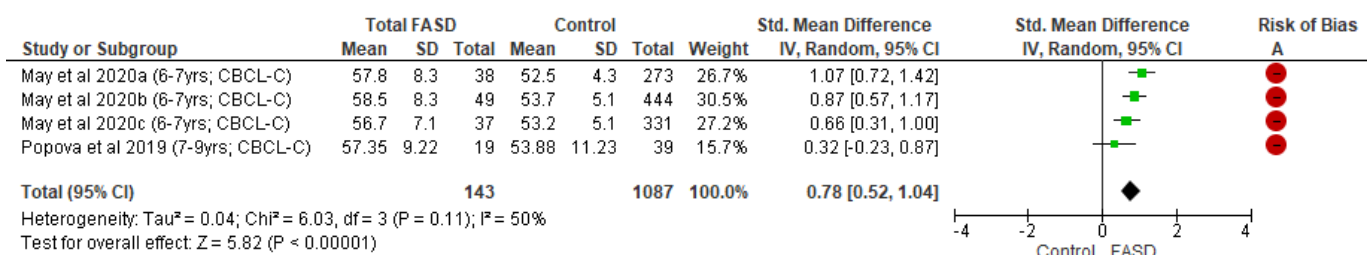Test for overall effect: Z = 10.19 (P < 0.00001)

Risk of bias legend
(A) Overall RoB
Note: Lynch et al 2017 also reports other minor CBCL subdomains.

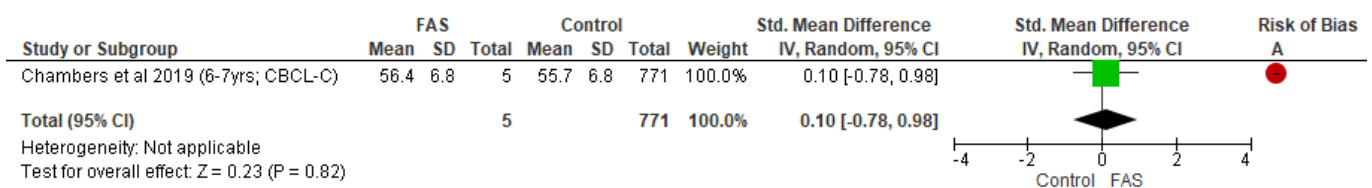## CBCL/CBRS Somatic Complaints Caregiver Report (T-score)

FASD and CBCL/CBRS Somatic Complaints – Caregiver (T-score) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Mattson & Riley 2000 (4-16yrs; CBCL-C)	61.6	11.2	33	55.2	9.09	33	35.4%	0.62 [0.13, 1.11]		🔴
Popova et al 2019 (7-9yrs; CBCL-C)	53.79	12.42	19	53.24	9.13	39	34.2%	0.05 [-0.50, 0.60]		🔴
Way et al 2012 (5-14yrs; CBRS-P)	72.1	18.6	24	49	9	17	30.4%	1.47 [0.76, 2.18]		🔴
Total (95% CI)			76			89	100.0%	0.68 [-0.05, 1.42]		

Heterogeneity: Tau² = 0.33; Chi² = 9.68, df = 2 (P = 0.008); I² = 79%
Test for overall effect: Z = 1.83 (P = 0.07)

ASR Somatic Complaints Self Report (T-score)

pFAS and ASR Somatic Complaints – Self-report (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR)	4.26	0.55	47	3.32	0.51	58	100.0%	1.77 [1.31, 2.22]		🔴
Total (95% CI)			47			58	100.0%	1.77 [1.31, 2.22]		

Heterogeneity: Not applicable
Test for overall effect: Z = 7.60 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and ASR Somatic Complaints – Self-report (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR; Cogn Affected)	4.42	0.76	34	3.32	0.51	58	100.0%	1.78 [1.28, 2.28]		🔴
Total (95% CI)			34			58	100.0%	1.78 [1.28, 2.28]		

Heterogeneity: Not applicable
Test for overall effect: Z = 6.99 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lynch et al 2017 also reports other minor CBCL subdomains.

CBCL/CBRS Thought Complaints Caregiver Report (T-score)

FASD and CBCL/CBRS Thought Problems – Caregiver (T-score) (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Popova et al 2019 (7-9yrs; CBCL-C)	58.9	15.16	19	55.07	10.14	39	51.3%	0.32 [-0.24, 0.87]		🔴
Way et al 2012 (5-14yrs; CBRS-P)	77.5	19	24	46.8	4.9	17	48.7%	2.02 [1.24, 2.79]		🔴
Total (95% CI)			43			56	100.0%	1.14 [-0.52, 2.81]		

Heterogeneity: Tau² = 1.33; Chi² = 12.35, df = 1 (P = 0.0004); I² = 92%
Test for overall effect: Z = 1.34 (P = 0.18)

Risk of bias legend
(A) Overall RoB

ASR Thought Complaints Self Report (T-score)

pFAS and ASR Thought Complaints – Self-report (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR)	3.8	0.39	47	3.49	0.36	58	100.0%	0.82 [0.42, 1.22]		🔴
Total (95% CI)			47			58	100.0%	0.82 [0.42, 1.22]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.02 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

ARND/Others and ASR Thought Complaints – Self-report (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lynch et al 2017 (22yrs; ASR; Cogn Affected)	5.06	0.54	34	3.49	0.36	58	100.0%	3.58 [2.90, 4.26]		🔴
Total (95% CI)			34			58	100.0%	3.58 [2.90, 4.26]		

Heterogeneity: Not applicable
Test for overall effect: Z = 10.36 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Note: Lynch et al 2017 also reports other minor CBCL subdomains.

CBCL Affective Problems Caregiver Report (T-score)

FASD and CBCL Affective Problems – Caregiver (T-score) (4 studies)

Study or Subgroup	Total FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; CBCL-C)	57.8	8.3	38	52.5	4.3	273	26.7%	1.07 [0.72, 1.42]		🔴
May et al 2020b (6-7yrs; CBCL-C)	58.5	8.3	49	53.7	5.1	444	30.5%	0.87 [0.57, 1.17]		🔴
May et al 2020c (6-7yrs; CBCL-C)	56.7	7.1	37	53.2	5.1	331	27.2%	0.66 [0.31, 1.00]		🔴
Popova et al 2019 (7-9yrs; CBCL-C)	57.35	9.22	19	53.88	11.23	39	15.7%	0.32 [-0.23, 0.87]		🔴
Total (95% CI)			143			1087	100.0%	0.78 [0.52, 1.04]		

Heterogeneity: Tau² = 0.04; Chi² = 6.03, df = 3 (P = 0.11); I² = 50%
Test for overall effect: Z = 5.82 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and CBCL Affective Problems – Caregiver (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	56.4	6.8	5	55.7	6.8	771	100.0%	0.10 [-0.78, 0.98]		🔴
Total (95% CI)			5			771	100.0%	0.10 [-0.78, 0.98]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.23 (P = 0.82)

Risk of bias legend
(A) Overall RoB

pFAS and CBCL Affective Problems – Caregiver (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C)	57.5	7.4	44	55.7	6.8	771	100.0%	0.26 [-0.04, 0.57]		🔴
Total (95% CI)			44			771	100.0%	0.26 [-0.04, 0.57]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.70 (P = 0.09)

Risk of bias legend
(A) Overall RoB

ARND/Others and CBCL Affective Problems – Caregiver (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-C; ARND)	59	8.4	44	55.7	6.8	771	100.0%	0.48 [0.17, 0.78]		🔴
Total (95% CI)			44			771	100.0%	0.48 [0.17, 0.78]		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.08 (P = 0.002)

Risk of bias legend
(A) Overall RoB

CBCL Affective Problems Teacher Report (T-score)

FASD and TRF Affective Problems – Teacher (T-score) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
May et al 2020a (6-7yrs; TRF-T)	57.9	8.3	38	52.6	5.4	273	29.8%	0.91 [0.56, 1.25]		🔴
May et al 2020b (6-7yrs; TRF-T)	56.2	7.7	49	52.2	4.9	444	40.1%	0.76 [0.46, 1.06]		🔴
May et al 2020c (6-7yrs; TRF-T)	55.6	6.6	37	52	3.9	331	30.1%	0.85 [0.50, 1.19]		🔴
Total (95% CI)			124			1048	100.0%	0.83 [0.64, 1.02]		

Heterogeneity: Tau² = 0.00; Chi² = 0.40, df = 2 (P = 0.82); I² = 0%
Test for overall effect: Z = 8.60 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

FAS and TRF Affective Problems – Teacher (T-score) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	53	6.7	5	53.1	5.8	771	100.0%	-0.02 [-0.90, 0.86]		🔴
Total (95% CI)			5			771	100.0%	-0.02 [-0.90, 0.86]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.04 (P = 0.97)

Risk of bias legend
(A) Overall RoB

pFAS and TRF Affective Problems – Teacher (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T)	54.1	6.1	44	53.1	5.8	771	100.0%	0.17 [-0.13, 0.48]		🔴
Total (95% CI)			44			771	100.0%	0.17 [-0.13, 0.48]		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.11 (P = 0.27)

Risk of bias legend
(A) Overall RoB

ARND/Others and TRF Affective Problems – Teacher (T-score) (1 study)

Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	56.9	6.8	44	53.1	5.8	771	100.0%	0.65 [0.34, 0.95]		🔴
Total (95% CI)			44			771	100.0%	0.65 [0.34, 0.95]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.16 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

Summary of available outcomes for social

Social			
Study type	**Outcome**	**Data**	**# studies**
Exposure Studies	**Theory of Mind**	N/A	
	Social-Emotional: BSID-III	mean/SD	**1 study:** 1 confirmed unquantifiable
	Social Problems – Caregiver Report: CBCL	T-score	**3 studies:** 2 confirmed unquantifiable, 1 Any PAE, 1 light, 1 moderate
	Social Problems – Caregiver Report: CBCL, SDQ	OR/Frequency	**4 studies:** 1 light, 2 moderate, 1 heavy, 1 confirmed unquantifiable
	Social Problems – Self Report: SDQ	OR/Frequency	**1 studies:** 1 confirmed unquantifiable
	Social Problems– Caregiver Report: CBCL Social Competency Sum, SSIS	mean/SD	**1 study:** 1 very heavy PAE, 1 confirmed unquantifiable
	Social Problems – Teacher Report: SDQ	OR/Frequency	**1 study:** 1 moderate
	Social – Self Report: YSR, SPSI, SRM-SF	mean/SD	**3 studies:** 1 light, 1 moderate, 2 confirmed unquantifiable
Diagnosed Studies	**NEPSY-II Theory of Mind Total**	mean/SD	**2 studies:** 2 FASD
	NEPSY-II Theory of Mind Contextual	mean/SD	**2 studies:** 1 FASD, 1 FAS
	NEPSY-II Theory of Mind Verbal	mean/SD	**2 studies:** 2 FASD
	Theory of Mind: Reading of the Mind's Eye	mean/SD	**2 studies:** 1 FASD, 1 FAS
	Social Skills: Vineland Social Maturity Scale (VSMS), Children's Interpersonal Problem Solving (ChIPS), Griffith Mental Development Scale – Social(GMDS)	mean/SD	**3 studies:** 2 FASD, 1 FAS
	Social Problems/Skills– Caregiver Report: CBCL, SRS	T-score	**7 studies:** 5 FASD, 1 pFAS, 1 ARND/Others
	Social Problems/Skills– Caregiver Report: SSRS, BASC, SIB-R	mean/SD	**4 studies:** 4 FASD
	Social Skills – Teacher Report: SSRS	mean/SD	**3 studies:** 3 FASD
	Social Problems/skills – Self Report	N/A	

GRADE ratings for social

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	Certainty
Certainty assessment							№ of patients		Effect		Certainty
EXPOSURE STUDIES										
Social-Emotional: BSID-III (mean/SD)										
Confirmed unquantifiable PAE										
1	serious[a]	not serious	serious[c]	very serious[d,e,f]	none	28	45	-	**SMD 0.79 lower** (1.28 lower to 0.3 lower)	⊕◯◯◯ Very low
Social Problems – Caregiver Report (T-score)										
Light										
1	serious[a]	not serious	not serious	serious[d]	none	93	6669	-	**SMD 0.04 lower** (0.25 lower to 0.16 higher)	⊕⊕◯◯ Low
Moderate										
1	serious[a]	not serious	not serious	not serious	none	755	66609	-	**SMD 0.13 higher** (0.05 higher to 0.2 higher)	⊕⊕⊕◯ Moderate
Any PAE										
1	serious[a]	not serious	not serious	serious[d]	none	2518	7201	-	**SMD 0.04 higher** (0.00 lower to 0.09 higher)	⊕⊕◯◯ Low
Confirmed unquantifiable PAE										
2	serious[a]	serious[b]	not serious	very serious[d,e,f]	none	140	188	-	**SMD 1.76 higher** (0.81 higher to 2.71 higher)	⊕◯◯◯ Very low
Social Problems – Caregiver Report (Odds of scoring in the 'clinical range'/scoring 'borderline or abnormal'/cut-off unclear)										
Light										
1	serious[a]	not serious	not serious	serious[d]	none	208	690	**OR 1.54** (0.61 to 3.89)	**2 fewer per 1,000** (from 4 fewer to 1 fewer)	⊕⊕◯◯ Low
Moderate										
2	serious[a]	not serious	not serious	serious[d]	none	584	875	**OR 1.12** (0.67 to 1.88)	**1 few per 1,000** (from 2 fewer to 1 fewer)	⊕⊕◯◯ Low
Heavy										
1	serious[a]	not serious	not serious	Serious[d,e]	none	57	690	**OR 2.20** (0.60 to 8.03)	**2 fewer per 1,000** (from 8 fewer to 1 fewer)	⊕⊕◯◯ Low
SDQ Peer Problems – Self-report (cut-off unclear)										
Confirmed unquantifiable										
1	serious[a]	not serious	not serious	serious[d]	none	850	5299	**aOR 1.20** (1.00 to 1.44)	**1 fewer per 1,000** (from 1 fewer to 1 fewer)	⊕⊕◯◯ Low
Social Problems: Social Competency Sum – Caregiver Report (mean/SD)										
Very Heavy										
1	serious[a]	not serious	not serious	serious[e,f]	none	23	22	-	**SMD 0.96 lower** (1.58 lower to 0.34 lower)	⊕⊕◯◯ Low
Social Communication: Social Skills Improvement System – Caregiver Report (mean/SD)										
Confirmed Unquantifiable										

1	seriousa	not serious	not serious	seriouse,f	none	31	39	-	**SMD 0.78 lower** (1.31 lower to 0.26 lower)	⊕⊕◯◯ Low
Social Problems – Teacher Report (Odds of scoring 'borderline or abnormal' score)										
Moderate										
1	seriousa	not serious	not serious	seriousd	none	195	758	**aOR 1.07** (0.50 to 2.30)		⊕⊕◯◯ Low
Social – Self Report (mean/SD)										
Light										
1	seriouss	not serious	not serious	seriousd	none	2536	2530	-	**SMD 0.00** (0.06 lower to 0.06 higher)	⊕⊕◯◯ Low
Moderate										
1	seriouss	not serious	not serious	seriousd	none	66	2530	-	**SMD 0.09 higher** (0.16 lower to 0.33 higher)	⊕⊕◯◯ Low
Confirmed unquantifiable										
2	seriousa	seriousb	not serious	seriouse,f	none	51	44	-	**SMD 1.12 lower** (2.19 lower to 0.06 lower)	⊕◯◯◯ Very low
DIAGNOSED STUDIES										
Theory of Mind Measures: NEPSY-II ToM Total (mean/SD)										
FASD										
2	seriousa	seriousb	not serious	very seriousd,e,f	none	69	51	-	**SMD 0.6 lower** (1.73 lower to 0.52 higher)	⊕◯◯◯ Very Low
Theory of Mind Measures: NEPSY-II ToM Contextual (mean/SD)										
FASD										
1	seriousa	not serious	not serious	seriouse,f	none	37	21	-	**SMD 0.66 lower** (1.21 lower to 0.11 lower)	⊕⊕◯◯ Low
FAS										
1	seriousa	not serious	seriousc	seriouse,f	none	8	19	-	**SMD 0.88 lower** (1.74 lower to 0.01 lower)	⊕◯◯◯ Very low
Theory of Mind Measures: NEPSY-II ToM Verbal (mean/SD)										
FASD										
2	seriousa	seriousb	not serious	very seriousd,e,f	none	69	51	-	**SMD 0.65 lower** (1.63 lower to 0.32 higher)	⊕◯◯◯ Very low
Theory of Mind Measures: Reading of the Mind's Eye (mean/SD)										
FASD										
1	seriousa	not serious	not serious	seriouse,f	none	35	21	-	**SMD 0.97 lower** (1.55 lower to 0.4 lower)	⊕⊕◯◯ Low
FAS										
1	seriousa	not serious	seriousc	Seriouse,f	none	8	19	-	**SMD 2.16 lower** (3.20 lower to 1.13 lower)	⊕◯◯◯ Very low
Social Skills: Higher Scores Favoured (mean/SD)										
FASD										

2	serious[a]	not serious	not serious	serious[e,f]	none	46	50	-	**SMD 0.81 lower** (1.22 lower to 0.39 lower)	⊕⊕◯◯ Low

FAS

1	serious[a]	not serious	serious[c]	very serious[d,e,f]	none	34	34	-	**SMD 0.24 lower** (0.72 lower to 0.24 higher)	⊕◯◯◯ Very low

Social Problems/Skills – Caregiver Report (T-score)

FASD

5	serious[a]	serious[b]	not serious	Serious[e,f]	none	153	154	-	**SMD 1.84 higher** (0.87 higher to 2.82 higher)	⊕◯◯◯ Very low

pFAS

1	serious[a]	not serious	not serious	Serious[e,f]	none	20	16	-	**SMD 1.85 higher** (1.05 higher to 2.64 higher)	⊕⊕◯◯ Low

ARND/Others

1	serious[a]	not serious	not serious	Serious[e,f]	none	24	16	-	**SMD 1.91 higher** (1.14 higher to 2.68 higher)	⊕⊕◯◯ Low

Social Problems/Skills – Caregiver Report (mean/SD)

FASD

3	serious[a]	serious[b]	not serious	serious[e,f]	none	111	110	-	**SMD 0.74 lower** (1.25 lower to 0.23 lower)	⊕◯◯◯ Very low

Social Skills – Teacher Report (mean/SD)

FASD

3	serious[a]	not serious	not serious	very serious[d,e,f]	none	91	81	-	**SMD 0.38 lower** (0.79 lower to 0.02 higher)	⊕◯◯◯ Very Low

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.

Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I^2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CI for overall estimate crossed the line of no effect; e) Wide CIs for overall estimate; f) Optimal information size criteria not met.

Meta-analyses for social

Exposure studies

Theory of Mind Scores
N/A

Social-Emotional: BSID-III

Confirmed PAE-Level Unquantifiable and BSID-III Social-Emotional Score (1 study)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Donald et al 2016 (6mnths; BSID-III)	101.25	13.15	28	113.7	17	45	100.0%	-0.79 [-1.28, -0.30]		−
Total (95% CI)			28			45	100.0%	**-0.79 [-1.28, -0.30]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.15 (P = 0.002)

Risk of bias legend
(A) Overall RoB

Social Problems: CBCL – Caregiver Report (T-score)

Light PAE and CBCL Social Problems (T-scores) (1 study)

Study or Subgroup	Light PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Lees et al 2020 (9-11yrs; CBCL-C)	52.4	4.1	93	52.6	4.6	6669	100.0%	-0.04 [-0.25, 0.16]		−
Total (95% CI)			93			6669	100.0%	**-0.04 [-0.25, 0.16]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.42 (P = 0.68)

Risk of bias legend
(A) Overall RoB

Moderate PAE and CBCL Social Problems (T-scores) (1 study)

Study or Subgroup	Moderate PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Lees et al 2020 (9-11yrs; CBCL-C)	53.2	5.1	755	52.6	4.6	6669	100.0%	0.13 [0.05, 0.20]		−
Total (95% CI)			755			6669	100.0%	**0.13 [0.05, 0.20]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 3.36 (P = 0.0008)

Risk of bias legend
(A) Overall RoB

Any PAE and CBCL Social Problems (1 study)

Study or Subgroup	Any PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Lees et al 2020 (9-11yrs; CBCL-C)	52.8	4.6	2518	52.6	4.6	7201	100.0%	0.04 [-0.00, 0.09]		−
Total (95% CI)			2518			7201	100.0%	**0.04 [-0.00, 0.09]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.88 (P = 0.06)

Risk of bias legend
(A) Overall RoB

Confirmed PAE-Level Unquantifiable and CBCL Social Problems (2 studies)

Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Vaurio et al 2011 (6-16yrs; CBCL-C)	69.96	12.86	55	55.96	8.71	55	49.3%	1.27 [0.86, 1.68]		−
Ware et al 2013 (8-16 yrs; CBCL-C)	66.11	9.16	85	51.8	3.63	133	50.7%	2.24 [1.89, 2.58]		−
Total (95% CI)			140			188	100.0%	**1.76 [0.81, 2.71]**		

Heterogeneity: Tau² = 0.43; Chi² = 12.56, df = 1 (P = 0.0004); I² = 92%
Test for overall effect: Z = 3.62 (P = 0.0003)

Risk of bias legend
(A) Overall RoB

Social Problems: CBCL and SDQ – Caregiver Report (Frequency/OR)

Light PAE and CBCL/SDQ Social Problems (Frequency/OR) (1 study)

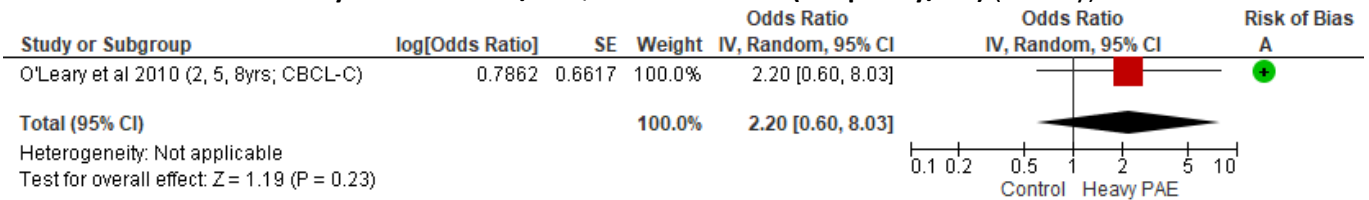| Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2, 5, 8yrs; CBCL-C)	0.4318	0.4725	100.0%	1.54 [0.61, 3.89]		+
Total (95% CI)			**100.0%**	**1.54 [0.61, 3.89]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.91 (P = 0.36)

Risk of bias legend
(A) Overall RoB

Moderate PAE and CBCL/SDQ Social Problems (Frequency/OR) (2 studies)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2013 (5yrs; SDQ-C)	0	0.3537	55.2%	1.00 [0.50, 2.00]		+
Sood et al 2001 (6-7yrs; CBCL-C)	0.2594	0.393	44.8%	1.30 [0.60, 2.80]		−
Total (95% CI)			**100.0%**	**1.12 [0.67, 1.88]**		

Heterogeneity: Tau² = 0.00; Chi² = 0.24, df = 1 (P = 0.62); I² = 0%
Test for overall effect: Z = 0.44 (P = 0.66)

Risk of bias legend
(A) Overall RoB

Heavy PAE and CBCL/SDQ Social Problems (Frequency/OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
O'Leary et al 2010 (2, 5, 8yrs; CBCL-C)	0.7862	0.6617	100.0%	2.20 [0.60, 8.03]		+
Total (95% CI)			**100.0%**	**2.20 [0.60, 8.03]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.19 (P = 0.23)

Risk of bias legend
(A) Overall RoB

Note: O'Leary et al 2010 reports data from 1st trimester and 3rd trimester exposure, 1st trimester exposure was used in the meta-analysis. O'Leary et al 2010 also reports frequency data at separately at 2, 5, and 8yrs. Sood et al 2001 also reports frequency and MD data. Skogerbo et al 2013 reports adjusted OR.

Social Problems: CBCL and SDQ – Self Report (Frequency/OR)

Confirmed PAE-Level Unquantifiable and SDQ Social Problems (aOR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Pfinder et al 2020 (11-17yrs; SDQ-C)	0.1823	0.093	100.0%	1.20 [1.00, 1.44]		?
Total (95% CI)			**100.0%**	**1.20 [1.00, 1.44]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.96 (P = 0.05)

Risk of bias legend
(A) Overall RoB

CBCL Social Competency Sum – Caregiver Report (mean/SD)

Very Heavy PAE and CBCL Social Competency Sum (mean/SD) (1 study)

Study or Subgroup	Very Heavy PAE Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Brown et al 1991 (4-6yrs; CBCL-C)	13.54	3.35	23	16.57	2.84	22	100.0%	-0.96 [-1.58, -0.34]		−
Total (95% CI)			**23**			**22**	**100.0%**	**-0.96 [-1.58, -0.34]**		

Heterogeneity: Not applicable
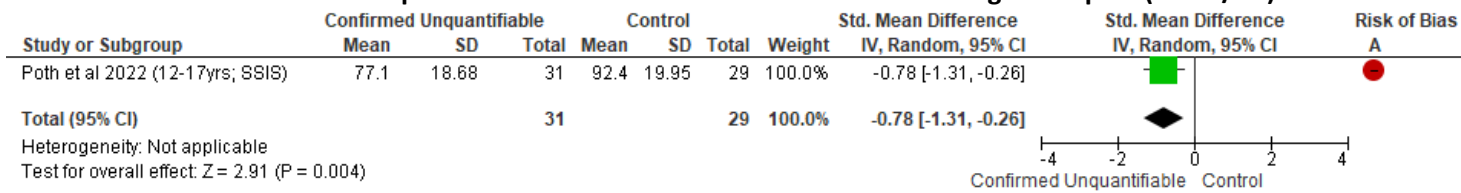Test for overall effect: Z = 3.02 (P = 0.002)

Risk of bias legend
(A) Overall RoB

Social Communication: SSIS – Caregiver Report (mean/SD)

Confirmed PAE-Level Unquantifiable and Social Communication SSIS Caregiver Report (mean/SD)
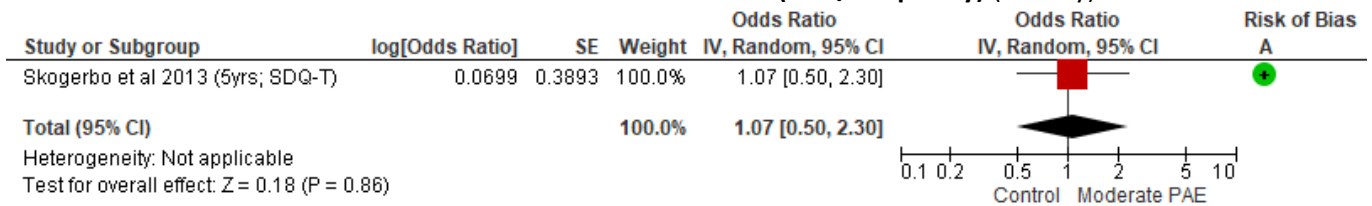
Study or Subgroup	Confirmed Unquantifiable			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Poth et al 2022 (12-17yrs; SSIS)	77.1	18.68	31	92.4	19.95	29	100.0%	-0.78 [-1.31, -0.26]		⊖
Total (95% CI)			31			29	100.0%	-0.78 [-1.31, -0.26]		

