# Supplemental File F

# GRADE Ratings and meta-analyses for neurodevelopmental outcomes

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# Summary of outcomes available for IQ/cognition

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

# GRADE ratings for IQ/cognition

			Certainty assessme	ent		Nº of	patients		Certainty	
Nº of studies	Risk of bias	Inconsisten	icy Indirectness	Imprecisi	on Other	PAE	Control	Relative (95% CI)	Absolute (95% CI) <sup>1</sup>	
EXPOSU	JRE STUDI	ES						1		
Compos	site IQ – In	fants (6 moi	nths–2 years of ag	e)						
Light pr	renatal alco	ohol exposu	ıre (1-20g/w in at	least one t	rimester)					
1	serious	not	serious <sup>c</sup>	serious <sup>d,</sup>	none	68	213	-	SMD 0.09 lower	000
	а	serious		f					(0.37 lower to 0.18 higher)	Very Low
Modera	ate prenata	al alcohol e	kposure (21-100g/	w in at leas	st one trimest	ter)	•			
4	serious	serious <sup>b</sup>	not serious	serious <sup>d,</sup>	none	182	918	-	SMD 0.06 lower	000
	а			e					(0.37 lower to 0.26 higher)	Very Low
Heavy p	orenatal al	cohol expos	sure (101-200g/w	in at least o	one trimester	)				
1	serious	not	not serious	serious <sup>d</sup>	none	186	525	-	SMD 0.06	$\oplus \oplus \bigcirc \bigcirc$
	а	serious							<b>higher</b> (0.11	
									lower to 0.22 higher)	Low
Very he	avy prena	tal alcohol (	exposure (201g+/v	w in at leas	t one trimeste	er)			ingrici /	
2	serious	serious <sup>b</sup>	not serious	serious <sup>e,</sup>	none	46	268	-	SMD 0.89 lower	000
	а			f					(1.76 lower to	Very Low
									0.01 lower)	
	=		posure (Exposure			no studi	es			
	- T		xposure-Level Un	quantifiabl	e			1	T	1
2	serious	coriouch	the set of a set of a set of			40				
2		serious <sup>b</sup>	not serious	very	none	40	57	-	SMD 0.66 lower	
2	a	senous	not serious	very serious <sup>d,</sup> <sub>e,f</sub>	none	40	57	-	(1.45 lower to	⊕⊖⊖⊖ Very Low
	а			serious <sup>d,</sup>	none	40	57	-		
Full-Sca	a le IQ – Sch	ool-Age (4-2	17 yrs)	serious <sup>d,</sup> <sub>e,f</sub>		40	57	-	(1.45 lower to	
Full-Sca Light pr	a le IQ – Sch renatal alco	ool-Age (4-1 ohol exposu	17 γrs) Ire (1-20g/w in at	serious <sup>d,</sup> <sub>e,f</sub> least one tr	rimester)			-	(1.45 lower to 0.13 higher)	Very Low
Full-Sca	a le IQ – Sch	ool-Age (4-2	17 yrs)	serious <sup>d,</sup> <sub>e,f</sub>		2471	2688	-	(1.45 lower to	
Full-Sca <b>Light pr</b>	a ile IQ – Sch renatal alco serious	ool-Age (4-1 ohol exposu not	17 γrs) Ire (1-20g/w in at	serious <sup>d,</sup> <sub>e,f</sub> least one tr	rimester)			-	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10	Very Low
Full-Sca Light pr 2	a lle IQ – Sch renatal alco serious a	ool-Age (4-2 ohol exposu not serious	17 yrs) I <b>re (1-20g/w in at</b> not serious	serious <sup>d,</sup> e,f least one ti serious <sup>d</sup>	r <b>imester)</b> none	2471		-	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01	Very Low
Full-Sca Light pr 2 Modera	a le IQ – Sch renatal alco serious a ate prenata	ool-Age (4-2 ohol exposu not serious al alcohol ex	17 yrs) Ire (1-20g/w in at not serious xposure (21-100g/	serious <sup>d,</sup> e,f least one tr serious <sup>d</sup> /w in at leas	rimester) none st one trimest	2471 :er)	2688	-	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher)	Very Low
Full-Sca Light pr 2	a Ile IQ – Sch renatal alco serious a ate prenata serious	ool-Age (4-2 ohol exposu not serious	17 yrs) I <b>re (1-20g/w in at</b> not serious	serious <sup>d,</sup> e,f least one tr serious <sup>d</sup> /w in at leas serious <sup>d,</sup>	r <b>imester)</b> none	2471		-	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower	Very Low
Full-Sca Light pr 2 Modera	a le IQ – Sch renatal alco serious a ate prenata	ool-Age (4-2 ohol exposu not serious al alcohol ex	17 yrs) Ire (1-20g/w in at not serious xposure (21-100g/	serious <sup>d,</sup> e,f least one tr serious <sup>d</sup> /w in at leas	rimester) none st one trimest	2471 :er)	2688	-	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower (0.47 lower to	Very Low
Full-Sca Light pr 2 Modera 5	a le IQ – Sch renatal alco serious a ate prenata serious a	ool-Age (4-2 ohol exposu not serious al alcohol ex serious <sup>b</sup>	17 yrs) Ire (1-20g/w in at not serious xposure (21-100g/ not serious	serious <sup>d,</sup> e,f least one to serious <sup>d</sup> <b>'w in at leas</b> serious <sup>d,</sup> e	rimester) none st one trimest	2471 ter) 1183	2688	-	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower	Very Low
Full-Sca Light pr 2 Modera 5 Heavy p	a le IQ – Sch renatal alco serious a ate prenata serious a prenatal al	ool-Age (4-2 ohol exposu not serious al alcohol ex serious <sup>b</sup> cohol expos	17 yrs) <b>ire (1-20g/w in at</b> not serious <b>kposure (21-100g/</b> not serious <b>sure (101-200g/w</b>	serious <sup>d,</sup> e,f least one tr serious <sup>d</sup> /w in at least serious <sup>d,</sup> e	rimester) none st one trimest none	2471 (cer) (1183)	2688	-	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower (0.47 lower to 0.11 higher)	Very Low
Full-Sca Light pr 2 Modera 5	a le IQ – Sch renatal alco serious a ate prenata serious a	ool-Age (4-2 ohol exposu not serious al alcohol ex serious <sup>b</sup>	17 yrs) Ire (1-20g/w in at not serious xposure (21-100g/ not serious	serious <sup>d,</sup> e,f least one to serious <sup>d</sup> <b>'w in at leas</b> serious <sup>d,</sup> e	rimester) none st one trimest	2471 ter) 1183	2688	-	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower (0.47 lower to	Very Low
Full-Sca Light pr 2 Modera 5 Heavy p	a le IQ – Sch renatal alco serious a ate prenata serious a orenatal al serious	ool-Age (4-2 ohol exposu not serious al alcohol ex serious <sup>b</sup> cohol expos	17 yrs) <b>ire (1-20g/w in at</b> not serious <b>kposure (21-100g/</b> not serious <b>sure (101-200g/w</b>	serious <sup>d,</sup> e,f least one to serious <sup>d</sup> /w in at least serious <sup>d,</sup> e in at least o serious <sup>d,</sup>	rimester) none st one trimest none	2471 (cer) (1183)	2688	-	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower (0.47 lower to 0.11 higher) SMD 0.98 higher (0.46 lower to 2.42	Very Low
Full-Sca Light pr 2 Modera 5 Heavy p 3	a le IQ – Sch renatal alco serious a ate prenatal serious a orenatal al serious a	ool-Age (4-: ohol exposu not serious al alcohol ex serious <sup>b</sup> cohol expose serious <sup>b</sup>	17 γrs) re (1-20g/w in at not serious xposure (21-100g/ not serious sure (101-200g/w not serious	serious <sup>d,</sup> e,f least one tr serious <sup>d</sup> /w in at least serious <sup>d,</sup> e in at least c serious <sup>d,</sup> e	rimester) none st one trimest none one trimester none	2471 (cer) 1183 ) 374	2688	- -	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower (0.47 lower to 0.11 higher) SMD 0.98 higher (0.46	Very Low
Full-Sca Light pr 2 Modera 5 Heavy p 3	a le IQ – Sch renatal alco serious a ate prenatal serious a orenatal al serious a	ool-Age (4-2 ohol exposu not serious al alcohol ex serious <sup>b</sup> cohol expos serious <sup>b</sup>	17 yrs) <b>ire (1-20g/w in at</b> not serious <b>kposure (21-100g/</b> not serious <b>sure (101-200g/w</b>	serious <sup>d,</sup> e,f least one tr serious <sup>d</sup> /w in at least serious <sup>d,</sup> e in at least c serious <sup>d,</sup> e	rimester) none st one trimest none one trimester none	2471 (cer) 1183 ) 374	2688 3126 1095	-	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower (0.47 lower to 0.11 higher) SMD 0.98 higher (0.46 lower to 2.42	Very Low
Full-Sca Light pr 2 Modera 5 Heavy p 3	a le IQ – Sch renatal alco serious a ate prenatal serious a prenatal al serious a serious a serious a serious a serious a	ool-Age (4-: ohol exposu not serious al alcohol ex serious <sup>b</sup> cohol expose serious <sup>b</sup>	17 γrs) re (1-20g/w in at not serious xposure (21-100g/ not serious sure (101-200g/w not serious	serious <sup>d,</sup> e,f least one tr serious <sup>d</sup> /w in at least serious <sup>d,</sup> e in at least of serious <sup>d,</sup> e w in at least	rimester) none st one trimest none one trimester none	2471 (cer) 1183 ) 374	2688	- -	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower (0.47 lower to 0.11 higher) SMD 0.98 higher (0.46 lower to 2.42 higher) SMD 0.12	Very Low
Full-Sca Light pr 2 Modera 5 Heavy p 3 Very he	a le IQ – Sch renatal alco serious a ate prenata serious a orenatal al serious a a	ool-Age (4-2 ohol exposu not serious al alcohol ex serious <sup>b</sup> cohol expos serious <sup>b</sup>	17 yrs) re (1-20g/w in at not serious xposure (21-100g/ not serious sure (101-200g/w not serious exposure (201g+/m	serious <sup>d,</sup> e,f least one tr serious <sup>d</sup> /w in at least serious <sup>d,</sup> e in at least of serious <sup>d,</sup> e w in at least	rimester) none st one trimest none one trimester none	2471 ter) 1183 ) 374	2688 3126 1095	- -	(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower (0.47 lower to 0.11 higher) SMD 0.98 higher (0.46 lower to 2.42 higher) SMD 0.12 higher (1.30	Very Low
Full-Sca Light pr 2 Modera 5 Heavy p 3 Very he	a le IQ – Sch renatal alco serious a ate prenatal serious a prenatal al serious a serious a serious a serious a serious a	ool-Age (4-2 ohol exposu not serious al alcohol ex serious <sup>b</sup> cohol expos serious <sup>b</sup>	17 yrs) re (1-20g/w in at not serious xposure (21-100g/ not serious sure (101-200g/w not serious exposure (201g+/m	serious <sup>d,</sup> e,f least one tr serious <sup>d</sup> /w in at least serious <sup>d,</sup> e in at least of serious <sup>d,</sup> e w in at least	rimester) none st one trimest none one trimester none	2471 ter) 1183 ) 374	2688 3126 1095		(1.45 lower to 0.13 higher) SMD 0.04 higher (0.01 lower to 0.10 higher) SMD 0.1 lower (0.47 lower to 0.11 higher) SMD 0.98 higher (0.46 lower to 2.42 higher) SMD 0.12	<ul> <li>⊕⊕○○</li> <li>Low</li> <li>⊕○○○</li> <li>Very Low</li> <li>⊕○○○</li> <li>Very</li> <li>Low</li> </ul>

1	serious	not	not serious	very	none	28	28	-	SMD 0.01	000
	а	serious		serious <sup>d,</sup> <sub>e,f</sub>					higher (0.52 lower to 0.53	
									higher)	Very Low
Confirm	ned prenat	al alcohol ex	posure-Level Un	quantifiable	2					
9	serious	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	785	942	-	SMD 1.05 lower	000
	а								(1.32 lower to 0.79 lower)	Very Low
Verbal I	Q – School	-Age (4-17 y	ears of age)							
			re (1-20g/w in at	least one tr	imester)					
2	serious	not serious	s not serious	serious	none	2471	2688	-	SMD 0.04	$\oplus \oplus \bigcirc \bigcirc$
	а								higher (0.01	Low
									lower to 0.10 higher)	
Modera	te prenata	al alcohol ex	 posure (21-100g/	/w in at leas	t one trimes	Ler)			liighei	
3	serious	not seriou		serious		. 1120	2977	-	SMD 0 (0.10	$\oplus \oplus \bigcirc \bigcirc$
	а								lower to 0.09 higher)	Low
Heavy p	prenatal al	cohol exposi	ure (101-200g/w	in at least o	ne trimester	)			1	
3	serious	serious <sup>b</sup>	not	serious <sup>d</sup>	<sup>,e</sup> none	523	1073	-	SMD 0.32 lower	$\oplus OOO$
	а		serious						(0.66 lower to 0.02 higher)	Very Low
Very he	avy prena	tal alcohol e	xposure (201+g/v	w in at least	one trimest	<b>er)</b> – 0 st	udies			
Any leve	el prenata	l alcohol exp	osure (exposure	dichotomiz	ed to yes/no	)				
1	serious <sup>a</sup>	not serious	s not serious	very serious <sup>d,</sup>	e,f	28	28	-	<b>SMD 0.14 lower</b> (0.67 lower to 0.38 higher)	000
										Very Low
	ned prenat		posure-Level un	-		1	T	T		
2	serious a	serious <sup>b</sup>	not serious	serious€	<sup>,f</sup> none	143	90	-	SMD 0.90 lower	<b>@</b> 000
	ŭ								(2.21 lower to 0.40 lower)	Very Low
Perform	nance IQ –	School-Age (	4-17 years of age	.)	• 		• 	•	•	
Light pr	enatal alco	ohol exposu	re (1-20g/w in at	1						
2	serious ª	not serious	s not serious	serious	none	2471	2688	-	SMD 0.02	$\oplus \oplus \bigcirc \bigcirc$
	a								<b>higher</b> (0.03 lower to 0.07 higher)	Low
Modera	te prenata	al alcohol ex	posure (21-100g/	w in at leas	t one trimes	ter)	•		•	
2	serious	not serious	s not serious	serious	none	236	2688	-	SMD 0.05	$\oplus \oplus \bigcirc \bigcirc$
	а								lower	Low

2	a a vi a v a	a a ri a wah	n et eerieue	a a ri a wad e		100	784	1		*
2	serious a	serious <sup>b</sup>	not serious	serious <sup>d,e</sup>	none	189	784	-	SMD 0.60 lower	000
									(1.63 lower to	Very Low
									0.43 higher)	Very Low
Very he	avy prena	tal alcohol exp	osure (201g+/\	w in at least one	trimeste	e <b>r)</b> – 0 stu	udies		0 - ,	
Any lev	el prenata	l alcohol expos	ure (exposure	dichotomized to	o yes/no)					
1	serious	not serious	not serious	very	none	28	28	-	SMD 0.25	000
	а			serious <sup>d,e,f</sup>					higher (0.28	
									lower to 0.77	
									higher)	Very Low
Confirm	ed prenat	al alcohol expo	osure-Level un	quantifiable						
2	serious	serious <sup>b</sup>	not serious	serious <sup>e, f</sup>	none	143	90	-	SMD 0.52 lower	$\oplus OOO$
	а								(1.09 lower to	Very Low
									0.05 lower)	
Non-Ve	rbal IQ – So	chool-Age (4-17	years of age)							
Light pr	enatal alco	ohol exposure (	(1-20g/w in at	least one trimes	<b>ter)</b> – no	studies				
Modera	ite prenata	al alcohol expo	sure (21-100g/	w in at least on	e trimest	er)				
2	serious	serious <sup>b</sup>	not serious	not serious	none	968	1831	-	SMD 0.30	$\oplus \oplus \bigcirc \bigcirc$
	а								higher (0.08	Low
									higher to 0.53	
									higher)	
Heavy p	orenatal al	cohol exposure	e (101-200g/w	in at least one t	rimester)				-	
3	serious	serious <sup>b</sup>	not serious	serious <sup>d,e</sup>	none	481	2004	-	SMD 0.03	$\oplus OOO$
	а								lower	Very Low
									(0.32 lower to	
Verv he	avy prena	tal alcohol exp	osure (201g+/\	w in at least one	trimeste	er)			0.25 higher)	
1	serious	not serious	not serious	very	none	25	21	-	SMD 0.55	000
-	a	not serious	not serious	serious <sup>d,e,f</sup>	none	20			lower	0000
									(1.14 lower to	
									0.04 higher)	Very Low
Any lev	el prenata	l alcohol expos	ure (exposure	dichotomized to	o yes/no)	– no stu	ıdies			
Confirm	ed prenat	al alcohol expo	sure-Level Un	quantifiable						
2	serious	not serious	not serious	serious <sup>e, f</sup>	none	82	82	-	SMD 0.91	$\oplus \oplus \bigcirc \bigcirc$
	а								lower	
									(1.25 lower to	Low
	(MDI<85)								0.58 lower)	
		cohol exposure	(101-200g/w	in at least one t	rimester					
1	serious	not serious	serious <sup>c</sup>	serious <sup>f</sup>	none	243	323	OR 2.11	-	⊕00
	а				_	-	-	(1.49 to		$\sim$
								2.99)		$\bigcirc$
										Very Low
Light, N	loderate, V	/ery Heavy, Any	Level, Confirm	ned-Unquantifia	ble – no s	studies			•	
Low Ful	I-Scale IQ (	< 1 SD)								
Light pr	enatal alco	ohol exposure	(1-20g/w in at	least one trimes	ster)					
1	serious	not serious	not serious	serious <sup>d, f</sup>	none	675	758	OR 1.10	-	$\oplus \oplus \bigcirc \bigcirc$
	а							(0.70 to		
								1.73)		Low
										LOW

1	serious	not serious	not serious	serious <sup>d, f</sup>	none	175	758	OR 1.10	-	$\oplus \oplus \bigcirc \bigcirc$
	а							(0.50 to		
								2.42)		Low
Heavy p	prenatal al	cohol exposure	(101-200g/w	in at least one t	rimester					•
1	serious	not serious	not serious	serious <sup>e,f</sup>	none	20	758	OR 4.60	-	$\oplus \oplus \bigcirc \bigcirc$
-	a			0011000				(1.20 to		
								17.63)		Low
Vonulla		aval Canfirma		<b>ntifichle</b> no st	udios.			17.007		Low
-			d-Level unqua	ntifiable – no st	ludies					
	rbal IQ (< 1	•								
Light pr	renatal alco	ohol exposure (	1-20g/w in at	least one trime	ster)					
1	serious	not serious	not serious	serious <sup>d, f</sup>	none	675	758	OR 0.90	-	$\oplus \oplus \bigcirc \bigcirc$
	а							(0.50 to		
								1.62)		Low
Modera	ate prenata	al alcohol expo	sure (21-100g/	w in at least on	e trimest	er)				2011
1	serious	not serious	not serious	serious <sup>d,f</sup>	none	175	758	OR 1.30		
Т	a	not serious	not senous	Serious	none	1/5	750	(0.60 to		$\oplus \oplus \bigcirc \bigcirc$
								2.82)		
			(101 000 (					2.82)		Low
Heavy p	prenatal al	cohol exposure	(101-200g/w	in at least one t	trimester					
1	serious	not serious	not serious	serious <sup>e, f</sup>	none	20	758	OR 5.90	-	$\oplus \oplus \bigcirc \bigcirc$
	а							(1.40 to		
								24.86)		Low
Very He	eavy, Any I	evel, Confirme	d-Level Unqua	i <b>ntifiable</b> – no st	tudies					
Low Per	rformance	IQ (< 1 SD)								
		. ,	1-20g/w in at	least one trime	ster)					
	1		-		-	C75	750	00.1.00		
1	serious a	not serious	not serious	serious <sup>d,f</sup>	none	675	758	OR 1.00	-	$\oplus \oplus \bigcirc \bigcirc$
	a							(0.60 to		
								1.67)		Low
Modera	ate prenata	al alcohol expo	sure (21-100g/	w in at least on	e trimest	er)				
1	serious	not serious	not serious	serious <sup>d, f</sup>	none	175	758	OR 1.20	-	$\oplus \oplus \bigcirc \bigcirc$
	а							(0.60 to		
								2.40)		Low
Heavy p	prenatal al	cohol exposure	(101-200g/w	in at least one t	rimester			1		
1	serious	not serious	not serious	very	none	20	758	OR 2.70	-	00
1	a	not serious	not serious	serious <sup>d,e,f</sup>	none	20	/30	(0.80 to		
				3011003				9.11)		0
								5.11)		
										Very Low
-			d-Level Unqua	<b>ntifiable</b> – no si	tudies					
Low No	on-Verbal IC	ር (< 85)								
Light pr	renatal alco	ohol exposure (	1-20g/w in at	least one trime	<b>ster)</b> – no	studies				
Modera	ate prenat	al alcohol expo	sure (21-100g/	w in at least on	e trimest	er)				
1	serious	not serious	not serious	serious <sup>d, f</sup>	none	84	1542	OR 0.70	-	$\oplus \oplus \bigcirc \bigcirc$
-	a	not schous	100301003	JEHOUS	none	54	1072	(0.30 to		
								1.63)		
			1101 200-6-					1.05)		Low
	-	-		in at least one t	-					
1	serious	not serious	not serious	serious <sup>d,f</sup>	none	39	1542	OR 0.80	-	$\oplus \oplus \bigcirc \bigcirc$
	а							(0.40 to		
								1.60)		Low
Very He	eavy, Any I	evel, Confirme	d-Level Unqua	<b>ntifiable</b> – no st	tudies					
DIAGNO	OSED STUD	DIES								
Full-Sca										
FASD										

16	serious ª	serious <sup>b</sup>	not seriou	serious <sup>e</sup>	none	750	543	-	<b>SMD 1.71 lower</b> (2.11 lower to	⊕○○○ Very Low
FAS			S						1.31 lower)	
7	serious a	serious <sup>b</sup>	not serio us	serious <sup>e</sup>	none	193	621	-	SMD 2.19 lower (3.18 lower to 1.20 lower)	⊕○○○ Very Low
pFAS (	oFAS or pF/	AS/FAS or dysn	norphic)		-					
7	serious ª	serious⁵	not serious	serious <sup>e</sup>	none	194	440	-	SMD 1.98 lower (2.82 lower to 1.13 lower)	⊕○○○ Very Low
Other I	FASDs (ARN	ND, ND-AE, SE-	AE, Non-synd	Iromal)					· · ·	
7	serious ª	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	203	256	-	<b>SMD 2.91</b> <b>lower</b> (4.04 lower to 1.78 lower)	⊕○○○ Very Low
Verbal	IQ									
FASD										
4	serious ª	serious⁵	not serious	serious <sup>e,f</sup>	none	172	122	-	<b>SMD 3.02</b> <b>lower</b> (4.56 lower to 1.48 lower)	⊕○○○ Very Low
FAS						-	-			
8	serious ª	serious <sup>b</sup>	serious <sup>c</sup>	serious <sup>e</sup>	none	362	883	-	SMD 1.75 lower (2.44 lower to 1.05 lower)	⊕○○○ Very Low
pFAS (	pFAS or pF/	AS/FAS or dysn	norphic)						1.05 lower)	
5	serious a	not serious	serious <sup>c</sup>	serious <sup>e</sup>	none	199	668	-	SMD 0.62 lower (0.88 lower to 0.36 lower)	⊕○○○ Very Low
Other I	FASDs (ARM	ND, ND-AE, SE-	AE, Non-synd	lromal)					0.3010Well)	
4	serious <sup>a</sup>	serious⁵	not serious	serious <sup>e</sup>	none	145	399	-	SMD 1.89 lower (3.00 lower to 0.78 lower)	⊕○○○ Very Low
Perform	nance IQ	L						•	· · · ·	
FASD										
4	serious ª	serious⁵	not serious	serious <sup>e,f</sup>	none	172	122	-	SMD 2.81 lower (4.30 lower to 1.33 lower)	⊕○○○ Very Low
FAS		L	1	1	1	1	1	1		1
4	serious a	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	143	334	-	SMD 2.65 lower (4.29 lower to 1.01 lower)	⊕○○○ Very Low
pFAS ()	FAS or pF4	AS/FAS or dysn	norphic)						1	
1	serious a	not serious	not serious	serious <sup>e,f</sup>	none	23	56	-	SMD 0.95 lower (1.45	$\Phi \Phi \bigcirc \bigcirc$
										Low

		1		T						
									lower to	
)thar [				<b>omal)</b> - 2 studies					0.44 lower)	
	-		-	-	-	60	100			
2	serious ª	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	69	106	-	SMD 2.88 lower (6.01 lower to	⊕○○○ Very Low
									0.25 lower)	
Non-Ve	erbal IQ				<u> </u>				- <b>1</b> - <b>'</b> 1	
ASD										
7	serious	serious <sup>b</sup>	not	serious <sup>e</sup>	none	229	216	-	SMD 1.16	000
	а		serious			_	-		lower (1.57	Very Low
									lower to	,
									0.75 lower)	
FAS	-		-							
8	serious	serious <sup>b</sup>	serious <sup>c</sup>	not serious	none	290	714	-	SMD 0.93	$\oplus OOO$
	а								<b>lower</b> (1.16	Very Low
									lower to 0.70 lower)	
oFAS (r	DFAS or pF/	L AS/FAS or dysn	norphic)						0.701000017	
7	serious	not serious	serious <sup>c</sup>	not serious	none	218	771	_	SMD 0.57	$\Theta \Theta \bigcirc \bigcirc$
,	a	not serious	Schous	not schous	none	210	,,1		lower (0.75	Low
									lower to	2011
									0.40 lower)	
Other F	FASDs (ARN	ND, ND-AE, SE-	AE, Non-syndr	omal)						
4	serious	not serious	serious <sup>c</sup>	not serious	none	103	383	-	SMD 0.76	$\oplus \oplus \bigcirc \bigcirc$
	а								<b>lower</b> (1.03	Low
									lower to 0.49 lower)	
Genera	l Ability Pe	rcentile							0.49 lower)	
FASD	in , is ney i e									
3	serious	not	not	not serious	none	91	843		SMD 0.58	
5	a	serious	serious	not senous	none	91	045	-	lower (0.80	⊕⊕⊕⊖ Moderate
			00.100.0						lower to	Woderate
									0.37 lower)	
FAS										
2	serious	not serious	not	serious <sup>e</sup>	none	43	1034	-	SMD 0.61	$\oplus \oplus \bigcirc \bigcirc$
	а		serious						<b>lower</b> (0.93	Low
									lower to 0.29 lower)	
nFAS (r	EAS or nE	AS/FAS or dysn	norphic)						0.29 lower)	
2	serious	not serious	not	not serious	none	82	1034		SMD 0.46	
Z	a	not senous	serious	not serious	none	02	1054	-	lower (0.69	⊕⊕⊕⊖ Moderate
									lower to	Woderate
									0.23 lower)	
Other F	FASDs (ARM	ND-AE, SE-/	AE, Non-syndr	l omal)					· _ ·	
Other F	FASDs (ARI serious	ND, ND-AE, SE-A	AE, Non-syndro not serious	omal) serious <sup>d</sup>	none	44	761	-	SMD 0.19	$\oplus \oplus \bigcirc \bigcirc$
	-		-	-	none	44	761	-	<b>lower</b> (0.50	⊕⊕⊖⊖ Low
	serious		-	-	none	44	761	-	<b>lower</b> (0.50 lower to	
1	serious a	not serious	-	-	none	44	761	-	<b>lower</b> (0.50	
1 Verbal	serious	not serious	-	-	none	44	761	-	<b>lower</b> (0.50 lower to	
1 Verbal FASD	serious <sup>a</sup> Ability Pero	not serious centile	not serious	serious <sup>d</sup>				-	lower (0.50 lower to 0.11 higher)	Low
1 Verbal	serious <sup>a</sup> Ability Pero serious	not serious centile not	not serious	-	none	44 91	761	-	lower (0.50 lower to 0.11 higher) SMD 0.58	Low $\oplus \oplus \oplus \odot$
1 Verbal FASD	serious <sup>a</sup> Ability Pero	not serious centile	not serious	serious <sup>d</sup>				-	lower (0.50 lower to 0.11 higher)	Low

FAS										
2	a serious	not serious	not serious	serious <sup>d,e</sup>	none	43	1034	-	SMD 0.31 lower (0.63 lower to 0.01 higher)	⊕⊕⊖⊖ Low
pFAS (p	FAS or pF	AS/FAS or dysm	norphic)				•	•		
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 I	ASDs (ARM	ND-AE, SE-A	AE, Non-syndro	omal)						
1	serious ª	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	<b>SMD 0.05</b> <b>lower</b> (0.35 lower to 0.25 higher)	⊕⊕⊖⊖ Low
Non-Ve	erbal 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 <sup>e</sup>	none	43	1034	-	SMD 0.61 lower (1.07 lower to 0.15 lower)	⊕⊕⊖⊖ Low
pFAS (p	FAS or pF	AS/FAS or dysm	norphic)				•			
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 I	ASDs (ARM	ND-AE, SE-A	AE, Non-syndro	omal)						
1	serious ª	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	<b>SMD 0.22</b> <b>lower</b> (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 (l<sup>2</sup> >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)

	Lig	ht PA	E	Control				Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	Mean SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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]	•
Total (95% CI)			68			213	100.0%	-0.09 [-0.37, 0.18]	•
Heterogeneity: Not applicable									- <del>         </del> -10 -5 0 5 10
Test for overall effect: Z = 0.67 (P = 0.51)									Light PAE Control
Risk of bias legend									
(A) Overall Risk of Bias									

#### Moderate PAE and Composite IQ (4 studies)

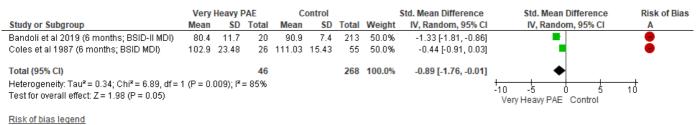
	Mode	erate PAE			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
2.1.1 Low-Moderate Risk of Bias										
Bakhireva et al 2018 (6months; BSID-III Cog) Subtotal (95% CI)	102.4	7.5	39 <b>39</b>	101.3	9.3	54 <b>54</b>	23.2% <b>23.2%</b>	0.13 [-0.29, 0.54] 0.13 [-0.29, 0.54]	<b>†</b>	?
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]	-	•
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]	+	•
McCormack et al 2018 (11-16months; BSID-III Cog) Subtotal (95% CI)	107.95	11.2726	55 <b>143</b>	106.72	10.5399	525 <b>864</b>	29.7% <b>76.8%</b>	0.12 [-0.16, 0.39] - <b>0.13 [-0.55, 0.29]</b>	4	•
Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 8.66, df = 2 (P = 0. Test for overall effect: Z = 0.63 (P = 0.53)	01); I² = 779	6								
Total (95% CI)			182			918	100.0%	-0.06 [-0.37, 0.26]	•	
Heterogeneity: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 9.04, df = 3 (P = 0.1	03); l² = 679	6								10
Test for overall effect: Z = 0.37 (P = 0.71)									Moderate PAE Control	10
Test for subgroup differences: Chi <sup>2</sup> = 0.76, df = 1 (P = Risk of bias legend	: 0.38), I <sup>z</sup> = (	D%								

Risk of bias legend (A) Overall Risk of Bias

#### Heavy PAE and Composite IQ (1 study)

	He	avy PAE			Control			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	I IV, Random, 95% CI 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]	
Total (95% CI)			186			525	100.0%	0.06 [-0.11, 0.22]	
Heterogeneity: Not applicable									-10 -5 0 5 10
Test for overall effect: Z = 0.65 (P = 0.51)									Heavy PAE Control
Risk of bias legend									
(A) Overall Risk of Bias									