Heterogeneity: Not applicable
Test for overall effect: Z = 2.91 (P = 0.004)

Risk of bias legend
(A) Overall RoB

Social Problems: SDQ – Teacher Report (aOR/Frequency)

Moderate PAE and CBCL Social Problems (aOR/Frequency) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Skogerbo et al 2013 (5yrs; SDQ-T)	0.0699	0.3893	100.0%	1.07 [0.50, 2.30]		⊕
Total (95% CI)			100.0%	1.07 [0.50, 2.30]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.18 (P = 0.86)

Risk of bias legend
(A) Overall RoB

Social Problems: YSR, SPSI, SRM-SF – Self Report (mean/SD)

Light PAE and Self Report Social Problems (mean/SD) (1 study)

Study or Subgroup	Light PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Alati et al 2009 (14yrs; YSR)	4	2.2	2536	4	2.3	2530	100.0%	0.00 [-0.06, 0.06]		⊖
Total (95% CI)			2536			2530	100.0%	0.00 [-0.06, 0.06]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

Risk of bias legend
(A) Overall RoB

Moderate PAE and YSR Social Problems (mean/SD) (1 study)

Study or Subgroup	Moderate PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
Alati et al 2009 (14yrs; YSR)	4.2	2.2	66	4	2.3	2530	100.0%	0.09 [-0.16, 0.33]		⊖
Total (95% CI)			66			2530	100.0%	0.09 [-0.16, 0.33]		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.70 (P = 0.49)

Risk of bias legend
(A) Overall RoB

Confirmed unquantifiable PAE and SPSI/SRM-SF Self Report Social Problems (mean/SD) (2 studies)

Study or Subgroup	Confirmed Unquantifiable PAE			Control			Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
	Mean	SD	Total	Mean	SD	Total				
McGee et al 2008a (13-18yrs; SPSI-R)	83.38	22.26	24	118.33	15.92	15	46.9%	-1.70 [-2.46, -0.95]		?
Schonfeld et al 2005 (10-18yrs; SRM-SF)	227.7	43.17	27	254.6	43.48	29	53.1%	-0.61 [-1.15, -0.07]		⊖
Total (95% CI)			51			44	100.0%	-1.12 [-2.19, -0.06]		

Heterogeneity: Tau² = 0.48; Chi² = 5.30, df = 1 (P = 0.02); I² = 81%
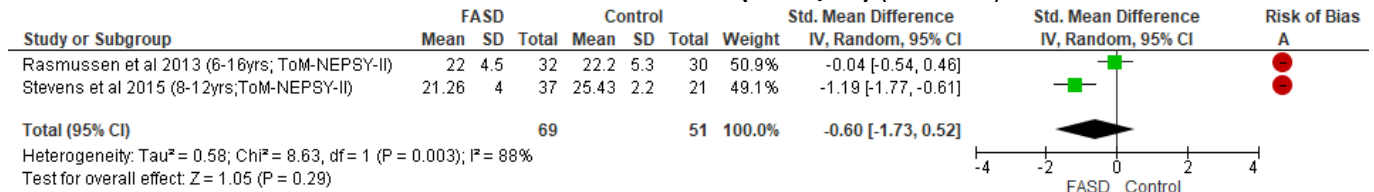Test for overall effect: Z = 2.06 (P = 0.04)

Risk of bias legend
(A) Overall RoB

Note: McGee et al 2008a also reports SPSI-R subdomains. Schonfeld et al 2005 also reports SRM-SF subdomains.

Diagnostic studies

Theory of Mind Scores: NEPSY-II ToM Total (mean/SD)
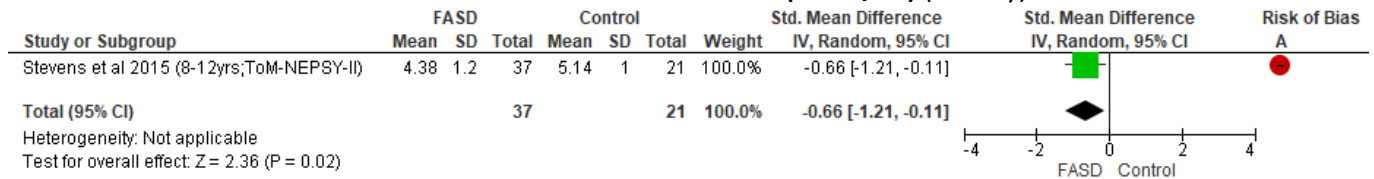
FASD and NEPSY-II ToM Total (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Rasmussen et al 2013 (6-16yrs; ToM-NEPSY-II)	22	4.5	32	22.2	5.3	30	50.9%	-0.04 [-0.54, 0.46]
Stevens et al 2015 (8-12yrs;ToM-NEPSY-II)	21.26	4	37	25.43	2.2	21	49.1%	-1.19 [-1.77, -0.61]
Total (95% CI)			69			51	100.0%	-0.60 [-1.73, 0.52]

Heterogeneity: Tau² = 0.58; Chi² = 8.63, df = 1 (P = 0.003); I² = 88%
Test for overall effect: Z = 1.05 (P = 0.29)

Risk of bias legend
(A) Overall RoB

Theory of Mind Scores: NEPSY-II ToM Contextual (mean/SD)

FASD and NEPSY-II ToM Contextual (mean/SD) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Stevens et al 2015 (8-12yrs;ToM-NEPSY-II)	4.38	1.2	37	5.14	1	21	100.0%	-0.66 [-1.21, -0.11]
Total (95% CI)			37			21	100.0%	-0.66 [-1.21, -0.11]

Heterogeneity: Not applicable
Test for overall effect: Z = 2.36 (P = 0.02)

Risk of bias legend
(A) Overall RoB

FAS and NEPSY-II ToM Contextual (mean/SD) (1 study)

Study or Subgroup	FAS Mean	FAS SD	FAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Lindinger et al 2016 (9-11yrs; ToM-NEPSY-II)	3.5	1.2	8	4.4	0.9	19	100.0%	-0.88 [-1.74, -0.01]
Total (95% CI)			8			19	100.0%	-0.88 [-1.74, -0.01]

Heterogeneity: Not applicable
Test for overall effect: Z = 1.99 (P = 0.05)

Risk of bias legend
(A) Overall RoB

Note: Lindinger et al 2016 also reports other ToM subdomains.

Theory of Mind Scores: NEPSY-II ToM Verbal (mean/SD)

FASD and NEPSY-II ToM Verbal (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Rasmussen et al 2013 (6-16yrs; ToM-NEPSY-II)	17.2	4.6	32	17.9	3.6	30	51.1%	-0.17 [-0.67, 0.33]
Stevens et al 2015 (8-12yrs;ToM-NEPSY-II)	16.88	3.4	37	20.29	1.6	21	48.9%	-1.16 [-1.74, -0.59]
Total (95% CI)			69			51	100.0%	-0.65 [-1.63, 0.32]

Heterogeneity: Tau² = 0.42; Chi² = 6.55, df = 1 (P = 0.01); I² = 85%
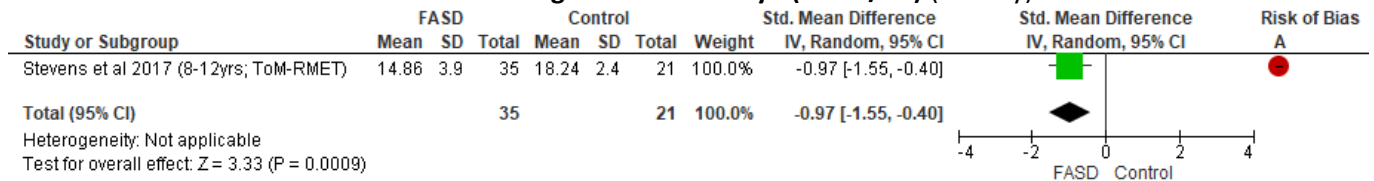Test for overall effect: Z = 1.31 (P = 0.19)

Risk of bias legend
(A) Overall RoB

Theory of Mind Scores: Reading of the Mind's Eye (mean/SD)

FASD and Reading of the Mind's Eye (mean/SD) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Stevens et al 2017 (8-12yrs; ToM-RMET)	14.86	3.9	35	18.24	2.4	21	100.0%	-0.97 [-1.55, -0.40]
Total (95% CI)			35			21	100.0%	-0.97 [-1.55, -0.40]

Heterogeneity: Not applicable
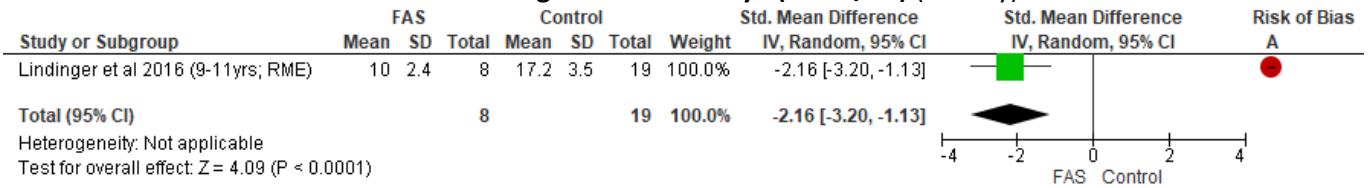Test for overall effect: Z = 3.33 (P = 0.0009)

Risk of bias legend
(A) Overall RoB

Note: Stevens et al 2017 also reports ToM-RMET subdomains.