#### Very Heavy PAE and Composite IQ (2 studies)



(A) Overall Risk of Bias

# Any Level PAE and Composite IQ (0 studies)

#### **Confirmed PAE-Level Unquantifiable (2 studies)**

	Confirmed	-Unquanti	fiable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.21; Chi <sup>2</sup> = 2.61, df = 1	(P = 0.11); I <sup>2</sup>	= 62%							10 -5 0 5	10
Test for overall effect: Z = 1.65 (P = 0.10)									-1U -5 U 5 ed-Unquantifiable Control	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)

a		ight PAE			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD.	Total	Mean	\$D	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
1.2.1 Mean and/or SD estimated - Low-Mode	rate 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]	Т	
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.02, df = 1	(P = 0.89)	): I <sup>2</sup> = 0%								
Test for overall effect: Z = 1.46 (P = 0.14)	· ·								-10 -5 0 5	10
Test for subgroup differences: Chi <sup>2</sup> = 0.02, df:	= 1 (P = 0.	.89), I <sup>2</sup> = 0	%						Light PAE Control	
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)

		woue	ale	FAL	ани ги	111-20	ale iQ	(5 studies)		
	Mo	derate PA	E		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Subtotal (95% CI)	95.3	12	38 99	92.6	12.7	101 <b>2031</b>	17.8% <b>39.1%</b>	0.21 [-0.16, 0.59] 0.04 [-0.23, 0.31]	<b>†</b>	•
Heterogeneity: Tau² = 0.01; Chi² = 1.50, df = 1 Test for overall effect: Z = 0.28 (P = 0.78)	(P = 0.22	2); I² = 33%	)							
2.2.3 Meand and/or SD estimated - Low-Mod	erate Ris	sk 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) Subtotal (95% CI)	96.8	1.9056	25 <b>200</b>	99.7	1.9056	48 <b>806</b>	13.4% <b>36.8%</b>	-1.51 [-2.05, -0.96] - <b>0.74 [-2.19, 0.71]</b>	<b>→</b>	?
Heterogeneity: Tau <sup>2</sup> = 1.06; Chi <sup>2</sup> = 26.07, df = : Test for overall effect: Z = 1.00 (P = 0.32)	1 (P < 0.0	)0001); I² =	96%							
2.2.4 Mean and/or SD estimated - High Risk (	of Bias^									
Maher et al 2022 (5 yrs; K-BIT) Subtotal (95% CI)	104	8.15	884 <mark>884</mark>	104	8.89	289 <b>289</b>	24.1% <b>24.1%</b>	0.00 [-0.13, 0.13] 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: Tau <sup>2</sup> = 0.09; Chi <sup>2</sup> = 30.01, df =	4 (P < 0.0	)0001); P=	: 87%							10
Test for overall effect: Z = 1.24 (P = 0.22)									-10 -5 0 5 Moderate PAE Control	10
Test for subgroup differences: Chi <sup>2</sup> = 1.08, df	= 2 (P = 0	).58), I <sup>2</sup> = 0	%						Moderater AE Colligo	
Risk of bias legend										
(A) Overall Risk of Rias										

(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)

	н	leavy PAE			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
3.2.1 Mean and/or SD estimated - Low-Mode	erate Risl	k 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) Subtotal (95% CI)	106.3	1.9162	20 <b>40</b>	99.7	1.9162	48 <b>806</b>	31.6% <b>65.3%</b>	3.41 [2.62, 4.19] 1.54 [-2.08, 5.17]	-	?
Heterogeneity: Tau <sup>2</sup> = 6.73; Chi <sup>2</sup> = 64.33, df = Test for overall effect: Z = 0.83 (P = 0.40)	1 (P ≺ 0.0	00001); I² =	98%							
3.2.2 Mean and/or SD estimated - High Risk	of Bias^									
Maher et al 2022 (5 yrs; K-BIT) Subtotal (95% CI)	104	8.15	334 <b>334</b>		8.89	289 <b>289</b>	34.7% <b>34.7%</b>	0.00 [-0.16, 0.16] <b>0.00 [-0.16, 0.16]</b>	<b>†</b>	•
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: Tau <sup>2</sup> = 1.55; Chi <sup>2</sup> = 72.24, df = Test for overall effect: Z = 1.33 (P = 0.18) Test for subgroup differences: Chi <sup>2</sup> = 0.69, df <u>Risk of bias legend</u> (A) Overall Risk of Bias	-								-10 -5 0 5 Heavy PAE Control	10

*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)

v	/ery H	eavy P	AE		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup Me	ean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
4.2.1 High Risk of Bias										
Coles et al 1991 (5-6yrs; K-ABC Mental Composite) 83. Subtotal (95% CI)	.91	12.61	25 <b>25</b>	91.91	13.81	21 <b>21</b>	50.6% <mark>50.6%</mark>	-0.60 [-1.19, -0.00] - <b>0.60 [-1.19, -0.00]</b>	•	•
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) 10 Subtotal (95% CI)	1.5 2	.0941	11 <b>11</b>	99.7	2.0941	48 <b>48</b>	49.4% <b>49.4%</b>	0.85 [0.17, 1.52] 0.85 [0.17, 1.52]	<b>—</b> ◆	?
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: Tau <sup>2</sup> = 0.94; Chi <sup>2</sup> = 9.94, df = 1 (P = 0.002);	l² = 90	)%								
Test for overall effect: Z = 0.16 (P = 0.87)									-10 -5 U 5 Very Heavy PAE Control	10
Test for subgroup differences: Chi <sup>2</sup> = 9.94, df = 1 (P = 0.00	12), I <sup>2</sup> =	89.9%	,						Very neavy FAE Control	
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)

	Any	Level P			Control			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									-10 -5 0 5	10
Test for overall effect: Z = 0.03 (P = 0.98)									Any Level PAE Control	
Risk of bias legend										
(A) Overall Risk of Bias										

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

	Confirme	ed-Unquanti	fiable		Control			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.12; Chi <sup>2</sup> = 41.03, df = 8 (P	< 0.00001)	; I <b>²</b> = 81%							-10 -5 0 5	10
Test for overall effect: Z = 7.75 (P < 0.00001)								Confirm	ned-Unquantifiable Control	

Risk of bias legend (A) Overall Risk of Bias

### Verbal IQ

#### Light PAE and Verbal IQ (2 studies)

	Li	ght PAE			Control		1	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
1.3.1 Mean and/or SD estimated - Low-Moder	ate Risk	of Bias^								
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R) Subtotal (95% CI)	105.2	14.4613	675 675	104.3	14.4613	758 <b>758</b>	27.7% <b>27.7%</b>	0.06 [-0.04, 0.17] <b>0.06 [-0.04, 0.17]</b>	ţ	?
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) Subtotal (95% CI)	109.2	16.7	1796 <b>1796</b>	108.6	16.5	1930 <b>1930</b>	72.3% <b>72.3%</b>	0.04 [-0.03, 0.10] 0.04 [-0.03, 0.10]	•	•
Heterogeneity: Not applicable Test for overall effect: Z = 1.10 (P = 0.27)										
Testion overall effect. $\Sigma = 1.10 (\Gamma = 0.27)$										
Total (95% CI)			2471			2688	100.0%	0.04 [-0.01, 0.10]		
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.18, df = 1 (	P = 0.68	1 <sup>2</sup> = 0%								
Test for overall effect: $Z = 1.56$ (P = 0.12)	,								-10 -5 0 5	10
Test for subgroup differences: Chi <sup>2</sup> = 0.18, df =	1 (P = 0.6)	68), <b>I<sup>2</sup> = O</b>	%						Light PAE Control	
Risk of bias legend		/1								
(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)

	Mo	derate PA	E		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
2.3.1 High Risk of Bias										
Alati et al 2008 (8yrs; WISC-III) Subtotal (95% CI)	108.8	17.2	61 <mark>61</mark>	108.6	16.5	1930 <b>1930</b>	14.1% <b>14.1%</b>	0.01 [-0.24, 0.27] 0.01 [-0.24, 0.27]	<b>•</b>	•
Heterogeneity: Not applicable										
Test for overall effect: Z = 0.09 (P = 0.93)										
2.3.2 Mean and/or SD estimated - High Risk of	of Bias^									
Maher et al 2022 (5 yrs; K-BIT) Subtotal (95% CI)	109	9.63	884 <mark>884</mark>	109	9.63	289 <b>289</b>	52.0% <b>52.0%</b>	0.00 [-0.13, 0.13] <b>0.00 [-0.13, 0.13]</b>	•	•
Heterogeneity: Not applicable Test for overall effect: Z = 0.00 (P = 1.00)										
2.3.3 Mean and/or SD estimated - Low-Mode	rate Risk	of Bias^								
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R)	104	13.9789		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]	1	
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.05, df = 2	(P = 0.98	); I <sup>2</sup> = 0%								
Test for overall effect: Z = 0.09 (P = 0.93)	`								-10 -5 Ó Ś Moderate PAE Control	10
Test for subgroup differences: Chi <sup>2</sup> = 0.05, df =	= 2 (P = 0	.98), I <sup>2</sup> = 0	%						Moderate FAE Control	
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)

	H	eavy PAE			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD.	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
3.3.1 High Risk of Bias										
Korkman et al 1998 (5-9yrs; WISC-R) Subtotal (95% CI)	84.2	14.3	14 <b>14</b>	102	11.8	26 <b>26</b>	15.0% <b>15.0%</b>	-1.37 [-2.10, -0.65] - <b>1.37 [-2.10, -0.65]</b>		•
Heterogeneity: Not applicable										
Test for overall effect: Z = 3.72 (P = 0.0002)										
3.3.2 Mean and/or SD estimated - Low-Moder	rate Risk	of Bias^								
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R) Subtotal (95% CI)	101	46.2358	175 <b>175</b>	104.3	46.2358	758 <b>758</b>	42.3% <b>42.3%</b>	-0.07 [-0.24, 0.09] - <b>0.07 [-0.24, 0.09]</b>		?
Heterogeneity: Not applicable Test for overall effect: Z = 0.85 (P = 0.40)										
3.3.3 Mean and/or SD estimated - High Risk o	f Bias^									
Maher et al 2022 (5 yrs; K-BIT) Subtotal (95% CI)	107	10.37	334 <b>334</b>	109	9.63	289 <b>289</b>	42.7% <b>42.7%</b>	-0.20 [-0.36, -0.04] - <b>0.20 [-0.36, -0.04]</b>	7	•
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: Tau <sup>z</sup> = 0.06; Chi <sup>z</sup> = 12.15, df = 2 Test for overall effect: Z = 1.85 (P = 0.06) Test for subgroup differences: Chi <sup>z</sup> = 12.15, df <u>Risk of bias legend</u> (A) Overall Risk of Bias				6					-10 -5 0 5 Heavy PAE Control	10

*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 L Mean	evel P SD		C Mean	ontrol SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% Cl	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]	, i terretaria de la competitiva de la competi	•
Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.54 (P = 0.59)			28			28	100.0%	-0.14 [-0.67, 0.38]	-10 -5 0 5 Any Level PAE Control	10
<u>Risk of bias legend</u> (A) Overall Risk of Bias										

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

	Confirmed	l-Unquantif	fiable	0	ontrol			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.83; Chi <sup>2</sup> = 15 Test for overall effect: Z = 1.35 (P = 0.		< 0.0001);	I² = 94%					⊢ -1 Confirmed	0 -5 0 5 I-Unquantifiable Control	10

<u>Risk of bias legend</u> (A) Overall Risk of Bias

### Performance IQ

#### Light PAE and Performance IQ (2 studies)

Study or Subgroup	Li Mean	ght PAE SD	Total		Control SD	Total		Std. Mean Difference IV, Random, 95% CI		Std. Mean D IV, Random		Risk of E A
1.4.1 Mean and/or SD estimated - Low-Mode	rate Risk	of Bias/										
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R) Subtotal (95% CI)	105	22.174	675 675	104.8	22.174	758 <b>758</b>	27.7% <b>27.7%</b>	0.01 [-0.09, 0.11] 0.01 [-0.09, 0.11]		t		?
Heterogeneity: Not applicable Test for overall effect: Z = 0.17 (P = 0.86)												
1.4.2 High Risk of Bias												
Alati et al 2008 (8yrs; WISC-III) Subtotal (95% CI)	101.5	16.8	1796 <b>1796</b>	101.1	16.8	1930 <b>1930</b>	72.3% <b>72.3%</b>	0.02 [-0.04, 0.09] 0.02 [-0.04, 0.09]		-		•
Heterogeneity: Not applicable Test for overall effect: Z = 0.73 (P = 0.47)												
Total (95% CI)			2471			2688	100.0%	0.02 [-0.03, 0.07]				
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.06, df = 1	(P = 0.81)	); I <sup>2</sup> = 0%							H-	- Ļ _ ļ	<u> </u>	
Test for overall effect: Z = 0.71 (P = 0.48)									-10	-5 0 Light PAE	Control	10
Test for subgroup differences: Chi <sup>2</sup> = 0.06, df =	= 1 (P = 0.	.81), I² =	0%								Control	
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 Performance IQ (2

					stu	dies)				
	Мо	derate PA	E		Control		:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	\$D	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
2.4.1 Mean and/or SD estimated - Low-Moder	ate Risk	c of Bias^								
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R) Subtotal (95% CI)	104.1	21.9012	175 <b>175</b>	104.3	21.9012	758 <b>758</b>	70.6% <b>70.6%</b>	-0.01 [-0.17, 0.16] - <b>0.01 [-0.17, 0.16]</b>		?
Heterogeneity: Not applicable Test for overall effect: Z = 0.11 (P = 0.91)										
2.4.2 High Risk of Bias										
Alati et al 2008 (8yrs; WISC-III) Subtotal (95% CI)	98.6	16.3	61 61	101.1	16.8	1930 <b>1930</b>	29.4% <b>29.4%</b>	-0.15 [-0.40, 0.11] - <b>0.15 [-0.40, 0.11]</b>		•
Heterogeneity: Not applicable Test for overall effect: Z = 1.14 (P = 0.25)										
Total (95% CI)			236			2688	100.0%	-0.05 [-0.19, 0.09]		
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.82, df = 1 (	P = 0.37	"); l² = 0%								
Test for overall effect: Z = 0.71 (P = 0.48)									-10 -5 0 5 Moderate PAE Control	10
Test for subgroup differences: Chi <sup>2</sup> = 0.82, df =	1 (P = 0)	).37), I² = 0	%						Moderate FAL Control	
<u>Risk of bias legend</u> (A) Overall Risk of Bias										

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

#### Heavy PAE and Performance IQ (2 studies)

Study or Subgroup	He Mean	avy PAE		Mean	Control SD	Total		Std. Mean Difference IV, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl	Risk of Bias A
3.4.1 High Risk of Bias	mean	30	Total	moun	30	Total	reight	iv, Rundom, 55% cr	10, Rundoni, 35% Cl	6
Korkman et al 1998 (5-9yrs; WISC-R) Subtotal (95% CI)	90	11.1	14 <b>14</b>	104.5	12.4	26 <b>26</b>	44.6% <b>44.6%</b>	-1.19 [-1.89, -0.48] - <b>1.19 [-1.89, -0.48]</b>	<b>‡</b>	•
Heterogeneity: Not applicable Test for overall effect: Z = 3.30 (P = 0.0010)										
3.4.2 Mean and/or SD estimated - Low-Moder	rate Risk	of Bias^								
Falgreen Eriksen et al 2012 (5yrs; WPPSI-R) Subtotal (95% CI)	97.9	50.4944	175 <b>175</b>	104.3	50.4944	758 <b>758</b>	55.4% <b>55.4%</b>	-0.13 [-0.29, 0.04] - <b>0.13 [-0.29, 0.04]</b>	7	?
Heterogeneity: Not applicable Test for overall effect: Z = 1.51 (P = 0.13)										
Total (95% CI)			189			784	100.0%	-0.60 [-1.63, 0.43]	•	
Heterogeneity: Tau <sup>2</sup> = 0.49; Chi <sup>2</sup> = 8.24, df = 1	(P = 0.004	4); I <sup>2</sup> = 88 <sup>4</sup>	%						-10 -5 0 5	10
Test for overall effect: Z = 1.14 (P = 0.26)									Heavy PAE Control	10
Test for subgroup differences: Chi <sup>2</sup> = 8.24, df =	: 1 (P = 0.	004), I² =	87.9%						noul, ne contor	
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.

Very Heavy PAE and Performance IQ (0 studies)

#### Any Level PAE and Performance IQ (1 study)

	Any L	evel PA	E	C	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD.	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									-10 -5 0 5 Any Level PAE Control	10
									Any Leven AL Control	
<u>Risk of bias legend</u> (A) Overall Risk of Bias										

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

	Confirmed	nfirmed-Unquantifiable Contr						Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.12; Chi <sup>2</sup> = 3.4 Test for overall effect: Z = 1.78 (P = 0.		0.06); l² =	71%					-10 −10 Confirmed-	) -5 0 5 Unquantifiable Control	10

#### <u>Risk of bias legend</u> (A) Overall Risk of Bias

# Non-Verbal IQ

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

#### Moderate PAE and Non-Verbal IQ (2 studies)

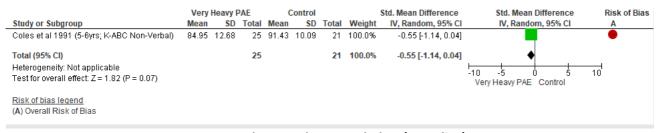
	Mo	derate PA	E	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
2.5.1 Mean and/or SD estimated - Low-Moderate Ris	k of Bia	s^								
O'Callaghan et al 2007 (14yrs; Ravens Non-Verbal) Subtotal (95% CI)	102.5	14.5372	84 <mark>84</mark>	99.9	15.2	1542 <b>1542</b>	42.7% <b>42.7%</b>	0.17 [-0.05, 0.39] <b>0.17 [-0.05, 0.39]</b>	<del>,</del>	?
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) Subtotal (95% CI)	100	7.41	884 <b>884</b>	97	7.41	289 <b>289</b>	57.3% 57.3%	0.40 [0.27, 0.54] <b>0.40 [0.27, 0.54]</b>	,	•
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: Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> = 3.16, df = 1 (P = 0.0 Test for overall effect: $Z = 2.64$ (P = 0.008)	8); I² = 6	8%							-10 -5 0 5 Moderate PAE Control	10
Test for subgroup differences: Chi <sup>2</sup> = 3.16, df = 1 (P = Disk of bios logand	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.

	He	avy P	AE a	nd N	on-V	'erba	al IQ (S	3 studies)		
	He	avy PAE		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD.	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
3.5.1 High Risk of Bias										
Coles et al 2021 (4yrs; DAS-II Non-verbal Composit Subtotal (95% CI)	96.44	16.67	108 <b>108</b>	100.93	13.19	173 <b>173</b>	33.2% <b>33.2%</b>	-0.31 [-0.55, -0.06] - <b>0.31 [-0.55, -0.06]</b>	•	•
Heterogeneity: Not applicable Test for overall effect: Z = 2.48 (P = 0.01)										
3.5.2 Mean and/or SD estimated - Low-Moderate Ris	sk of Bias	٨								
O'Callaghan et al 2007 (1 4yrs; Ravens Non-Verbal) Subtotal (95% CI)	100.8	14.4562	39 <b>39</b>	99.9	15.2	1542 <b>1542</b>		0.06 [-0.26, 0.38] 0.06 [-0.26, 0.38]	<b>†</b>	?
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	<b>x</b>									
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: Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 8.97, df = 2 (P = 0.0	01); I <sup>2</sup> = 78	3%								10
Test for overall effect: Z = 0.23 (P = 0.81)									Heavy PAE Control	10
Test for subgroup differences: Chi <sup>2</sup> = 8.97, df = 2 (P =	0.01), l <sup>z</sup> =	: 77.7%							Heavy The Condor	
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)



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

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

	Confirmed	I-Unquanti	fiable	0	Control		:	Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.05, df = Test for overall effect: Z = 5.37 (P < 0.00001		I <sup>2</sup> = 0%							-10 -5 0 5 ed-Unquantifiable Control	10

<u>Risk of bias legend</u> (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)

			Heavy PAE	Control		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)							0.05 0.2 1 5 Control Heavy PAE	20

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)

	-		Light PAE	Control		Odds Ratio		Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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							0.2	0.5 1 2	5
Test for overall effect: Z = 0.41 (P = 0.68)							0.2	Control Light PAE	Ū
Risk of bias legend									
(A) Overall Risk of Bias									

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

log[Odds Ratio]	SE	Moderate PAE Total		Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio IV, Random, 95% Cl	Risk of Bias A
0.0953	0.4023	175	758	100.0%	1.10 [0.50, 2.42]		?
		175	758	100.0%	1.10 [0.50, 2.42]	0.2 0.5 1 2	
			log[Odds Ratio]         SE         Total           0.0953         0.4023         175	log[Odds Ratio]         SE         Total         Total           0.0953         0.4023         175         758	log[Odds Ratio]         SE         Total         Total         Weight           0.0953         0.4023         175         758         100.0%	log[Odds Ratio]         SE         Total         Total         Weight         IV, Random, 95% CI           0.0953         0.4023         175         758         100.0%         1.10 [0.50, 2.42]	log[Odds Ratio]         SE         Total         Total         Weight         IV, Random, 95% Cl         IV, Random, 95% Cl           0.0953         0.4023         175         758         100.0%         1.10 [0.50, 2.42]         Image: Cl         Image: Cl

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

Study or Subgroup	log[Odds Ratio]	SE	Heavy PAE Total		Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio Risk of Bia IV, Random, 95% Cl 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) Heterogeneity: Not applicable Test for overall effect: Z = 2.23 (P = 0.03)			20	758	100.0%	4.60 [1.20, 17.63]	0.05 0.2 1 5 20 Control Heavy PAE

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		Weight	Odds Ratio IV, Random, 95% CI		Odds Ratio IV, Random, 95% Cl	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) Heterogeneity: Not applicable Test for overall effect: Z = 0.35 (P = 0.73)			675	758	100.0%	0.90 [0.50, 1.62]	0.2	0.5 1 2 Control Light PAE	5
<u>Risk of bias legend</u> (A) Overall Risk of Bias									

#### Moderate PAE and Low Verbal IQ (1 study)

Study or Subgroup	log[Odds Ratio]		Moderate PAE Total	Control Total	Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio Risk of Bias IV, Random, 95% Cl 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) Heterogeneity: Not applicable Test for overall effect: Z = 0.67 (P = 0.51)			175	758	100.0%	1.30 [0.60, 2.82]	0.2 0.5 1 2 5 Control Moderate PAE
<u>Risk of bias legend</u> (A) Overall Risk of Bias							

#### Heavy PAE and Low Verbal IQ (1 study)

			Heavy PAE	Control		Odds Ratio	Odds	s Ratio	<b>Risk of Bias</b>
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Rando	om, 95% Cl	Α
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	1.775	0.7339	20	758	100.0%	5.90 [1.40, 24.86]			→ <u>?</u>
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 2.42 (P = 0.02)			20	758	100.0%	5.90 [1.40, 24.86]	0.05 0.2 Control	1 5 Heavy PAE	20

<u>Risk of bias legend</u> (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 Tota		Weight	Odds Ratio IV, Random, 95% Cl		Odds Ratio IV, Random, 95% Cl	Risk of Bias A
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	0	0.2606	675	758	100.0%	1.00 [0.60, 1.67]			?
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.00 (P = 1.00)			675	758	100.0%	1.00 [0.60, 1.67]	L0.2	0.5 1 2 Control Light PAE	5
<u>Risk of bias leqend</u> (A) Overall Risk of Bias									

#### Moderate PAE and Low Performance IQ (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Moderate PAE Total		Weight	Odds Ratio IV, Random, 95% Cl		Odds R IV, Random		1	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) Heterogeneity: Not applicable Test for overall effect: Z = 0.52 (P = 0.61)			175	758	100.0%	1.20 [0.60, 2.40]	0.2	0.5 1 Control	2 Iodera	te PAE	<b>⊣</b> 5
<u>Risk of bias legend</u> (A) Overall Risk of Bias											

#### Heavy PAE and Low Performance IQ (1 study)

			Heavy PAE	Control		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
FalgreenEriksen etal 2012 (5yrs; WPPSI-R less1SD)	0.9933	0.6206	20	758	100.0%	2.70 [0.80, 9.11]		?
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.60 (P = 0.11)			20	758	100.0%	2.70 [0.80, 9.11]	0.05 0.2 1 5 2 Control Heavy PAE	

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)

			Moderate PAE	Control		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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) Heterogeneity: Not applicable			84	1542	100.0%	0.70 [0.30, 1.63]	0.2 0.5 1 2	
Test for overall effect: Z = 0.83 (P = 0.41)							Control Moderate PAE	

Risk of bias legend (A) Overall Risk of Bias

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

			Heavy PAE C	ontrol		Odds Ratio		Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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								0.5 1 2	<u> </u>
Test for overall effect: Z = 0.63 (P = 0.53)							0.2	Control Heavy PAE	5
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)

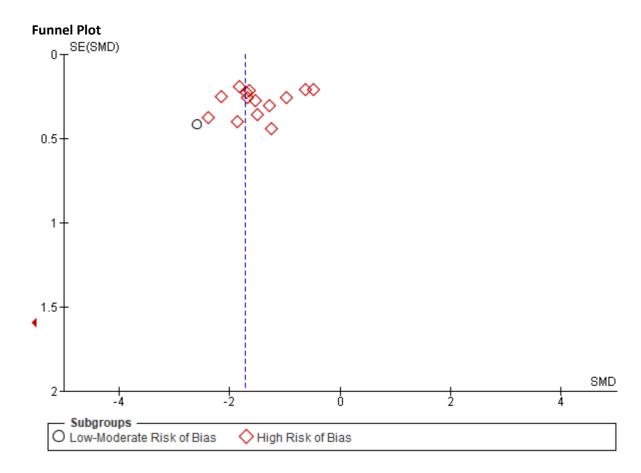
# **Diagnosed studies**

### Full-Scale IQ

#### FASD and Full-Scale IQ (16 studies)

		FASD		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
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]	_ <b>_</b>	?
Subtotal (95% CI)			42			42	7.2%	-7.82 [-18.27, 2.64]		
Heterogeneity: Tau <sup>2</sup> = 55.59; Chi <sup>2</sup> = 41.98, df = 1 (	P < 0.00	001); I <sup>z</sup> :	= 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]	_ <b>—</b>	•
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]	_ <b>—</b>	•
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]	I	•
Subtotal (95% CI)			708			501	92.8%	-1.48 [-1.78, -1.17]	•	
Heterogeneity: Tau <sup>2</sup> = 0.25; Chi <sup>2</sup> = 61.03, df = 13 (	P < 0.00	001); 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: Tau <sup>2</sup> = 0.55; Chi <sup>2</sup> = 123.40, df = 15	(P < 0.0	0001); P	²= 88%							+
Test for overall effect: Z = 8.31 (P < 0.00001)									FASD Control	4
Test for subgroup differences: Chi <sup>2</sup> = 1.41, df = 1	(P = 0.23	i), i <b>z</b> = 29	3.1%						1.100 001101	
Risk of bias legend										

(A) Risk of Bias



#### FAS and Full-Scale IQ (7 studies)

			/ <b>10</b> u					aarcoj			
		FAS		С	ontrol		-	Std. Mean Difference	Std. Mea	In Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Ran	dom, 95% Cl	Α
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: Tau <sup>2</sup> = 0.34; Chi <sup>2</sup> = 6.56, df = 1 (P	= 0.01);1	l² = 85%									
Test for overall effect: Z = 3.76 (P = 0.0002)											
2.1.2 High Risk of Bias											
Mattson et al 1997 (WPPSI-RAVISC-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		14.9%	-0.36 [-0.87, 0.15]		-	•
Subtotal (95% CI)			114			493	70.2%	-2.49 [-4.03, -0.94]	-	•	
Heterogeneity: Tau <sup>2</sup> = 2.93; Chi <sup>2</sup> = 116.52, df = 4	(P < 0.00	0001); I <sup>z</sup>	= 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: Tau <sup>2</sup> = 1.64; Chi <sup>2</sup> = 123.59, df = 6	(P < 0.00	0001); I <sup>z</sup>	= 95%						La t	<u> </u>	
Test for overall effect: Z = 4.34 (P < 0.0001)									-10 -5	U 5	10
Test for subgroup differences: Chi <sup>2</sup> = 0.76, df = 1	(P = 0.3)	8), I <sup>2</sup> = 0	1%						FA	S Control	
	,	~									

### pFAS and Full-Scale IQ (7 studies)

							1			
		pFAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of E
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.00, df = 1 (P = 0.99	); I <sup>z</sup> = 0%	6								
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;	0001); P	°= 95%								
· · ·										
Total (95% CI)			194			440	100.0%	-1.98 [-2.82, -1.13]	•	
Heterogeneity: Tau <sup>2</sup> = 1.09; Chi <sup>2</sup> = 86.95, df = 6 (P < 0.0	0001); l <sup>a</sup>	²= 93%							-10 -5 0 5 10	1
Test for overall effect: Z = 4.58 (P < 0.00001)									pFAS Control	,
Test for subgroup differences: Chi² = 8.01, df = 1 (P = 0	.005), I²:	= 87.5%	6							
Risk of bias legend										
(A) Risk of Bias										

### Other FASDs and Full-Scale IQ (7 studies)

	AR	ND/Othe	er	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
4.1.1 Low-Moderate Risk of Bias										
Sullivan et al 2020 FAE (WAIS-R; 13-37yrs) Subtotal (95% CI)	83.12	14.4	56 <b>56</b>	109.37	13.81	59 <b>59</b>	15.7% <b>15.7%</b>	-1.85 [-2.29, -1.41] - <b>1.85 [-2.29, -1.41]</b>	<b>↓</b>	?
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]	<b>←</b>	•
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) Subtotal (95% CI)	100.7	13.65	44 147	106.79	14.11	28 <b>197</b>	15.7% <b>84.3%</b>	-0.44 [-0.92, 0.04] - <b>3.21 [-4.69, -1.73</b> ]		•
Heterogeneity: Tau <sup>2</sup> = 3.11; Chi <sup>2</sup> = 115.52, df = 5 (P < 0.) Test for overall effect: Z = 4.25 (P < 0.0001)	00001); I	<b>*</b> = 96%							•	
Total (95% CI)			203			256	100.0%	-2.91 [-4.04, -1.78]	◆	
Heterogeneity: Tau <sup>2</sup> = 2.05; Chi <sup>2</sup> = 116.61, df = 6 (P < 0.)	00001); I	²= 95%								10
Test for overall effect: Z = 5.06 (P < 0.00001)									ARND/Other Control	10
Test for subgroup differences: Chi <sup>2</sup> = 2.99, df = 1 (P = 0.	.08), l² = l	66.5%							Addenotier Control	
Risk of bias legend										

(A) Risk of Bias

# Verbal IQ

### FASD and Verbal IQ (4 studies)

		FASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
1.2.1 Low-Moderate Risk of Bias										
Kaemingk et al 2003 (WISC-III; 6-16yrs) Subtotal (95% CI)	64.5	2.46	20 <b>20</b>	92.1	2.15	20 <b>20</b>		-11.71 [-14.48, -8.94] - <b>11.71 [-14.48, -8.94]</b>	•	?
Heterogeneity: Not applicable										
Test for overall effect: Z = 8.28 (P < 0.000	01)									
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, d	f= 2 (P =	0.01);1	<sup>2</sup> = 77%	5						
Test for overall effect: Z = 4.52 (P < 0.000)	01)									
Total (95% CI)			172			122	100.0%	-3.02 [-4.56, -1.48]	•	
Heterogeneity: Tau <sup>2</sup> = 2.09; Chi <sup>2</sup> = 58.68,	df = 3 (P	< 0.000	101); l <sup>e</sup> =	= 95%						
Test for overall effect: Z = 3.85 (P = 0.000	1)								-20 -10 0 10 FASD Control	20
Test for subgroup differences: Chi² = 49.3	31, df = 1	(P < 0.0	00001),	l² = 98.0	1%				FASD CONTO	
Risk of bias legend										

(A) Risk of Bias

			FAS	S and	Verb	al IC	<b>) (8 st</b> i	udies)		
		FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
2.3.1 Low-Moderate Risk of Bias										
Sullivan et al 2020 (VVAIS-R; 13-37yrs) Subtotal (95% CI)	79.74	12.51	57 <b>57</b>	108.27	11.98	59 <mark>59</mark>	12.8% <b>12.8%</b>	-2.31 [-2.79, -1.84] - <b>2.31 [-2.79, -1.84]</b>	•	?
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]	<b>_</b>	•
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) Subtotal (95% CI)	68.3	6.5	28 305	82.5	15.2	123 <b>824</b>	13.0% <b>87.2%</b>	-1.01 [-1.43, -0.58] - <b>1.65 [-2.36, -0.94]</b>	•	•
Heterogeneity: Tau <sup>2</sup> = 0.83; Chi <sup>2</sup> = 118.01, df = Test for overall effect: Z = 4.56 (P < 0.00001)	=6(P≺(	).00001	); <b>I²</b> = 96	5%						
Total (95% CI)			362			883	100.0%	-1.75 [-2.44, -1.05]	•	
Heterogeneity: Tau <sup>2</sup> = 0.92; Chi <sup>2</sup> = 148.34, df = Test for overall effect: $Z = 4.94$ (P < 0.00001) Test for subgroup differences: Chi <sup>2</sup> = 2.35, df Risk of bias legend									-10 -5 0 5 FAS Control	10
(A) Risk of Bias										