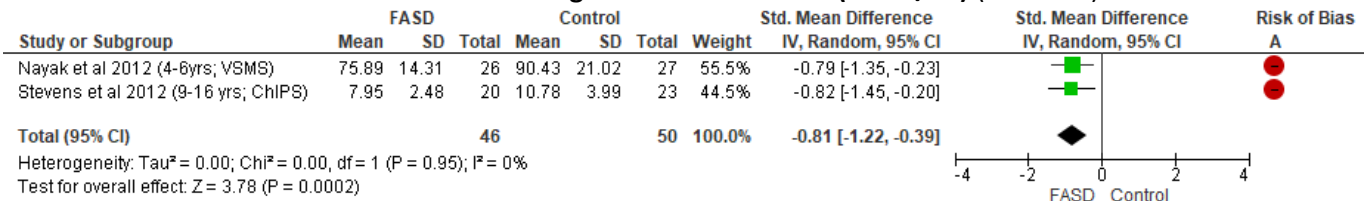## FAS and Reading of the Mind's Eye (mean/SD) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Lindinger et al 2016 (9-11yrs; RME)	10	2.4	8	17.2	3.5	19	100.0%	-2.16 [-3.20, -1.13]	■	●
Total (95% CI)			8			19	100.0%	-2.16 [-3.20, -1.13]	◆	

Heterogeneity: Not applicable
Test for overall effect: Z = 4.09 (P < 0.0001)

Risk of bias legend
(A) Overall RoB

Note: Lindinger et al 2016 also reports other ToM subdomains.

Social Skills: Higher Scores Favoured – Direct Measures (mean/SD)

FASD and Social Skills: Higher Scores Favoured (mean/SD) (2 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Nayak et al 2012 (4-6yrs; VSMS)	75.89	14.31	26	90.43	21.02	27	55.5%	-0.79 [-1.35, -0.23]	■	●
Stevens et al 2012 (9-16 yrs; ChIPS)	7.95	2.48	20	10.78	3.99	23	44.5%	-0.82 [-1.45, -0.20]	■	●
Total (95% CI)			46			50	100.0%	-0.81 [-1.22, -0.39]	◆	

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.95); I² = 0%
Test for overall effect: Z = 3.78 (P = 0.0002)

Risk of bias legend
(A) Overall RoB

Note: Stevens et al 2012 also reports ChIPS subdomains.

FAS and Social Skills: Higher Scores Favoured (mean/SD) (1 study)

Study or Subgroup	FAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Adnams et al 2001 (6-8yrs; GMDS-PS)	88.88	12.245	34	91.68	10.9622	34	100.0%	-0.24 [-0.72, 0.24]	■	●
Total (95% CI)			34			34	100.0%	-0.24 [-0.72, 0.24]	◆	

Heterogeneity: Not applicable
Test for overall effect: Z = 0.98 (P = 0.33)

Risk of bias legend
(A) Overall RoB

Social Problems/Skills: CBCL, SRS – Caregiver Report (T-score)

FASD and Social Problems: CBCL/SRS – Caregiver Report (T-score) (5 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
de Water et al 2021 (8-16yrs; CBCL-C)	64.15	8.99	41	52.4	3.33	43	21.1%	1.73 [1.23, 2.24]	■	●
Mattson & Riley 2000 (4-16yrs; CBCL-C)	64.6	9.55	33	55.6	9.77	33	21.0%	0.92 [0.41, 1.43]	■	●
Popova et al 2019 (7-9yrs; CBCL-C)	58.08	13.97	19	53.33	10.41	39	20.8%	0.40 [-0.15, 0.95]	■	●
Stevens et al 2015 (8-12yrs; CBCL-C)	71.32	9.4	37	52.1	3.5	21	20.0%	2.42 [1.72, 3.13]	■	●
Way et al 2012 (5-14 yrs; SRS-C)	80	10.4	23	44.4	4.4	18	17.1%	4.19 [3.05, 5.32]	■	●
Total (95% CI)			153			154	100.0%	1.84 [0.87, 2.82]	◆	

Heterogeneity: Tau² = 1.11; Chi² = 48.83, df = 4 (P < 0.00001); I² = 92%
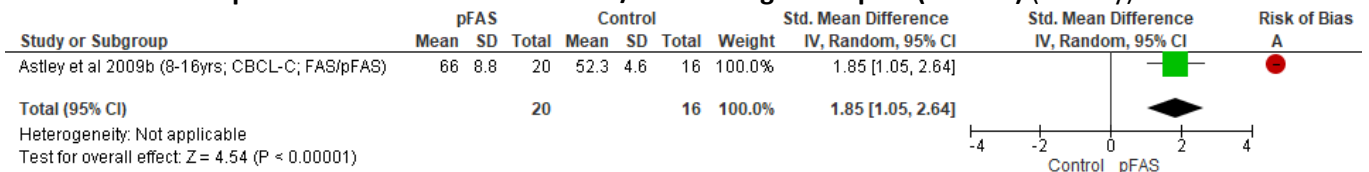Test for overall effect: Z = 3.71 (P = 0.0002)

Risk of bias legend
(A) Overall RoB

Note: Way et al 2012 also reports SRS-C subdomains.

pFAS and Social Problems: CBCL/SRS – Caregiver Report (T-score) (1 study)

Study or Subgroup	pFAS Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; CBCL-C; FAS/pFAS)	66	8.8	20	52.3	4.6	16	100.0%	1.85 [1.05, 2.64]	■	●
Total (95% CI)			20			16	100.0%	1.85 [1.05, 2.64]	◆	

Heterogeneity: Not applicable
Test for overall effect: Z = 4.54 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

ARND/Others and Social Problems: CBCL/SRS – Caregiver Report (T-score) (1 study)

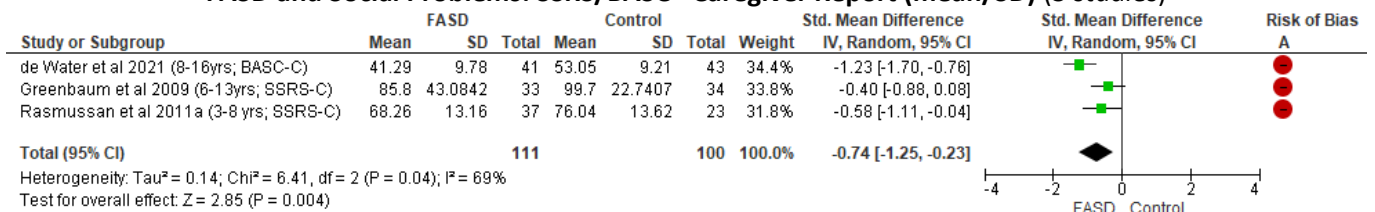| Study or Subgroup	ARND/Others Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; CBCL-C; SE/AE)	66.8	8.8	24	52.3	4.6	16	100.0%	1.91 [1.14, 2.68]		🔴
Total (95% CI)			24			16	100.0%	1.91 [1.14, 2.68]		

Heterogeneity: Not applicable
Test for overall effect: Z = 4.86 (P < 0.00001)

Risk of bias legend
(A) Overall RoB

Social Problems/Skills: SSRS/BASC – Caregiver Report (mean/SD)

FASD and Social Problems: SSRS/BASC– Caregiver Report (mean/SD) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
de Water et al 2021 (8-16yrs; BASC-C)	41.29	9.78	41	53.05	9.21	43	34.4%	-1.23 [-1.70, -0.76]		🔴
Greenbaum et al 2009 (6-13yrs; SSRS-C)	85.8	43.0842	33	99.7	22.7407	34	33.8%	-0.40 [-0.88, 0.08]		🔴
Rasmussan et al 2011a (3-8 yrs; SSRS-C)	68.26	13.16	37	76.04	13.62	23	31.8%	-0.58 [-1.11, -0.04]		🔴
Total (95% CI)			111			100	100.0%	-0.74 [-1.25, -0.23]		

Heterogeneity: Tau² = 0.14; Chi² = 6.41, df = 2 (P = 0.04); I² = 69%
Test for overall effect: Z = 2.85 (P = 0.004)

Risk of bias legend
(A) Overall RoB

Note: Rasmussen et al 2011a also reports SSRS subdomains. Greenbaum et al 2009 reported mean values adjusted for SES, tobacco exposure, abuse, adoption ⁄ foster home history.

Social Problems/Skills: SSRS – Teacher Report (mean/SD)

FASD and Social Problems: SSRS – Teacher Report (mean/SD) (3 studies)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Greenbaum et al 2009 (6-13yrs; SSRS-T)	81.7	33.8929	33	101.3	16.9098	34	36.2%	-0.73 [-1.22, -0.23]		🔴
Jirikowic et al 2008a (5-8yrs; SSRS-T)	96.8	14.4	21	101.3	10.5	24	29.5%	-0.35 [-0.95, 0.24]		🔴
Rasmussen et al 2011a (3-8yrs; SSRS-T)	91.89	18.02	37	92.75	21.14	23	34.3%	-0.04 [-0.56, 0.48]		🔴
Total (95% CI)			91			81	100.0%	-0.38 [-0.79, 0.02]		

Heterogeneity: Tau² = 0.06; Chi² = 3.48, df = 2 (P = 0.18); I² = 43%
Test for overall effect: Z = 1.84 (P = 0.07)

Risk of bias legend
(A) Overall RoB

Note: Greenbaum et al 2009 reported mean values adjusted for SES, tobacco exposure, abuse, adoption ⁄ foster home history.

Social Problems/Skills – Self Report

N/A

Summary of available outcomes for Sensory Processing and Soft Neurological Signs

Sensory Processing and Soft Neurological Signs			
Study type	**Outcome**	**Data**	**# studies**
Exposure Studies	Infant-Toddler Sensory Profile	aOR	1 study: Moderate PAE
	Infant-Toddler Sensory Profile	Frequency	1 study: Moderate PAE
Diagnosed Studies	Short Sensory Processing	mean/SD	1 study: 1 FASD
	Short Sensory Processing	Frequency/OR	1 study: 1 FASD
	Sensory Processing Measure Home	Frequency/OR	1 study: 1 FASD
	Quick Neurological Screen Test	Frequency/OR	1 study: 1 FASD
	Quick Neurological Screen Test	mean/SD	2 studies: 1 FASD, 1 pFAS, 1 ARND/Others

GRADE ratings for Sensory Processing and Soft Neurological Signs

№ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	Certainty
		Certainty assessment				**№ of patients**		**Effect**		**Certainty**
Exposure Studies										
Infant-Toddler Sensory Profile (adjusted odds of scoring <1SD below the mean): Low Registration										
Moderate PAE										
1	not serious	not serious	not serious	serious[d,f]	-	74	126	**aOR 1.21** (0.65 to 2.25)	-	⊕⊕⊕◯ Moderate
Infant-Toddler Sensory Profile (adjusted odds of scoring <1SD below the mean): Sensation Seeking										
Moderate PAE										
1	not serious	not serious	not serious	serious[d,f]	-	74	126	**aOR 0.52** (0.24 to 1.11)	-	⊕⊕⊕◯ Moderate
Infant-Toddler Sensory Profile (adjusted odds of scoring <1SD below the mean): Sensory Sensitivity										
Moderate PAE										
1	not serious	not serious	not serious	serious[d,f]	-	74	126	**aOR 1.36** (0.71 to 2.60)	-	⊕⊕⊕◯ Moderate
Infant-Toddler Sensory Profile (adjusted odds of scoring <1SD below the mean): Sensation Avoiding										
Moderate PAE										
1	not serious	not serious	not serious	serious[d,f]	-	74	126	**aOR 1.32** (0.70 to 2.49)	-	⊕⊕⊕◯ Moderate
Infant-Toddler Sensory Profile (Frequency of 'typical' scores): Low Registration										
Moderate PAE										
1	serious[a]	not serious	not serious	serious[d,f]	-	22/39	25/54	**OR 1.50** (0.66 to 3.44)	-	⊕⊕◯◯ Low
Infant-Toddler Sensory Profile (Frequency of 'typical' scores): Sensation Seeking										
Moderate PAE										
1	serious[a]	not serious	not serious	serious[d,f]	-	24/39	32/54	**OR 1.10** (0.47 to 2.56)	-	⊕⊕◯◯ Low
Infant-Toddler Sensory Profile (Frequency of 'typical' scores): Sensory Sensitivity										

Moderate PAE										
1	serious[a]	not serious	not serious	serious[d,f]	-	21/39	39/54	**OR 0.45** (0.19 to 1.07)	-	⊕⊕◯◯ Low

Infant-Toddler Sensory Profile (Frequency of 'typical' scores): Sensation Avoiding

Moderate PAE										
1	serious[a]	not serious	not serious	serious[d,f]	-	25/39	40/54	**OR 0.63** (0.26 to 1.53)	-	⊕⊕◯◯ Low

Diagnosed Studies

Short Sensory Profile (mean/SD)

FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	25	23	-	**SMD 1.45 lower** (2.09 lower to 0.8 lower)	⊕⊕◯◯ Low

Short Sensory Profile (Frequency/OR) (<1SD on SSP)

FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	11	12	**OR 175.0** (6.43 to 4764.19)	-	⊕⊕◯◯ Low

Sensory Processing Measure (Frequency/OR) (<1SD on SPM)

FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	11	12	**OR 95.0** (4.07 to 2219.98)	-	⊕⊕◯◯ Low

Quick Neurological Screen Test (Frequency/OR) (<24th centile on QNST-II)

FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	21	42	**OR 2.40** (0.67 to 8.65)	-	⊕⊕◯◯ Low

Quick Neurological Screen Test (mean/SD)

FASD										
1	serious[a]	not serious	not serious	serious[e,f]	none	25	26	-	**SMD 1.44 higher** (0.82 higher to 2.06 higher)	⊕⊕◯◯ Low

FAS/pFAS										
1	serious[a]	not serious	not serious	serious[e,f]	none	20	16	-	**SMD 1.47 higher** (0.72 higher to 2.22 higher)	⊕⊕◯◯ Low

ARND/Others										
1	serious[a]	not serious	not serious	serious[e,f]	none	24	16	-	**SMD 1.89 higher** (1.12 higher to 2.66 higher)	⊕⊕◯◯ Low

Notes: CI: confidence interval; **SMD:** standardized mean difference; **OR:** odds ratio.
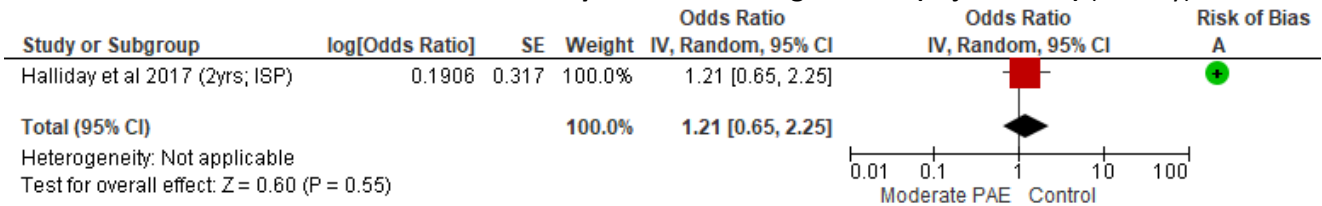
Explanations: a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I^2 >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CI for overall estimate crossed the line of no effect; e) Wide CIs for overall estimate; f) Optimal information size criteria not met.

Meta-analyses for Sensory Processing and Soft Neurological Signs
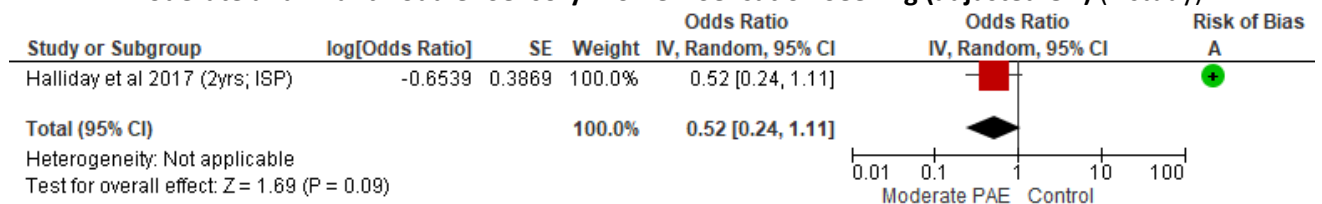
Exposure Studies

Infant-Toddler Sensory Profile – Low Registration (aOR)

Moderate and Infant-Toddler Sensory Profile - Low Registration (adjusted OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Halliday et al 2017 (2yrs; ISP)	0.1906	0.317	100.0%	1.21 [0.65, 2.25]		+
Total (95% CI)			100.0%	**1.21 [0.65, 2.25]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.60 (P = 0.55)
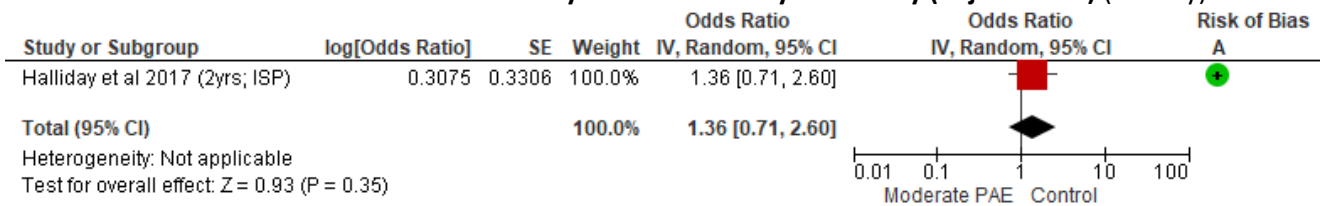
Risk of bias legend
(A) Overall RoB