#### pFAS and Verbal IQ (5 studies)

	. r.					( 10 00			
	pFAS		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
90.91	14.93	23 23	101.27	17.55	56 <mark>56</mark>	16.1% <mark>16.1%</mark>	-0.61 [-1.10, -0.11] - <b>0.61 [-1.10, -0.11]</b>		?
14	15.94	18	24.1	21.46	133	16.1%	-0.48 [-0.98, 0.01]	-	•
5.7	10.2	51	13.4	18.2	87	22.8%	-0.49 [-0.84, -0.14]	-	•
90.2	15.78	19	108.1	14.14	186	16.4%	-1.25 [-1.74, -0.76]	+	•
26.4	23.2	88	38.4	26.9	206	28.6%	-0.46 [-0.72, -0.21]		•
		176			612	83.9%	-0.64 [-0.95, -0.32]	•	
= 0.04);1	I² = 65%								
		199			668	100.0%	-0.62 [-0.88, -0.36]	•	
= 0.08);1	I <b>²</b> = 53%								
									10
(P = 0.9)	3), I² = 0	%						prAS Control	
	<u>Mean</u> 90.91 14 5.7 90.2 26.4 = 0.04); = 0.08);	pFAS           Mean         SD           90.91         14.93           14         15.94           5.7         10.2           90.2         15.78           26.4         23.2           =         0.04); I <sup>a</sup> = 65%	pFAS           Mean         SD         Total           90.91         14.93         23           14         15.94         18           5.7         10.2         51           90.2         15.78         19           26.4         23.2         88           176         =         0.04); I*= 65%	pFAS         C           Mean         SD         Total         Mean           90.91         14.93         23         101.27           23         101.27         23         101.27           14         15.94         18         24.1           5.7         10.2         51         13.4           90.2         15.78         19         108.1           26.4         23.2         88         38.4           176         176         199           = 0.04); I° = 65%         199         199	pFAS         Control Mean         Mean         SD           90.91         14.93         23         101.27         17.55           23         101.27         17.55         23           14         15.94         18         24.1         21.46           5.7         10.2         51         13.4         18.2           90.2         15.78         19         108.1         14.14           26.4         23.2         88         38.4         26.9           0.04); I° = 65%         199         199         199	pFAS         Control Mean         Control SD         Control Mean         SD         Total           90.91         14.93         23         101.27         17.55         56           14         15.94         18         24.1         21.46         133           5.7         10.2         51         13.4         18.2         87           90.2         15.78         19         108.1         14.14         186         26.4         23.2         88         38.4         26.9         206           176         612         176         612         612         668	pFAS         Control Mean         Mean         SD         Total         Weight           90.91         14.93         23         101.27         17.55         56         16.1%           14         15.94         18         24.1         21.46         133         16.1%           5.7         10.2         51         13.4         18.2         87         22.8%           90.2         15.78         19         108.1         14.14         186         16.4%           26.4         23.2         88         38.4         26.9         206         28.6%           0.04); IP = 65%         199         668         100.0%         668         100.0%	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           90.91         14.93         23         101.27         17.55         56         16.1%         -0.61 [-1.10, -0.11]           14         15.94         18         24.1         21.46         133         16.1%         -0.48 [-0.98, 0.01]           5.7         10.2         51         13.4         18.2         87         22.8%         -0.49 [-0.84, -0.14]           90.2         15.78         19         108.1         14.14         186         16.4%         -1.25 [-1.74, -0.76]           26.4         23.2         88         38.4         26.9         206         28.6%         -0.46 [-0.95, -0.32] $= 0.04$ ); I* = 65%         199         668         100.0%         -0.62 [-0.88, -0.36]	pFAS         Control         Std. Mean Difference         Std. Mean Difference         IV, Random, 95% CI         Std. Mean Difference           90.91         14.93         23         101.27         17.55         56         16.1%         -0.61 [-1.10, -0.11]         •           14         15.94         18         24.1         21.46         133         16.1%         -0.61 [-1.10, -0.11]         •           5.7         10.2         51         13.4         18.2         87         22.8%         -0.49 [-0.84, -0.14]         •           90.2         15.78         19         108.1         14.14         186         16.4%         -1.25 [-1.74, -0.76]         •           26.4         23.2         88         38.4         26.9         206         28.6%         -0.46 [-0.95, -0.32]         •           0.04); IP = 65%         -         -         668         100.0%         -0.62 [-0.88, -0.36]         •           -0.08); IP = 53%         -         668         100.0%         -0.62 [-0.88, -0.36]         •         •

### Other FASDs and Verbal IQ (4 studies)

	U	uner	FAS	us an	a ve	rbai	1Q (4 :	studiesj		
	AR	ND/Oth	ег	C	ontrol			Std. Mean Difference	Std. Mean Difference	ce Risk of Bi
Study or Subgroup	Mean	SD.	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% C	A I
4.2.1 Low-Moderate Risk of Bias										
Sullivan et al 2020 FAE (WAIS-R; 13-37yrs) Subtotal (95% CI)	82.55	13.47	58 <b>58</b>	108.27	11.98	59 <b>59</b>		-2.01 [-2.45, -1.56] - <b>2.01 [-2.45, -1.56]</b>		?
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-RAVISC-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) Subtotal (95% CI)	14.6	17.2	39 <b>87</b>	38.4	26.9	206 <b>340</b>	26.3% <b>74.1%</b>	-0.93 [-1.28, -0.57] - <b>1.88 [-3.32, -0.44]</b>		•
Heterogeneity: Tau <sup>2</sup> = 1.51; Chi <sup>2</sup> = 50.59, df = 2 (P < 0.0	00001); P	<sup>2</sup> = 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: Tau <sup>2</sup> = 1.18; Chi <sup>2</sup> = 66.05, df = 3 ( $P < 0.0$	00001); P	²= 95%								+
Test for overall effect: Z = 3.34 (P = 0.0008)									-10 -5 0 4 ARND/Other Control	J IU
Test for subgroup differences: Chi <sup>2</sup> = 0.03, df = 1 (P = 0	0.87), l² =	0%							ARREFORMET CONTROL	
Risk of bias legend										

# Performance IQ

#### FASD and Performance IQ (4 studies)

								~ (		
	I	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	e Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
1.3.1 Low-Moderate Risk of Bias										
Kaemingk et al 2003 (WISC-III; 6-16yrs) Subtotal (95% CI)	73.2	2.46	20 <b>20</b>	103.4	2.17	20 <b>20</b>			•	?
Heterogeneity: Not applicable										
Test for overall effect: Z = 8.31 (P < 0.000	01)									
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]	-	•
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]	-	•
Nayak et al 2012 (MISIC; 6yrs)	67.04	6.71	26	77.45	8.28	27	28.7%	-1.36 [-1.96, -0.76]	-	•
Subtotal (95% CI)			152			102	86.6%	-1.29 [-1.57, -1.01]	•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.26, d	f= 2 (P =	0.88)	; I² = 0%	6						
Test for overall effect: Z = 9.08 (P < 0.000	01)									
Total (95% CI)			172			122	100.0%	-2.81 [-4.30, -1.33]	•	
Heterogeneity: Tau <sup>2</sup> = 1.90; Chi <sup>2</sup> = 55.55,	df = 3 (P	< 0.00	)001); P	²= 95%						1 20
Test for overall effect: Z = 3.72 (P = 0.000	2)								-20 -10 0 10 FASD Control	20
Test for subgroup differences: Chi <sup>2</sup> = 55.	29, df = 1	(P < 0	.00001	), I <sup>z</sup> = 98.	.2%				FASD CONTO	
Risk of bias legend	-									
(A) Risk of Bias										
5 C										

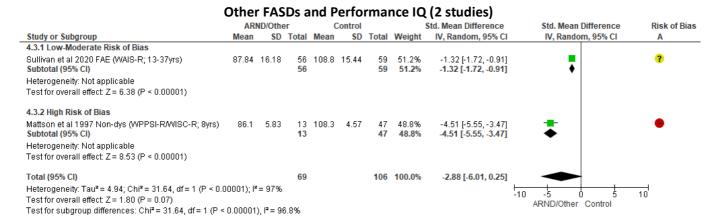
### FAS and Performance IQ (4 studies)

		FAS		0	Control			Std. Mean Difference	5	Std. Mean Difference	Risk of Bi
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% Cl	Α
2.4.1 Low-Moderate Risk of Bias											
Sullivan et al 2020 (WAIS-R; 13-37yrs) Subtotal (95% CI)	84.29	15.47	56 <mark>56</mark>	108.8	15.44	59 <mark>59</mark>	26.0% <b>26.0%</b>	-1.58 [-2.00, -1.16] - <b>1.58 [-2.00, -1.16]</b>		<b>.</b>	?
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-RAVISC-R; 8yrs)	75.35	5.51	34	108.3	3.78	47	23.1%	-7.12 [-8.33, -5.91]			•
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]		+	•
May et al 2015 (WASI; 6-7yrs) Subtotal (95% CI)	92.6	9.13	7 <b>87</b>	104.5	16.84	186 <b>275</b>		-0.71 [-1.47, 0.05] - <b>3.09 [-5.93, -0.26]</b>			•
Heterogeneity: Tau <sup>2</sup> = 6.08; Chi <sup>2</sup> = 82.53, df = Test for overall effect: Z = 2.14 (P = 0.03)	2 (P < 0.	00001);	² = 98	%							
Total (95% CI)			143			334	100.0%	-2.65 [-4.29, -1.01]		•	
Heterogeneity: Tau <sup>2</sup> = 2.64; Chi <sup>2</sup> = 84.12, df =	3 (P < 0.	00001);	I <sup>z</sup> = 96	%					-10		10
Test for overall effect: Z = 3.17 (P = 0.002)									-10	-5 U 5 FAS Control	10
Test for subgroup differences: Chi <sup>2</sup> = 1.08, df	= 1 (P =	0.30), I <b>²</b>	= 7.4%							The Sonitor	
Dick of bias logond											

Risk of bias legend (A) Risk of Bias

### pFAS and Performance IQ (1 study)

		pFAS		C	Control		-	Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD.	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									-20 -10 0 10	20
Test for overall effect: Z = 3.65 (P = 0.0003)									pFAS Control	



Non-Verbal IQ

FASD and Non-Verbal IQ (7 studies)

					011-0	CINC	ין אווע ע	studiesj		
		FASD		C	ontrol		-	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
1.4.1 Low-Moderate Risk of Bias										
Aragon et al 2008b (Leiter-R; 7-17yrs) Subtotal (95% CI)	84.16	15.2	24 <b>24</b>	101.96	16.12	32 <b>32</b>	15.3% <b>15.3%</b>	-1.12 [-1.69, -0.54] - <b>1.12 [-1.69, -0.54]</b>		?
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) Subtotal (95% CI)	91.2	15	25 <b>205</b>	109	14.1	23 <b>184</b>	14.5% <b>84.7%</b>	-1.20 [-1.82, -0.58] - <b>1.19 [-1.68, -0.70]</b>	<b>→</b>	•
Heterogeneity: Tau <sup>2</sup> = 0.26; Chi <sup>2</sup> = 20.85, df = Test for overall effect: Z = 4.77 (P < 0.00001)	5 (P = 0.	0009); l	²= 76%	, ,						
Total (95% CI)			229			216	100.0%	-1.16 [-1.57, -0.75]	•	
Heterogeneity: Tau <sup>2</sup> = 0.20; Chi <sup>2</sup> = 21.01, df =	6 (P = 0.	002); l²:	= 71%						-10 -5 0 5	10
Test for overall effect: Z = 5.52 (P < 0.00001)									FASD Control	10
Test for subgroup differences: Chi <sup>2</sup> = 0.04, df	= 1 (P =	0.84), I <sup>z</sup>	= 0%						11.00 001101	

Risk of bias legend

Risk of bias legend (A) Risk of Bias

(A) Risk of Bias

#### FAS and Non-Verbal IQ (8 studies)

			FAJ	anun	011- V	CINA	וו וע נס	sluuiesj		
		FAS		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD.	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
2.2.1 Low-Moderate Risk of Bias										
Aragon et al 2008b (Leiter-R; 7-17yrs) Subtotal (95% CI)	82.4	12.71	10 <b>10</b>	101.96	16.12	32 <b>32</b>		-1.24 [-2.01, -0.48] - <b>1.24 [-2.01, -0.48]</b>	<b>→</b>	?
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: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 14.02, df Test for overall effect: $Z = 7.29$ (P < 0.00001		0.03); l²	= 57%							
	/									
Total (95% CI)			290			714	100.0%	-0.93 [-1.16, -0.70]	•	
Heterogeneity: Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 14.99, df		0.04); l²	= 53%					-1		10
Test for overall effect: Z = 7.86 (P < 0.00001									FAS Control	
Test for subgroup differences: Chi <sup>2</sup> = 0.67, (	df=1 (P	= 0.41),	I <sup>2</sup> = 0%	, ,						
Dials of high langed										

#### pFAS and Non-Verbal IQ (7 studies)

		pFAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean		Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.84, df = 1 (P Test for overall effect: Z = 4.04 (P < 0.0001)	= 0.36);	I² = 0%								
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 (VVASI; 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		-0.41 [-0.67, -0.16]		•
Subtotal (95% CI)			181			682	82.5%	-0.51 [-0.68, -0.34]	•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 3.81, df = 4 (P	= 0.43);	I <sup>2</sup> = 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: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 6.62, df = 6 (P	= 0.36);	l² = 9%								
Test for overall effect: Z = 6.53 (P < 0.00001)									-10 -5 Ó Ś pFAS Control	10
Test for subgroup differences: Chi <sup>2</sup> = 1.97, df = 1	(P = 0.1	6), I <sup>2</sup> = 4	19.3%						pras control	
Risk of bias legend										
(A) Risk of Bias										

#### Other FASDs and Non-Verbal IQ (4 studies)

ARN	D/Oth	er	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
85.5	19.1	19	92.9	15.6	70	21.9%	-0.45 [-0.96, 0.06]	-	•
84.9	8.76	10	101.45	12.89	20	9.2%	-1.37 [-2.22, -0.53]		•
7.7	4.5	35	22.2	19.1	87	30.8%	-0.88 [-1.29, -0.47]	-	•
14.3	11.9	39	29.1	22.3	206	38.2%	-0.70 [-1.05, -0.35]	•	•
		103			383	100.0%	-0.76 [-1.03, -0.49]	•	
27); I² =	23%								10
								ARND/Other Control	10
	Mean 85.5 84.9 7.7 14.3	Mean         SD           85.5         19.1           84.9         8.76           7.7         4.5	85.5 19.1 19 84.9 8.76 10 7.7 4.5 35 14.3 11.9 39 103	Mean         SD         Total         Mean           85.5         19.1         19         92.9           84.9         8.76         10         101.45           7.7         4.5         35         22.2           14.3         11.9         39         29.1	Mean         SD         Total         Mean         SD           85.5         19.1         19         92.9         15.6           84.9         8.76         10         101.45         12.89           7.7         4.5         35         22.2         19.1           14.3         11.9         39         29.1         22.3	Mean         SD         Total         Mean         SD         Total           85.5         19.1         19         92.9         15.6         70           84.9         8.76         10         101.45         12.89         20           7.7         4.5         35         22.2         19.1         87           14.3         11.9         39         29.1         2.3         206	Mean         SD         Total         Mean         SD         Total         Weight           85.5         19.1         19         92.9         15.6         70         21.9%           84.9         8.76         10         101.45         12.89         20         9.2%           7.7         4.5         35         22.2         19.1         87         30.8%           14.3         11.9         39         29.1         22.3         206         38.2%	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           85.5         19.1         19         92.9         15.6         70         21.9%         -0.45 [-0.96, 0.06]           84.9         8.76         10         101.45         12.89         20         9.2%         -1.37 [-2.22, -0.53]           7.7         4.5         35         22.2         19.1         87         30.8%         -0.88 [-1.29, -0.47]           14.3         11.9         39         29.1         22.3         206         38.2%         -0.70 [-1.05, -0.35]           to 30         29.1         23.8         100.0%         -0.76 [-1.03, -0.49]	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           85.5         19.1         19         92.9         15.6         70         21.9%         -0.45 [-0.96, 0.06]         •           84.9         8.76         10         101.45         12.89         20         9.2%         -1.37 [-2.22, -0.53]         •           7.7         4.5         35         22.2         19.1         87         30.8%         -0.088 [-1.29, -0.47]         •           14.3         11.9         39         29.1         22.3         206         38.2%         -0.70 [-1.05, -0.35]         •           103         383         100.0%         -0.76 [-1.03, -0.49]         •         •           27); IP = 23%         -         -         -         5         0         5

<u>Risk of bias legend</u> (A) Risk of Bias

# General Ability Percentile

#### FASD and General Ability Percentile (3 studies)

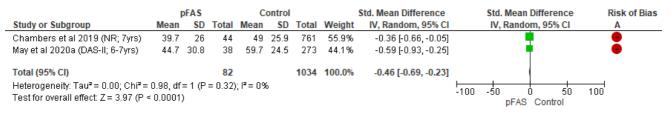
	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
May et al 2020b (DAS-II; 6-7yrs)	35.6	23.8	49	51.1	26	444	53.7%	-0.60 [-0.90, -0.30]	•	•
May et al 2020c (DAS-II; 6-7yrs)	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]	1	•
Total (95% CI)			91			843	100.0%	-0.58 [-0.80, -0.37]		
Heterogeneity: Tau <sup>z</sup> = 0.00; Chi <sup>z</sup> = Test for overall effect: Z = 5.24 (P	•		P = 0.82	?); I² = 09	%				-100 -50 0 50 FASD Control	100

Risk of bias legend (A) Risk of Bias

#### FAS and General Ability Percentile (2 studies)

		FAS		С	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = Test for overall effect: Z = 3.72 (P =			= 0.80)	; I² = 0%	ò				-100 -50 0 50 100 FAS Control

#### pFAS and General Ability Percentile (2 studies)



Risk of bias legend (A) Risk of Bias

#### Other FASDs and General Ability Percentile (1 study)

	ARM	ID/Oth	or	0	ontrol		•	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD SD	Total	Mean	SD.	Total	Weight		IV, Random, 95% Cl	A
Chambers et al 2019 ARND (NR; 7yrs)	44	27.8	44	49	25.9	761	100.0%	-0.19 [-0.50, 0.11]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.24 (P = 0.22)			44			761	100.0%	-0.19 [-0.50, 0.11]	-100 -50 0 50 - ARND/Other Control	
Disk of bias lagrand										