Infant-Toddler Sensory Profile – Sensation Seeking (aOR)

Moderate and Infant-Toddler Sensory Profile – Sensation Seeking (adjusted OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Halliday et al 2017 (2yrs; ISP)	-0.6539	0.3869	100.0%	0.52 [0.24, 1.11]		+
Total (95% CI)			100.0%	**0.52 [0.24, 1.11]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 1.69 (P = 0.09)
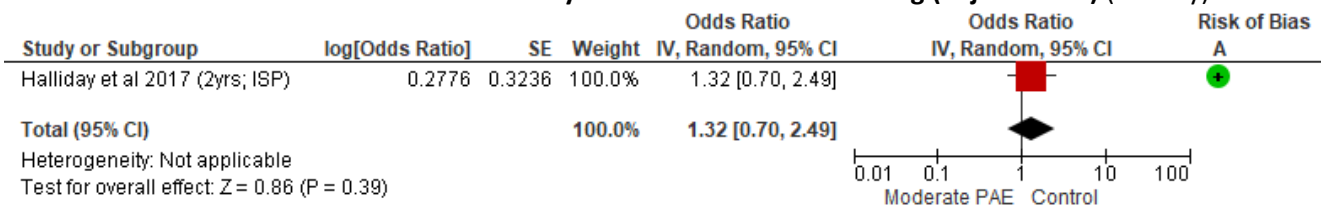
Risk of bias legend
(A) Overall RoB

Infant-Toddler Sensory Profile – Sensory Sensitivity (aOR)

Moderate and Infant-Toddler Sensory Profile – Sensory Sensitivity (adjusted OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Halliday et al 2017 (2yrs; ISP)	0.3075	0.3306	100.0%	1.36 [0.71, 2.60]		+
Total (95% CI)			100.0%	**1.36 [0.71, 2.60]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.93 (P = 0.35)

Risk of bias legend
(A) Overall RoB

Infant-Toddler Sensory Profile – Sensation Avoiding (aOR)

Moderate and Infant-Toddler Sensory Profile – Sensation Avoiding (adjusted OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Halliday et al 2017 (2yrs; ISP)	0.2776	0.3236	100.0%	1.32 [0.70, 2.49]		+
Total (95% CI)			100.0%	**1.32 [0.70, 2.49]**		

Heterogeneity: Not applicable
Test for overall effect: Z = 0.86 (P = 0.39)

Risk of bias legend
(A) Overall RoB

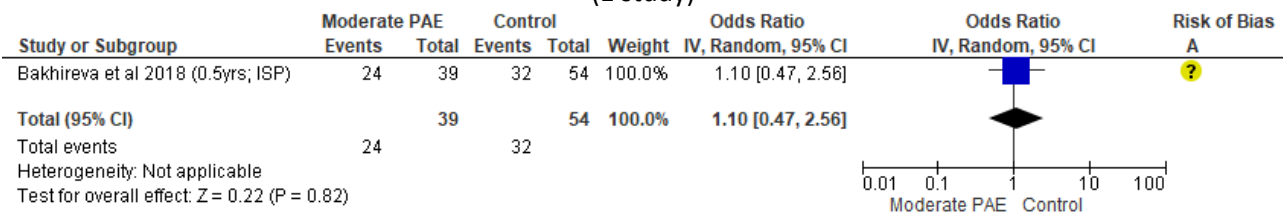Note: Halliday et al 2017 also reports another moderate PAE group and binge exposure.

Infant-Toddler Sensory Profile – Low Registration (Frequency)

Moderate and Infant-Toddler Sensory Profile – Frequency of typical performance for Low Registration (1 study)

Study or Subgroup	Moderate PAE Events	Moderate PAE Total	Control Events	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Bakhireva et al 2018 (0.5yrs; ISP)	22	39	25	54	100.0%	1.50 [0.66, 3.44]		?
Total (95% CI)		39		54	100.0%	**1.50 [0.66, 3.44]**		
Total events	22		25					

Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)
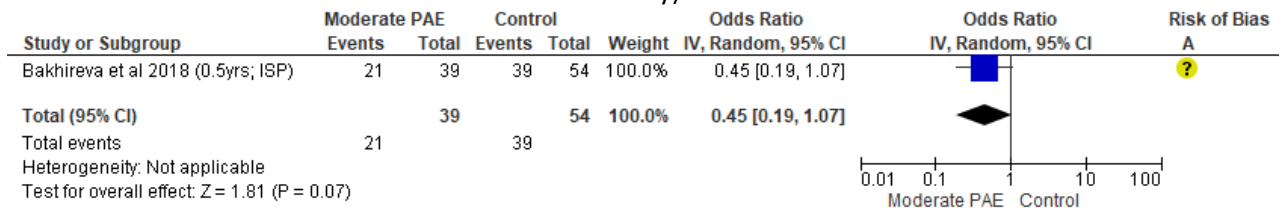
Risk of bias legend
(A) Overall RoB

Infant-Toddler Sensory Profile – Sensation Seeking (Frequency)

Moderate and Infant-Toddler Sensory Profile – Frequency of typical performance for Sensation Seeking (1 study)

Study or Subgroup	Moderate PAE Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Bakhireva et al 2018 (0.5yrs; ISP)	24	39	32	54	100.0%	1.10 [0.47, 2.56]		?
Total (95% CI)		39		54	100.0%	**1.10 [0.47, 2.56]**		
Total events	24		32					

Heterogeneity: Not applicable
Test for overall effect: Z = 0.22 (P = 0.82)

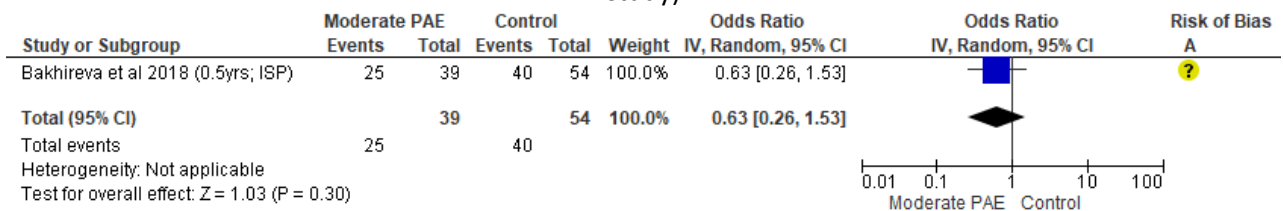0.01 0.1 1 10 100
Moderate PAE   Control

Infant-Toddler Sensory Profile – Sensory Sensitivity (Frequency)

Moderate and Infant-Toddler Sensory Profile – Frequency of typical performance for Sensory Sensitivity (1 study)

Study or Subgroup	Moderate PAE Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Bakhireva et al 2018 (0.5yrs; ISP)	21	39	39	54	100.0%	0.45 [0.19, 1.07]		?
Total (95% CI)		39		54	100.0%	**0.45 [0.19, 1.07]**		
Total events	21		39					

Heterogeneity: Not applicable
Test for overall effect: Z = 1.81 (P = 0.07)

0.01 0.1 1 10 100
Moderate PAE   Control
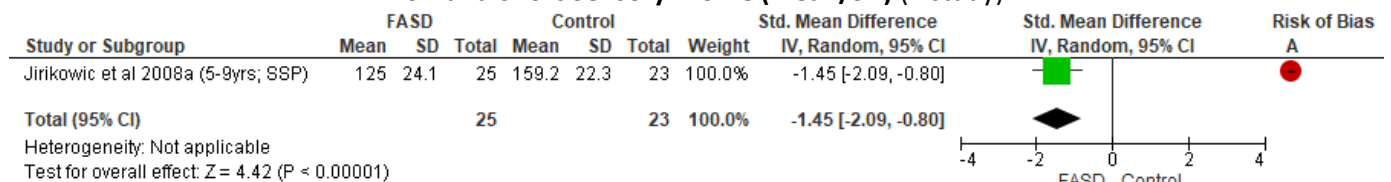
Infant-Toddler Sensory Profile – Sensation Avoiding (Frequency)

Moderate and Infant-Toddler Sensory Profile – Frequency of typical performance for Sensation Avoiding (1 study)

Study or Subgroup	Moderate PAE Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Bakhireva et al 2018 (0.5yrs; ISP)	25	39	40	54	100.0%	0.63 [0.26, 1.53]		?
Total (95% CI)		39		54	100.0%	**0.63 [0.26, 1.53]**		
Total events	25		40					

Heterogeneity: Not applicable
Test for overall effect: Z = 1.03 (P = 0.30)

0.01 0.1 1 10 100
Moderate PAE   Control

Diagnosed studies

Short Sensory Profile (mean/SD)

FASD and Short Sensory Profile (mean/SD) (1 study)

Study or Subgroup	FASD Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Jirikowic et al 2008a (5-9yrs; SSP)	125	24.1	25	159.2	22.3	23	100.0%	-1.45 [-2.09, -0.80]		●
Total (95% CI)			25			23	100.0%	**-1.45 [-2.09, -0.80]**		