Risk of bias legend (A) Risk of Bias

#### Verbal Ability Percentile

#### FASD and Verbal Ability Percentile (3 studies)

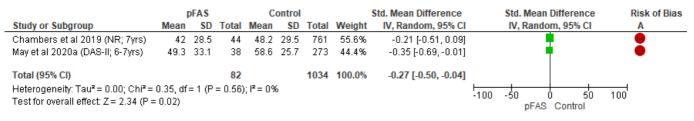
	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl A
May et al 2020b (DAS-II; 6-7yrs)	42.3	26.1	49	54	27.5	444	51.4%	-0.43 [-0.72, -0.13]	<b>•</b> •
May et al 2020c (DAS-II; 6-7yrs)	40.4	25.6	37	60.1	25	331	41.2%	-0.78 [-1.13, -0.44]	<b>•</b> •
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 = Test for overall effect: Z = 4.47 (P			P = 0.30	l); l² = 18	3%				-100 -50 0 50 100 FASD Control

#### Risk of bias legend (A) Risk of Bias

#### FAS and Verbal Ability Percentile (2 studies)

	F	AS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
Chambers et al 2019 (NR; 7yrs)	46.5	27.6	5	48.2	29.5	761	13.0%	-0.06 [-0.94, 0.82]	_ <u>+</u>	•
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: Tau <sup>z</sup> = 0.00; Chi <sup>z</sup> = Test for overall effect: Z = 1.91 (P =		= 1 (P	= 0.55)	; I² = 0%					-100 -50 0 50 - FAS Control	100

#### pFAS and Verbal Ability Percentile (2 studies)



#### Risk of bias legend

(A) Risk of Bias

#### Other FASDs and Verbal Ability Percentile (1 study)

	ARN	D/Oth	ег	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	•	•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.33 (P = 0.74)			44			761	100.0%	-0.05 [-0.35, 0.25]	-100 -50 0 50 1 ARND/Other Control	00
Risk of bias legend										

(A) Risk of Bias

#### Non-Verbal Ability Percentile

#### FASD and Non-Verbal Ability Percentile (3 studies)

	F	ASD		С	ontrol			Std. Mean Difference	Std. Mean Difference Ris	k of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = Test for overall effect: Z = 3.58 (P	•		P = 0.85	i); I² = 0°	%				-100 -50 0 50 100 FASD Control	

#### Risk of bias legend (A) Risk of Bias

(A) NISK UI DIAS

#### FAS and Non-Verbal Ability Percentile (2 studies)

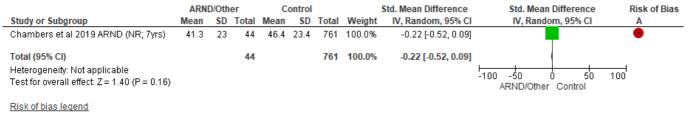
		FAS		C	ontrol		•	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
Chambers et al 2019 (NR; 7yrs)	22	14.1	5	46.4	23.4	761	22.6%	-1.04 [-1.92, -0.16]	•	•
May et al 2020a (DAS-II; 6-7yrs)	43.1	28.1	38	56	26.4	273	77.4%	-0.48 [-0.83, -0.14]	-	•
Total (95% CI)			43			1034	100.0%	-0.61 [-1.07, -0.15]		
Heterogeneity: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> =	1.35, df	= 1 (P	= 0.25)	; I² = 26	%					<u> </u>
Test for overall effect: Z = 2.61 (P =	0.009)								FAS Control	0

Risk of bias legend (A) Risk of Bias

#### pFAS and Non-Verbal Ability Percentile (2 studies)

	i	<b>pFAS</b>		С	ontrol		•	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = Test for overall effect: Z = 3.24 (P =		= 1 (P	= 0.41)	; I² = 0%	ó				-100 -50 0 50 10 pFAS Control	Τo

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



(A) Risk of Bias

# Summary of available outcomes for language

	Langu	iage	
Study type	Outcome	Data	# studies
	2yrs: Ages & Stages	Frequency/OR	1 study: light & moderate
Exposure studies	<3yrs: Bayley Score of Infant Development (BSID)	mean/SD	<b>3 studies:</b> 2 moderate, 1 confirmed/unquantifiable
	3-5yrs: Clinical Evaluation of Language Fundamentals – Preschool (CELF-P)	mean/SD	<b>1 study:</b> 1 confirmed/unquantifiable
	>5yrs: Peabody Picture Vocabulary Test (PPVT-R)	mean/SD	<b>1 studies:</b> 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	<b>1 study:</b> 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)	tmean/SD	3 studies: 3 FASD
	<ul> <li>&gt; 5 yrs &amp; 3-16 yrs: NEPSY</li> <li>Incl: Word Generation, Comprehension of Instructions</li> </ul>	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	<b>7 studies:</b> 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

		Certainty	assessment			Nº of p	oatients		Effect	Certainty
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% Cl)	Absolute (95% Cl)	
	RE STUDIE	S								
2 years:	Ages & Sta	ges (Delayed La	nguage as defi	ined by the Com	nmunica	ition Sca	les of the	Ages & Sta	ges)	
Light										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	none	554	934	OR <b>0.97</b> (0.65 to 1.43)	-	⊕⊕⊖⊖ Low
Moderat	te							1.45)		
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	none	202	934	OR <b>0.71</b>	_	$\oplus \oplus \bigcirc \bigcirc$
1	Schous	not schous	not schous	Schous	none	202	554	(0.40 to 1.27)		Low
0 studies	s for heavy	/ & very heavy								
< 3 yrs: E	Bayley Scal	es of Infant Dev	elopment							
0 studies	s for light,	heavy & very h	eavy							
Moderat	te									
2	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	none	113	180	-	SMD <b>0.05 higher</b> (0.19 lower to 0.29 higher)	⊕⊕⊖⊖ Low
Confirm	ed unquar	tifiable								
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	very serious <sup>d,e,f</sup>	none	28	45	-	SMD <b>0.16 higher</b> (0.31 lower to 0.64 higher)	⊕⊖⊖⊖ Very Low
3 – 5 yrs:	: Clinical Ev	valuation of Lan	guage Fundam	entals – Presch	ool (CEL	F-P)	<u> </u>			
Confirm	ed unquar	tifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	25	26	-	SMD <b>0.96 lower</b> (1.54 lower to 0.38 lower)	⊕⊕⊖⊖ Low
0 studies	s for light,	moderate, hear	vy & very heav	/y						
>5 yrs: P	eabody Pio	cture Vocabular	y Test							
Confirm	ed unquar	tifiable								
1	seriousª	not serious	not serious	very serious <sup>d,e,f</sup>	none	53	53	-	SMD 0.13 lower (0.51 lower lower to 0.25 higher)	⊕○○○ Very low
0 studies	s for light,	moderate, hea	vy & very heav	/y						
>5 yrs: N	IEPSY Lang	uage sub-tests								
Confirm	ed unquar	tifiable								
3	serious <sup>a</sup>	serious⁵	not serious	serious <sup>e</sup>	none	222	238	-	SMD <b>0.61 lower</b> (1.00 lower to 0.21 lower)	⊕○○○ Very low
0 studies	s for light,	moderate, hear	vy & very heav	/y						
		f Language Fundow the mean)	damentals – 5	(CELF-5) (CELF-5	5 Core L	anguage	e Index ≤ 1	L SD below t	the mean or 2 or mo	ore core
Confirm	ed unquar	tifiable								

1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	31	29	<b>OR 1.04</b> (0.36 to	-	⊕○○○ Very Low
								3.02)		VELVLOW
>5yrs: G	FTA-3 Spee	ech Sound	•				•			
Confirm	ed unquan	tifiable								
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	31	29	-	SMD 0.34 lower	$\oplus OOO$
									(0.85 lower to 0.17 higher)	Very Low
>5yrs: C	hildren's Co	ommunication (	Checklist-Seco	nd Edition – Pare	ent Rep	ort			•	
Confirm	ed unquan	tifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	31	29	-	<b>SMD 0.92 lower</b> (1.45 lower to 0.38 lower)	⊕⊕⊖⊖ Low
DIAGNO	SED STUD	IES							0.30 10 wery	
>5 yrs: E	valuation	of Language Fur	idamentals – 4	4 (CELF-4)						
FASD		0.0		· ·						
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	38	29	-	SMD 3.03 lower	$\oplus \oplus \bigcirc \bigcirc$
									(3.75 lower to	Low
			. Toot Douise						2.32 lower)	
	eabody Pic	cture Vocabular	y Test - Revise	ed (PPVT-R)						
FASD				· of		60	60			
3	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	69	60	-	<b>SMD 1.13 lower</b> (1.52 lower to	$\oplus \oplus \bigcirc \bigcirc$
									0.75 lower)	Low
>5 yrs &	3-16 yrs: N	NEPSY Language	sub-tests	<u>.</u>					• •	
FASD										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	53	110	-	SMD 1.5 lower	$\oplus O O O$
									(3.56 lower to	Very Low
>5 vrs· H	ligher scor	es favoured (me	an/SD)	1				l	0.55 higher)	
FASD	ingriter Score									
	seriousa	not serious	not serious	serious <sup>e, f</sup>	none	108	95	_	SMD 0.70 lower	
2	Schous	not schous	not schous	Schous	none	100	55		(1.06 lower to	Low
									0.35 lower)	2011
FAS										
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	serious <sup>e,f</sup>	none	34	34	-	SMD 6.8 lower	000
									(8.07 lower to 5.53 lower)	Very Low
pFAS									5.55 lower)	
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	51	122	-	SMD 0.95 lower	000
5	serious	5011045	not serious	5011003	none	51			(1.68 lower to	Very Low
									0.21 lower)	,
ARND/C	1		1	1	1		1	1	•	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	6	5	-	SMD 5.26 lower	$\Theta \Theta O O$
									(8.25 lower to 2.27 lower)	Low
>5 yrs: R	Rustioni Tes	st of Language (	Comprehensio	n (Errors)	<u> </u>				•	
pFAS										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	45	117	-	SMD 0.76 higher	⊕000
									(0.13 higher to	Very Low
N. F. 1. 1994 A	larrativa	Total Number	f Difformative						1.39 higher)	
>5 yrs: N	varrative –	Total Number o	Different Wo	uras						

FASD										
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	69	69	-	<b>SMD 0.49 lower</b> (0.83 lower to 0.15 lower)	⊕⊕⊖⊖ Low
>5 yrs: C	Connors Co	mprehensive Be	ehaviour Ratin	g Scale – Parent	Report					
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	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)												
	-		-	Odds Ratio	Odds Ratio	Risk of Bias						
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α						
O'Leary et al 2009 (2yrs; Ages & Stages)	-0.0305	0.205	100.0%	0.97 [0.65, 1.45]		•						
Total (95% CI)			100.0%	0.97 [0.65, 1.45]	•							
Heterogeneity: Not applicable						<u>          </u>   5   10						
Test for overall effect: Z = 0.15 (P = 0.88)					Control Light PAE	) 10						

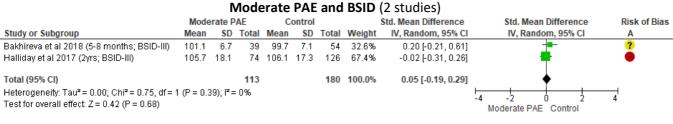
Risk of bias legend (A) Overall RoB

#### Moderate PAE & Ages and Stages (1 study)

			U	Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
O'Leary et al 2009 (2yrs; Ages & Stages)	-0.3386	0.2947	100.0%	0.71 [0.40, 1.27]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.15 (P = 0.25)			100.0%	0.71 [0.40, 1.27]	0.1 0.2 0.5 1 2 5 Control Moderate PA	 E

Risk of bias legend (A) Overall RoB

#### Bayley Scale of Infant Development – Language (<3yrs)



Risk of bias legend (A) Overall RoB

#### **Confirmed PAE-Level Unquantifiable and BSID** (1 study)

Confirmed	l Unquantif	fiable	C	Control			Std. Mean Differenc	e Std. Mean Difference	Risk of Bias
Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95%	CI IV, Random, 95% CI	Α
104.13	15.24	28	101.7	14.49	45	100.0%	0.16 [-0.31, 0.6	4]	•
		28			45	100.0%	0.16 [-0.31, 0.6	4] 🔶	
							Con	irmed Unquantifiable Control	4
	Mean	Mean SD	104.13 15.24 28	Mean         SD         Total         Mean           104.13         15.24         28         101.7	Mean         SD         Total         Mean         SD           104.13         15.24         28         101.7         14.49	Mean         SD         Total         Mean         SD         Total           104.13         15.24         28         101.7         14.49         45	Mean         SD         Total         Mean         SD         Total         Weight           104.13         15.24         28         101.7         14.49         45         100.0%	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95%           104.13         15.24         28         101.7         14.49         45         100.0%         0.16 [-0.31, 0.6           28         45         100.0%         0.16 [-0.31, 0.6	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           104.13         15.24         28         101.7         14.49         45         100.0%         0.16 [-0.31, 0.64]         Image: Comparison of the second

(A) Overall RoB

#### Language Measures (3 - 5 years)

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

	Confirme	d Unquanti	fiable	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								-4	-2 0 2	4
Test for overall effect: Z = 3.23 (P = 0.001)								Confirmed	d Unquantifiable Control	

Risk of bias legend (A) Overall RoB

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

### Language: Peabody Picture Vocabulary Test (>5yrs)

	Confirmed	l Unquanti	ifiable	0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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										<u> </u>
Test for overall effect: Z = 0.67 (P = 0.50)	)							Confirm	-4 -2 U Z	4

Risk of bias legend (A) Overall RoB

# Language: NEPSY Measures (>5yrs)

	Confirmed	Unquanti	fiable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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]		•
otal (95% CI)			222			238	100.0%	-0.61 [-1.00, -0.21]	•	
leterogeneity: Tau <sup>2</sup> = 0.08; Chi <sup>2</sup> = 6.52, df =	2 (P = 0.04); i	<b>=</b> 69%								
Fest for overall effect: Z = 3.01 (P = 0.003)								Confirm	ed Unguantifiable Control	4

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)

	Confirmed Unquan	tifiable	Cont	ol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 Heterogeneity: Not applicable Test for overall effect: Z = 0.08 (P = 0.9	4)		10			Confirm	0.01 0.1 1 10 ned Unquantifiable Control	100
Risk of bias legend								

(A) Overall RoB

	Confirmed	Unquantif	ïable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								⊢ ⊢	<u> </u>	7
Test for overall effect: Z = 1.30 (P = 0.19)								-4 Confirmed	Unquantifiable Control	4
Risk of bias legend										
(A) Overall RoB										
Confirmed	PAE – Le	vel Ur	nquar	ntifia	ble a	and	Childr	en's Communica	ation	
	Checklist	t-2 Ge	neral	Lan	guag	e – I	Parent	t (1 study)		
	Confirm	ed Unquai	ntifiable		Contr	ol		Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Tot	tal Me	an S	SD To	tal Weig	ht IV, Random, 95% Cl	IV, Random, 95% CI	Α
Poth et al 2022 (12-17yrs; CCC-2 General Language)	) 79	22.62	3	31 98	.7 19.6	67	29 100.0	-0.92 [-1.45, -0.38]		•

Potretal 2022 (12-17)(S, COC-2 General Language)	73	22.02	51	30.7 13.07	29 100.0%	-0.32 [-1.40, -0.30]			•
Total (95% CI)			31		29 100.0%	-0.92 [-1.45, -0.38]	•		
Heterogeneity: Not applicable						H-4	-2		4
Test for overall effect: Z = 3.36 (P = 0.0008)						Confirmed	l 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	Clinic	al Ev	valua	tion (	of La	ingua	age Fur	ndamentals – 4	<b>(CELF-4)</b> (1 study)	
	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable			38			29	100.0%	-3.03 [-3.75, -2.32]		
Test for overall effect: Z = 8.29 (P < 0.000	001)								FASD Control	4

Risk of bias legend (A) Overall RoB

# Language: Peabody Picture Vocabulary Test (>4yrs)

		FASD		0	Control		1	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.04, df =	2 (P = 0.	.59); l² =	:0%					-4		
Test for overall effect: Z = 5.77 (P < 0.00001)								-4	FASD Control	4

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)

				•	•		•	,		
	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	-8-	•
Rasmussen et al 2013 (3-16yrs; NEPSY-II; Col)	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: Tau <sup>2</sup> = 2.11; Chi <sup>2</sup> = 24.15, df = 1 (P < 0	0.00001)	; I² = 9	6%							
Test for overall effect: Z = 1.43 (P = 0.15)									FASD Control	4

Risk of bias legend (A) Overall RoB

Note: WG-Letter – Word Generation (Letters) and Col – 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) Std. Mean Difference FASD Control Std. Mean Difference Risk of Bias Study or Subgroup SD SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Mean Total Mean 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 9.93 2.85 -0.62 [-1.05, -0.19] 97 28 70.0% Total (95% CI) 108 95 100.0% -0.70 [-1.06, -0.35] Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.48, df = 1 (P = 0.49); l<sup>2</sup> = 0% ⊢\_4 4 Ó Test for overall effect: Z = 3.86 (P = 0.0001) FASD Control

#### Risk of bias legend (A) Overall RoB

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

		FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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]	- <mark>-</mark>
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)	)							-10 -5 0 5 10 FAS Control

# Risk of bias legend

(A) Overall RoB

pFAS a	and H	ighe	er Sc	ores	Fav	oure	d (me	an/SD) (3 studies)	)	
		FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.25; Chi <sup>2</sup> = 6.18, df = 2 (P = 0.0 Test for overall effect: Z = 2.53 (P = 0.01)	5); I <sup>z</sup> = 6	8%						-10	-5 0 5 pFAS Contorl	10

#### 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)

	ARND	/Othe	ers	Co	ontro	l i		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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]	<b>•</b>	
Heterogeneity: Not applicable Test for overall effect: Z = 3.45 (P = 0.0006)									-10 -5 0 5 ARND/Others Control	10

Risk of bias legend (A) Overall RoB

# Other Language Measures:

#### pFAS and Rustioni Test of Language Comprehension (Errors) (2 studies) Std. Mean Difference Std. Mean Difference pFAS Control Risk of Bias Study or Subgroup SD Total Weight IV, Random, 95% CI SD Total Mean IV. Random, 95% CI Mean 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] 117 100.0% 0.76 [0.13, 1.39] Total (95% CI) 45 Heterogeneity: Tau<sup>2</sup> = 0.14; Chi<sup>2</sup> = 3.11, df = 1 (P = 0.08); l<sup>2</sup> = 68% - 4 -2 'n 4 Test for overall effect: Z = 2.38 (P = 0.02) Control pFAS

	F	ASD		C	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								H	4 -2 0 2	4
Test for overall effect: Z = 2.85 (P = 0.004)	)								FASD Control	

(A) Overall RoB

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

	F	ASD		C	ontrol			Std. Mean Difference		Std. Mean Diffe	rence	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Random, 9	5% CI	Α
Vay et al 2012 (5-14yrs; CCBRS)	88.2	21.3	17	51.1	11.8	24	100.0%	2.22 [1.42, 3.02]			-	•
otal (95% CI)			17			24	100.0%	2.22 [1.42, 3.02]			٠	
leterogeneity: Not applicable fest for overall effect: Z = 5.43 (P < 0.1	000043							 	-4	-2 0	2	4
estion overall ellect. Z = 5.45 (F < 0.)	00001)									Control FAS	D	

Summary of available outcomes for motor

		Motor	
Study type	Outcome	Data	# studies
Exposure Studies	<12 months Total Motor Measures: BSID and BNBAS	mean/SD	<b>6 studies:</b> 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	<b>1 study:</b> 1 light, 1 moderate, 1 heavy
	<1yrs Gross Motor: BSID	OR/Frequency	1 study: 1 confirmed/unquantifiable
	1-4yrs Gross Motor: BSID	mean/SD	<b>1 study:</b> 1 light, 1 moderate, 1 heavy
	>5yrs Gross Motor: Motor Age Test	mean/SD	<b>1 study:</b> 1 confirmed/unquantifiable
	<1yrs Fine Motor: BSID	OR/Frequency	<b>1 study:</b> 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	<b>1 study:</b> 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	<b>Total Motor</b> : GMDS, BOTMP, COMPS and BOT-2	mean/SD	4 studies: 3 FASD, 1 FAS
	Total Motor: M-Fun Draw-a-kid	mean/SD	<b>1 study:</b> 1 FASD and 1 ARND/other

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

Note. all diagnosed studies > 5 years.

# GRADE ratings for motor

		Certainty	assessment			Nº of p	atients		Effect	Certainty
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% Cl)	
EXPOSU	RE STUDIE	S								
< 12 Mo	nths Total	Motor Measure	es (BSID)							
Moderat	te									
3	serious <sup>a</sup>	serious <sup>b</sup>	serious <sup>c</sup>	serious <sup>d,e</sup>	none	245	562	-	SMD 0.26 lower (0.6 lower to 0.08 higher)	⊕○○○ Very low
Very Hea	avy								•	
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	46	332	-	<b>SMD 0.83 lower</b> (1.33 lower to 0.32 lower)	⊕⊕⊖⊖ Low
Confirm	ed Unqua	ntifiable								
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	40	57	-	<b>SMD 0.63 lower</b> (1.53 lower to 0.28 higher)	⊕○○○ Very low
0 studies	s for light a	and heavy								
<12 mon	ths Total	Motor Measures	s (BSID) (Psycho	omotor Develop	ment lı	ndex <85	5)			
Modera	te PAE									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	89/243	75/323	<b>OR 1.91</b> (1.32 to 2.76)	-	⊕⊕⊖⊖ Low
1-4 yrs T	otal Moto	r Measures (BSI	D)							
Moderat	te									
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>d,e</sup>	none	75	403	-	<b>SMD 0.46 lower</b> (1.18 lower to 0.26 higher)	⊕○○○ Very low

Very He	eavy									
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	serious <sup>e,f</sup>	none	24	277	-	<b>SMD 1.1 lower</b> (1.53 lower to 0.67 lower)	⊕○○○ Very low
0 studie	es for light a	ind heavy			1 1					
>5yrs To	otal Motor	Measures (<5 <sup>th</sup>	percentile on t	he M-ABC: Total	Impair	ment Sco	ore)			
Light										
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	325	267	<b>aOR 0.79</b> (0.35 to 1.78)	-	⊕⊕⊕⊖ Moderate
Modera	ate			•				•		
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	82	325	<b>aOR 0.18</b> (0.03 to 1.08)	-	⊕⊕⊕⊖ Moderate
Heavy	•			•						
1	not serious	not serious	not serious	very serious <sup>d,e,f</sup>	none	11	325	<b>aOR 2.05</b> (0.12 to 34.85)	-	⊕⊕⊖⊖ Low
	es for very h									
-		(BSID-III) (Cut-c	offs unclear)							
Confirm	ned unquar	ntifiable						•		
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	serious <sup>e,f</sup>	none	105	52	<b>OR 0.16</b> (0.06 to 0.44)	-	⊕○○○ Very Low
	Gross Moto	or (BSID) (adjust	ed mean/95%	CI)						
Light				• 4	<u> </u>	204	544			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	291	514	-	<b>SMD 0.14 lower</b> (0.28 lower to 0.01 higher)	⊕⊕⊖⊖ Low
Modera	ate									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	none	55	514	-	<b>SMD 0.24 lower</b> (0.51 lower to 0.04 higher)	⊕⊕⊖⊖ Low
Heavy								T		-
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	184	514	-	<b>SMD 0.02 lower</b> (0.19 lower to 0.15 higher)	⊕⊕⊖⊖ Low
0 studie	es for very h	neavy								
•		r (Motor Age Te	st)							
Confirm	ned unquar		1	1				T		1
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	21	21	-	SMD 1.18 higher (0.52 higher to 1.84 higher)	⊕⊕⊖⊖ Low
<1yr Fir	e Motor (B	SID-III) (Cut-offs	s unclear)							
Confirm	ned Unquar	ntifiable								
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	serious <sup>e,f</sup>	none	52	104	<b>OR 0.16</b> (0.06 to 0.43)	-	⊕○○○ Very Low
1-4 yrs	Fine Motor	(Hand Game)								
Heavy										

1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	serious <sup>d,e</sup>	none	101	158	-	<b>SMD 0.13 lower</b> (0.38 lower to 0.12 higher)	⊕○○○ Very Low
0 studie	s for light, i	moderate or ve	ry heavy							
>5 yrs Fi	ine Motor (	Motor Age Test	t, GPT complet	ion time mean, G	GPT cor	npletion	time z-so	core domina	nt and non-domina	nt
respecti										
	ed unquan	tifiable	1	-					1	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	21	21	-	SMD 0.97 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.61 lower to 0.33 lower)	Low
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	55	55	-	SMD 0.33 higher	000
				,					(0.04 lower to	Very Low
				_					0.71 higher)	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	38	60	-	SMD 1.1 higher	$\oplus \oplus \bigcirc \bigcirc$
									(0.67 higher to 1.54 higher)	Low
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	38	60	-	SMD 0.92 higher	$\oplus \oplus \bigcirc \bigcirc$
									(0.49 higher to	Low
									1.35 higher)	
		moderate, heav		У						
>5yrs Vi	sual Motor	Integration (Be	ery)							
Confirm	ed unquan	tifiable (mean/	/SD)							
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	93	115	-	SMD 0.57 lower	$\oplus O O O$
									(1.15 lower to 0)	Very low
		moderate, or ve	ery heavy							
DIAGNO	DSED STUD	IES								
Fotal Me	otor >5yrs (	GMDS, BOTMP	, COMPS, BOT	-2)						
FASD										
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	76	108	-	SMD 0.97 lower	$\oplus OOO$
									(1.49 lower to	Very low
FAS									0.44 lower)	
				a a ut a u a e f		24	24		CMD 2 04 I	
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	serious <sup>e,f</sup>	none	34	34	-	SMD 2.01 lower (2.60 lower to	⊕○○○ Very low
									1.42 lower)	veryiow
Total M	otor M-Fun	Draw-a-kid (m	/SD)						· · ·	
FASD										
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	21	43	-	SMD 0.29 lower	000
				,					(0.81 lower to	Very low
									0.24 higher)	
ARND/C	Others									
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	39	43	-	SMD 0.14 lower	$\oplus O O O$
									(0.58 lower to	Very low
Total M	otor (<5 <sup>th</sup> >	ercentile on the	M-ARC total	impairment score	2)				0.29 higher)	
	otor (<5 þ									
		not serious	not corious	serious <sup>e,f</sup>	nore	14/20	2/39	OR 16.19	<b>115 mans</b>	
FASD			not serious	serious	none	14/30	2/39	(3.29 to	<b>415 more per</b> <b>1000</b> (from 100	⊕⊕⊖⊖ Low
FASD 1	serious <sup>a</sup>	not senous						(3.2.) (0		
	seriousª	not senous						79.65)	•	LOW
	serious <sup>a</sup>	Hot serious						79.65)	more to 760 more)	LOW
1		on the BOT-2)						79.65)	more to 760	LOW

							-		
serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	2/21	1/43	OR 4.42	72 more per 1000	$\oplus O O O$
					(9.5%)	(2.3%)	(0.38 to	(from 14 fewer to	Very Low
							51.79)	529 more)	
lotor (<1SD	on the BOT-2)								
serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	5/21	8/43	OR 1.37		$\oplus O O O$
					(23.8%)	(18.6%)	-		Very Low
( )							4.84)		
tor (BOT-2)									
						-	-		
serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	21	43	-	<b>SMD 0.62 lower</b> (1.15 lower to 0.08 lower)	⊕⊕⊖⊖ Low
Other									
serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	39	43	-	SMD 0.15 lower	$\oplus O O O$
								(0.58 lower to 0.29 higher)	Very Low
tor (<3 <sup>rd</sup> pe	ercentile on the	BOT-2)	-			-			
serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	1/21	0/43	OR 6.37	0 fewer per 1,000	000
			,		(4.8%)	(0%)	(0.25 to	(from 0 fewer to 0	Very Low
							163.10)	fewer)	,
Other									
				none	0/39	0/43	Not	-	NA
					(0%)	(0%)	estimable		
tor (GPT co	ompletion time)								
serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	13	20	-	SMD 0.48 higher	$\oplus OOO$
								(0.23 lower to	Very Low
								1.18 higher)	
tor (GPT do	ominant hand c	ompletion time	e z-score)						
serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	24	32	-	SMD 0.02 higher	$\oplus O O O$
									Very Low
								0.55 higher)	
							[		
serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	51	78	-	SMD 0.69 higher	000
serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	51	78	-	<b>SMD 0.69 higher</b> (0.05 lower to	⊕○○○ Very low
		not serious	very serious <sup>d,e,f</sup>	none	51	78	-	SMD 0.69 higher	
k pFAS/FAS	;)						-	<b>SMD 0.69 higher</b> (0.05 lower to 1.43 higher)	Very low
		not serious not serious	very serious <sup>d,e,f</sup> very serious <sup>d,e,f</sup>	none	51 29	78	-	SMD 0.69 higher (0.05 lower to 1.43 higher) SMD 0.53 higher	Very low
k pFAS/FAS	;)						-	SMD 0.69 higher (0.05 lower to 1.43 higher) SMD 0.53 higher (0.19 lower to	Very low
k pFAS/FAS	;)						-	SMD 0.69 higher (0.05 lower to 1.43 higher) SMD 0.53 higher	Very low
x pFAS/FAS serious <sup>a</sup> Others	5) not serious	not serious	very serious <sup>d,e,f</sup>		29		-	<b>SMD 0.69 higher</b> (0.05 lower to 1.43 higher) <b>SMD 0.53 higher</b> (0.19 lower to 1.25 higher)	Very low ⊕⊕⊖⊖ Low
<b>x pFAS/FAS</b> serious <sup>a</sup>	;)			none		58	-	SMD 0.69 higher (0.05 lower to 1.43 higher) SMD 0.53 higher (0.19 lower to	Very low ⊕⊕⊖⊖ Low
x pFAS/FAS serious <sup>a</sup> Others	5) not serious	not serious	very serious <sup>d,e,f</sup>	none	29	58	-	SMD 0.69 higher (0.05 lower to 1.43 higher) SMD 0.53 higher (0.19 lower to 1.25 higher) SMD 1.96 higher	Very low ⊕⊕⊖⊖ Low
serious <sup>a</sup> Serious <sup>a</sup> Others Serious <sup>a</sup>	5) not serious	not serious not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup>	none	29	58	-	SMD 0.69 higher (0.05 lower to 1.43 higher) SMD 0.53 higher (0.19 lower to 1.25 higher) SMD 1.96 higher (1.09 higher to	Very low ⊕⊕⊖⊖ Low
serious <sup>a</sup> Serious <sup>a</sup> Others Serious <sup>a</sup>	not serious not serious not serious	not serious not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup>	none	29	58	-	SMD 0.69 higher (0.05 lower to 1.43 higher) SMD 0.53 higher (0.19 lower to 1.25 higher) SMD 1.96 higher (1.09 higher to	Very low ⊕⊕⊖⊖ Low
serious <sup>a</sup> Serious <sup>a</sup> Others Serious <sup>a</sup> tor (GPT no	not serious not serious not serious on-dominant ha	not serious not serious nd completior	very serious <sup>d,e,f</sup> serious <sup>e,f</sup>	none	29	26	- -	SMD 0.69 higher (0.05 lower to 1.43 higher) SMD 0.53 higher (0.19 lower to 1.25 higher) SMD 1.96 higher (1.09 higher to 2.84 higher)	Very low $\oplus \oplus \bigcirc \bigcirc$ Low $\oplus \oplus \bigcirc \bigcirc$ Low
serious <sup>a</sup> Serious <sup>a</sup> Others Serious <sup>a</sup>	not serious not serious not serious	not serious not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> time z-score)	none	29	58		SMD 0.69 higher (0.05 lower to 1.43 higher) SMD 0.53 higher (0.19 lower to 1.25 higher) SMD 1.96 higher (1.09 higher to	Very low ⊕⊕⊖⊖ Low
serious <sup>a</sup> Serious <sup>a</sup> Others Serious <sup>a</sup> tor (GPT no	not serious not serious not serious on-dominant ha	not serious not serious nd completior	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> time z-score)	none	29	26	-	SMD 0.69 higher (0.05 lower to 1.43 higher) SMD 0.53 higher (0.19 lower to 1.25 higher) SMD 1.96 higher (1.09 higher to 2.84 higher) SMD 0.55 higher	Very low ⊕⊕⊖⊖ Low Low
	otor (<1SD serious <sup>a</sup> tor (BOT-2) serious <sup>a</sup> other serious <sup>a</sup> tor (<3 <sup>rd</sup> pe serious <sup>a</sup> other tor (GPT co serious <sup>a</sup>	otor (<1SD on the BOT-2) serious <sup>a</sup> not serious tor (BOT-2) serious <sup>a</sup> not serious serious <sup>a</sup> not serious tor (<3 <sup>rd</sup> percentile on the serious <sup>a</sup> not serious tor (GPT completion time) serious <sup>a</sup> not serious	otor (<1SD on the BOT-2)	otor (<1SD on the BOT-2)	otor (<1SD on the BOT-2)	otor (<1SD on the BOT-2)	Image: constraint of the serious of the serie	Image: Serious and the BOT-2)Image: Serious and the	Image: Serious and serious are serious and serious and serious and serious and serious and serious are serious and serious and serious and serious are serious and serious and serious and serious are serious and serious are serious and serious are serious and serious are serious are serious and serious are serious and serious are serious are serious are serious and serious are serious are serious and serious are serious