Heterogeneity: Not applicable
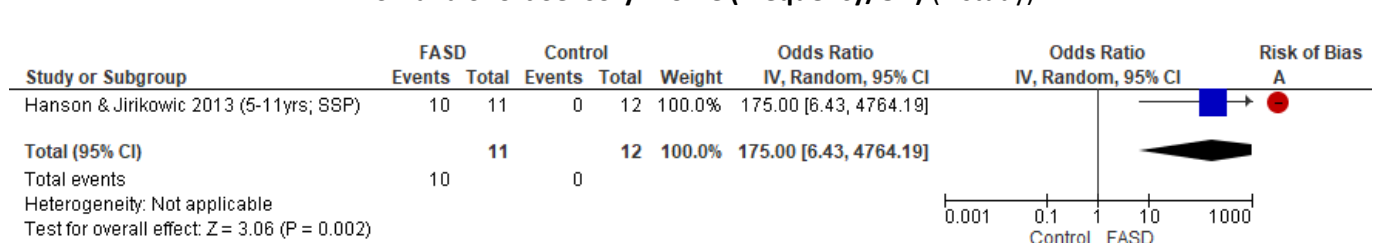Test for overall effect: Z = 4.42 (P < 0.00001)

-4 -2 0 2 4
FASD   Control

Risk of bias legend
(A) Overall RoB

Short Sensory Profile (Frequency/OR)

FASD and Short Sensory Profile (Frequency/OR) (1 study)

Study or Subgroup	FASD Events	Total	Control Events	Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Hanson & Jirikowic 2013 (5-11yrs; SSP)	10	11	0	12	100.0%	175.00 [6.43, 4764.19]		●
Total (95% CI)		11		12	100.0%	**175.00 [6.43, 4764.19]**		
Total events	10		0					

Heterogeneity: Not applicable
Test for overall effect: Z = 3.06 (P = 0.002)
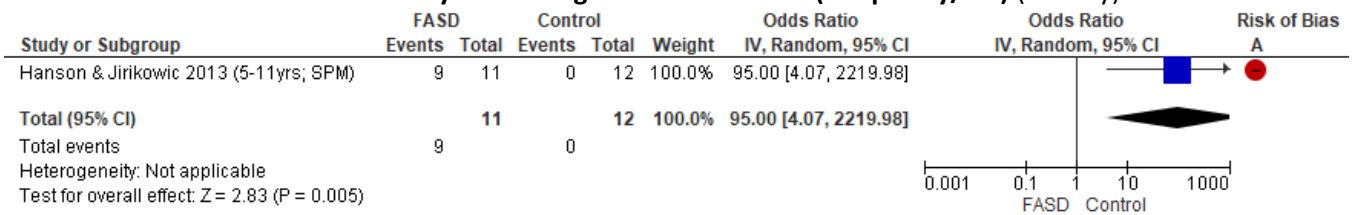
0.001 0.1 1 10 1000
Control   FASD

Risk of bias legend
(A) Overall RoB

Note: Frequency of atypical score on SSP (<1SD).

Sensory Processing Measure - HOME (Frequency/OR)

FASD and Sensory Processing Measure – HOME (Frequency/OR) (1 study)

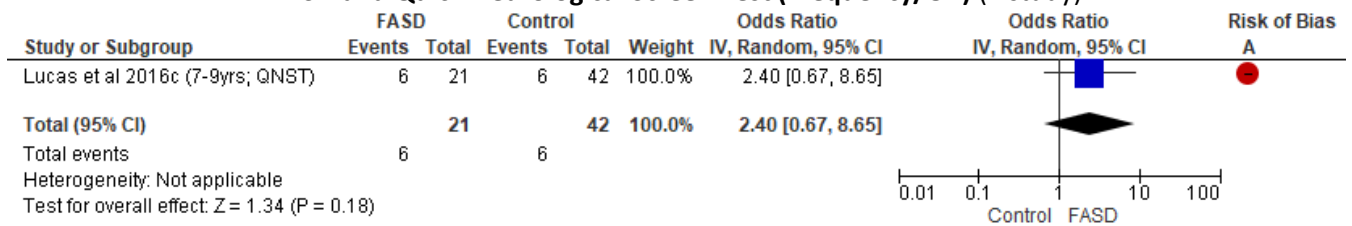| Study or Subgroup	FASD Events	FASD Total	Control Events	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Hanson & Jirikowic 2013 (5-11yrs; SPM)	9	11	0	12	100.0%	95.00 [4.07, 2219.98]		−
Total (95% CI)		11		12	100.0%	95.00 [4.07, 2219.98]		
Total events	9		0					
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.83 (P = 0.005)								

Risk of bias legend
(A) Overall RoB

Note: Frequency of atypical score on SSP (<1SD).

Quick Neurological Screen Test (Frequency/OR)

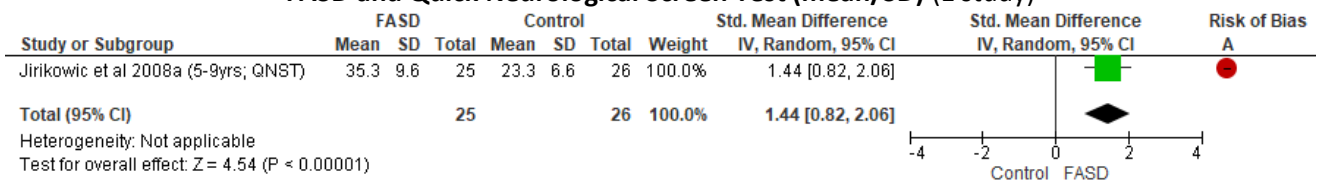**FASD and Quick Neurological Screen Test (Frequency/OR)** (1 study)

Study or Subgroup	FASD Events	FASD Total	Control Events	Control Total	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI	Risk of Bias A
Lucas et al 2016c (7-9yrs; QNST)	6	21	6	42	100.0%	2.40 [0.67, 8.65]		−
Total (95% CI)		21		42	100.0%	2.40 [0.67, 8.65]		
Total events	6		6					
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.34 (P = 0.18)								

Risk of bias legend
(A) Overall RoB

Note: Frequency of atypical score on SNS (<24th centile).
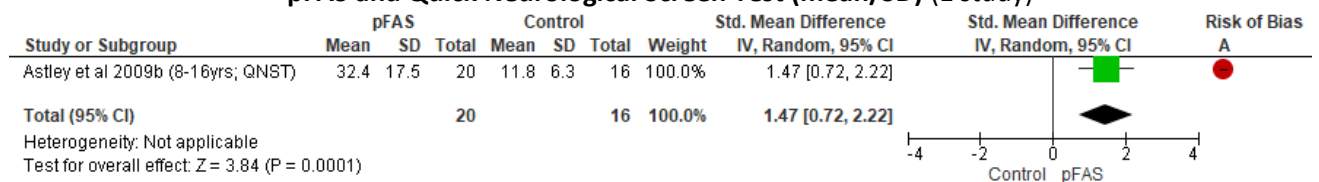
Quick Neurological Screen Test (mean/SD)

FASD and Quick Neurological Screen Test (mean/SD) (1 study)

Study or Subgroup	FASD Mean	FASD SD	FASD Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Jirikowic et al 2008a (5-9yrs; QNST)	35.3	9.6	25	23.3	6.6	26	100.0%	1.44 [0.82, 2.06]		−
Total (95% CI)			25			26	100.0%	1.44 [0.82, 2.06]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 4.54 (P < 0.00001)										

Risk of bias legend
(A) Overall RoB

pFAS and Quick Neurological Screen Test (mean/SD) (1 study)

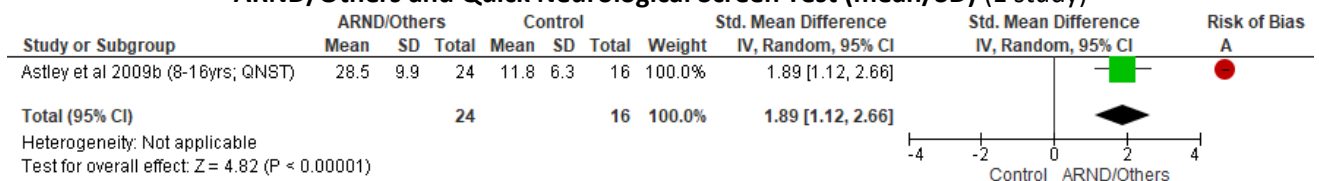| Study or Subgroup	pFAS Mean	pFAS SD	pFAS Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; QNST)	32.4	17.5	20	11.8	6.3	16	100.0%	1.47 [0.72, 2.22]		−
Total (95% CI)			20			16	100.0%	1.47 [0.72, 2.22]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 3.84 (P = 0.0001)										

Risk of bias legend
(A) Overall RoB

Note: Astley 2009 reports FAS/pFAS.

ARND/Others and Quick Neurological Screen Test (mean/SD) (1 study)

Study or Subgroup	ARND/Others Mean	ARND/Others SD	ARND/Others Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI	Risk of Bias A
Astley et al 2009b (8-16yrs; QNST)	28.5	9.9	24	11.8	6.3	16	100.0%	1.89 [1.12, 2.66]		−
Total (95% CI)			24			16	100.0%	1.89 [1.12, 2.66]		
Heterogeneity: Not applicable										
Test for overall effect: Z = 4.82 (P < 0.00001)										

Risk of bias legend
(A) Overall RoB

Note: Astley 2009 reports SE/AE. Astley 2009 also reports ND/AE.