				-	-	-				
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	51	78	-	SMD 0.73 higher	$\oplus \oplus \bigcirc \bigcirc$
									(0.35 higher to 1.1	Low
		-							higher)	
pFAS (in	cluded FAS	•		T	1		1			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	15	26	-	SMD 4.72 higher	$\Theta \Theta O O$
									(3.47 higher to	Low
									5.95 higher)	
ARND/C	· · · · · ·		1	T			1 1		· · · · ·	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	10	26	-	SMD 2.13 higher	$\oplus \oplus \bigcirc \bigcirc$
									(1.23 higher to	Low
Vicual M	lotor Intog	ration (Beery VI	(ctandard o	(coro)					3.02 higher)	
	iotor integr		vii) (stanuaru s							
FASD				1	1				· · · · · · · · · · · · · · · · · · ·	
4	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	145	1091	-	SMD 0.46 lower	$\oplus \oplus \bigcirc \bigcirc$
									(0.73 lower to	Low
546									0.19 lower)	
FAS				1	1					
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	102	98	-	SMD 0.64 lower	$\Theta \Theta O O$
									(0.92 lower to 0.35 lower)	Low
DEAS (2)	x FAS/pFAS	2)							0.35 lower)	
	-	-		· of	1	42	54			*
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	43	51	-	SMD 1.38 lower (2.55 lower to	⊕○○○ Very low
									0.21 lower)	
ARND/C	Dther								0.211000017	
3	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	121	102		SMD 0.47 lower	$\Theta \Theta \bigcirc \bigcirc$
5	Scribus	not serious	not serious	Schous	none	121	102		(0.78 lower to	Low
									0.16 lower)	LOW
Visual M	lotor Integi	ration (Beery VI	MI) (raw score)	)	1		11		· · ·	
FASD										
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	36	46		SMD 0.97 lower	$\oplus \oplus \bigcirc \bigcirc$
-	5011043	not serious	not serious	5011045	none	50	10		(1.44 lower to	Low
										2011
									0.51 lower)	
Visual M	lotor Integ	ration (Beery VI	VI) (percentile	)					0.51 lower)	
Visual M <b>FASD</b>	lotor Integi	ration (Beery VI	VI) (percentile	)					0.51 lower)	
FASD	_				none	36	98		· · · ·	₽₽○○
	1otor Integr	ration (Beery VI not serious	MI) (percentile not serious	) serious <sup>e,f</sup>	none	36	98	-	0.51 lower) SMD 0.54 lower (0.93 lower to	⊕⊕⊖⊖ Low
FASD	_				none	36	98	-	SMD 0.54 lower	⊕⊕⊖⊖ Low
FASD 1	serious <sup>a</sup>		not serious	serious <sup>e,f</sup>	none	36	98	-	<b>SMD 0.54 lower</b> (0.93 lower to	
FASD 1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	36	98	-	<b>SMD 0.54 lower</b> (0.93 lower to	
FASD 1 Visual M FASD	seriousª 1otor Integr	not serious	not serious centile on the l	serious <sup>e,f</sup> Beery VMI)	none			- - OR 2.78	<b>SMD 0.54 lower</b> (0.93 lower to 0.16 lower)	Low
FASD 1 Visual M	serious <sup>a</sup>	not serious ration (<5 <sup>th</sup> pere	not serious	serious <sup>e,f</sup>		14/21	98 18/43 (41.9%)	- OR 2.78 (0.93 to	<b>SMD 0.54 lower</b> (0.93 lower to	
FASD 1 Visual M FASD	seriousª 1otor Integr	not serious ration (<5 <sup>th</sup> pere	not serious centile on the l	serious <sup>e,f</sup> Beery VMI)		14/21	18/43		<b>SMD 0.54 lower</b> (0.93 lower to 0.16 lower) 248 more per	Low ⊕○○○
FASD 1 Visual M FASD	seriousª 1otor Integr	not serious ration (<5 <sup>th</sup> pere	not serious centile on the l	serious <sup>e,f</sup> Beery VMI)		14/21	18/43	(0.93 to	SMD 0.54 lower (0.93 lower to 0.16 lower) 248 more per 1000 (from 18	Low ⊕○○○
FASD 1 Visual M FASD	serious <sup>a</sup> lotor Integi serious <sup>a</sup>	not serious ration (<5 <sup>th</sup> pere	not serious centile on the l	serious <sup>e,f</sup> Beery VMI)		14/21	18/43	(0.93 to	SMD 0.54 lower (0.93 lower to 0.16 lower) 248 more per 1000 (from 18 fewer to 438	Low ⊕○○○
FASD 1 Visual M FASD 1	serious <sup>a</sup> lotor Integi serious <sup>a</sup>	not serious ration (<5 <sup>th</sup> pere	not serious centile on the l	serious <sup>e,f</sup> Beery VMI)		14/21 (66.7%) 17/39	18/43 (41.9%) 18/43	(0.93 to	SMD 0.54 lower (0.93 lower to 0.16 lower) 248 more per 1000 (from 18 fewer to 438 more) 17 more per 1000	Low ⊕○○○ Very low
FASD 1 Visual M FASD 1 ARND/C	serious <sup>a</sup> lotor Integr serious <sup>a</sup> Dther	not serious ration (<5 <sup>th</sup> pero not serious	not serious centile on the I not serious	serious <sup>e,f</sup> Beery VMI) very serious <sup>d,e,f</sup>	none	14/21 (66.7%) 17/39	18/43 (41.9%)	(0.93 to 8.27)	SMD 0.54 lower (0.93 lower to 0.16 lower) 248 more per 1000 (from 18 fewer to 438 more)	Low O(0) 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<sup>2</sup> >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.

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# Meta-analyses for motor

# **EXPOSURE STUDIES**

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

	Mod	erate P	AE	0	Control		:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
3akhireva 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]	+	?
3andoli 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: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 5.97, df = 2	(P = 0.0	05); I <b>²</b> =	66%							-
fest for overall effect: Z = 1.52 (P = 0.13)									Moderate PAE Control	4

(A) Overall RoB

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

veryneuv	<b>y</b> 1 AL	una	1000				.5 ( ***	montilis) (mean		
	Very I	leavy F	PAE	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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: Tau <sup>2</sup> = 0.08; Chi <sup>2</sup> = 2.36, Taot for everyll effect: $Z = 2.32$ (D = 0.00)	``	= 0.12)	; <b>I²</b> = 58	3%					-4 -2 0 2	4
Test for overall effect: Z = 3.22 (P = 0.001	0								Very Heavy PAE Control	

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)

								•			,
	Confirme	d Unquantifi	iable	C	ontrol			Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.31; Chi <sup>2</sup> = 3.40, d	f= 1 (P = 0.0	17); I² = 71%							-4		
Test for overall effect: Z = 1.35 (P = 0.18)								Confirm	-	quantifiable Control	4
								Comm	ieu Of	Iquanunable Control	

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 PA	E and To	otal N	lotor S	Score	s (<12 i	months) (Frequ	ency/OR) (1 study)
	Moderate	e PAE	Cont	rol		Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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 Heterogeneity: Not applicable Test for overall effect: Z = 3.46 (P = 0.0005)	89 )		75				0.01 0.1 1 10 100 Control Moderate PAE

# Total Motor Measures (1-4 years)

#### Moderate PAE and Total Motor Scores (1-4 years) (2 studies) Moderate PAE Control Std. Mean Difference Std. Mean Difference **Risk of Bias** SD Total Weight IV, Random, 95% CI Study or Subgroup Mean SD Total Mean IV, Random, 95% CI Α 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 -0.11 [-0.43, 0.21] 126 52.0% Total (95% CI) 75 403 100.0% -0.46 [-1.18, 0.26] Heterogeneity: Tau<sup>2</sup> = 0.23; Chi<sup>2</sup> = 7.14, df = 1 (P = 0.008); l<sup>2</sup> = 86% -4 4 Test for overall effect: Z = 1.26 (P = 0.21) Moderate PAE Control

Risk of bias legend (A) Overall RoB

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

	Very I	leavy I	PAE	Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 < 0.000	01)								-4 -2 0 2	4
Dick of bigs legend									Very Heavy PAE Control	

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) Odds Ratio Odds Ratio Risk of Bias SE Weight IV, Random, 95% CI Study or Subgroup log[Odds Ratio] IV, Random, 95% CI Δ 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 0.01 100 10 0.1 Test for overall effect: Z = 0.57 (P = 0.57) Control Light PAE Risk of bias legend (A) Overall RoB

Moderate PA	E and M-ABC	Total I	mpairn	nent Score (>5 y	<b>/ears)</b> (1 study)	
				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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						H
Test for overall effect: Z = 1.88 (P = 0.06)					Control Moderate PAE	,
Risk of bias legend						
(A) Overall RoB						

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

				Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)					Control Heavy PAE
Risk of bias legend					
(A) Overall RoB					

# Gross Motor Measures (<1 years) (OR)

		Gros	ss M	otor	Mea	asur	es (<	1 years) (O	R)		
Confirmed	Unqu	uanti	fiabl	e PAI	E and	BSID		ross Motor (	<1 year	• • • • •	
Study or Subgroup		log[Odd	le Rat	iol	SE I	Weight		lds Ratio Indom, 95% Cl	IV	Odds Ratio , Random, 95% Cl	Risk of Bias A
Hendricks et al 2020 (6 months; BSID		ogload		-	5083 1	-		16 [0.06, 0.44]	_		?
	r					400.00		46 10 06 0 441			
Total (95% CI) Heterogeneity: Not applicable						100.0%	) U.	16 [0.06, 0.44] H			
Test for overall effect: Z = 3.58 (P = 0.0	)004)								0.01 0.1 0.01 0.1	1 10 tifiable Control	100
Risk of bias legend											
(A) Overall RoB											
Gross	Mot	or N	lead		: (1_/	1	ars) (	adjusted m	ean/9	5% (L)	
								s (1-4 years)			
	•	ght PAE		(	Control			Std. Mean Differe	nce	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup Hutchinson et al 2019 (0.5-2yrs; BSID-III)	Mean	2.7735	Total 291	Mean	2.7696		Weight 100.0%			IV, Random, 95% Cl	A ?
Hutchinson et al 2019 (0.5-29rs, BSID-III)	0.90	2.1130		9.30	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)									-4	-2 0 2 Light PAE Control	4'
Risk of bias legend										Eight / AE Control	
(A) Overall RoB											
Mo	derate	e PAE	and	Gros	ss Mo	otor N	Aeasu	ires (1-4 yea	<b>rs)</b> (1 st	udv)	
		erate PA			Control			Std. Mean Differe		Std. Mean Difference	Risk of Bias
Study or Subgroup Hutchinson et al 2019 (0.5-2yrs; BSID-III)	Mean 8.71	SD 2.6633	Total 55	Mean	2.7696	Total 514	Weight 100.0%			IV, Random, 95% Cl	A 2
	0.71	2.0033		9.50	2.7090				•		·
Total (95% CI) Heterogeneity: Not applicable			55			514	100.0%	-0.24 [-0.51,	0.04]		
Test for overall effect: Z = 1.66 (P = 0.10)									-4 M	-2 0 2 oderate PAE Control	4
Risk of bias legend											
(A) Overall RoB											
H	eavy F	PAE a	nd G	iross	Moto	or Me	easure	es (1-4 years	<b>)</b> (1 stud	dy)	
Study or Subgroup	Hea Mean	avy PAE	Total	-	ontrol SD	Total	Weight	Std. Mean Differer IV, Random, 95		Std. Mean Difference IV, Random, 95% Cl	Risk of Bias A
Hutchinson et al 2019 (0.5-2yrs; BSID-III)			184	9.36			100.0%	-0.02 [-0.19, 0		N, Rundon, 55% Cl	?
Total (95% CI)			184			514	100.0%	-0.02 [-0.19, 0	.151	•	
Heterogeneity: Not applicable									-4	-2 0 2	4
Test for overall effect: Z = 0.21 (P = 0.83)									-	Heavy PAE Control	-
Risk of bias legend											
<u>Risk of bias legend</u> (A) Overall RoB											
		G	ross	Mo	tor N	Леаs	ures	(>5 vears)			
(A) Overall RoB	۹E-Lev							(>5 years) Motor Score	s (>5 ve	ears) (1 studv)	
(A) Overall RoB Confirmed PA	Confi	vel U irmed Ur	nqua nquanti	antifia <sub>ifiable</sub>	able a	and G	Gross	Motor Score Std. Mean Diffe	erence	ears) (1 study) Std. Mean Difference	Risk of Bias
(A) Overall RoB Confirmed PA Study or Subgroup	Confi Me	vel U irmed Ur	nqua	antifia <sub>ifiable</sub>	able a Co Mean	and G	otal We	Motor Score Std. Mean Diffe	erence 95% Cl		Risk of Bias
(A) Overall RoB Confirmed PA <u>Study or Subgroup</u> Kyllerman et al 1985 (5-Byrs; Motor Age Test)	Confi Me	vel U irmed Ur ean	nqua nquanti SD	<b>antifi</b> a ifiable <u>Total</u> 21	able a Co <u>Mean</u> 87	and G ontrol SD To	otal We	Motor Score Std. Mean Diffe ight IV, Random, .0% 1.18 [0.5	erence 95% Cl 2, 1.84]	Std. Mean Difference	
(A) Overall RoB Confirmed PA Study or Subgroup	Confi Me	vel U irmed Ur ean	nqua nquanti SD	<b>antifi</b> a ifiable Total	able a Co <u>Mean</u> 87	and G ontrol SD To	otal We	Motor Score Std. Mean Diffe ight IV, Random, .0% 1.18 [0.5	erence 95% Cl 2, 1.84]	Std. Mean Difference	

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)

Con	firmed U	Inquan	tifiab	le and	Fine	Motor	Measures (<1	years) (1 stu	ıdy)	
							Odds Ratio		Ratio	Risk of Bia
Study or Subgroup		log[Od	ds Rati	-			Random, 95% Cl	IV, Rando	om, 95% Cl	A
Hendricks et al 2020 (6 month	s; BSID-III)		-1.832	26 0.500	04 100	0.0%	0.16 [0.06, 0.43]			?
Total (95% CI)					10	0.0%	0.16 [0.06, 0.43]			
Heterogeneity: Not applicable					10	0.070	0.10 [0.00, 0.40] F		ļ	
Test for overall effect: Z = 3.66 (	(P = 0.0002)	)					-	1.01 0.1	1 10	100
	() = 0.0002/	, ,					Confirme	d Unquantifiable	Control	
Risk of bias legend										
(A) Overall RoB										
		Fi	ine N	1otor	Mea	sures	(1-4 years)			
	Hoov						es (1-4 years) (	1 study)		
			anu n	Control			Std. Mean Difference		an Difference	Risk of Bia
Study or Subgroup	Mean		otal Me		Total		IV, Random, 95% C		dom, 95% Cl	A
Coles et al 2021 (4yrs; Hand Gan				23 3.13		100.0%	-0.13 [-0.38, 0.12]		-	ê
		0.00		20 0.10			0.10[0.00,0.12	,		•
Fotal (95% CI)		1	101		158	100.0%	-0.13 [-0.38, 0.12]	□ ◀	►	
Heterogeneity: Not applicable								-1 -0.5		
Test for overall effect: Z = 1.01 (P :	= 0.31)								E Control	
<u>Risk of bias legend</u> A) Overall RoB										
		г		Actor	Mar	acurac	$(\Sigma E voorc)$			
		Г	-me r	νιστοι	Iviea	asures	s (>5 years)			
Confir	rmed PAE	E-Level	l Unqu	uantifia	able a	and Mo	otor Age Test (>	>5 years) (1 :	study)	
	С	onfirmed		fiable	Cont	rol	Std. Mean Diffe	erence Sto	l. Mean Differenc	e Risk of E
itudy or Subgroup		Mean	SD		Mean S		Weight IV, Random,		<mark>, Random, 95% C</mark>	
yllerman et al 1985 (5-6yrs; Motor A	ge Test)	91	14	21	103 1	0 21	100.0% -0.97 <b>[</b> -1.61	1,-0.33]		?
otal (95% CI)				21		21	100.0% -0.97 [-1.61	I, -0.33]	◆	
leterogeneity: Not applicable							-	· · ·	<u> </u>	,, _
Fest for overall effect: Z = 2.95 (P = 0.	.003)							Confirmed Unguar	ntifiable Control	4
A) Overall RoB Confirmed	d PAE-Lev		-	ifiable		Groove	ed Pegboard Te Std. Mean Difference		) (1 study) ean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total			tal Weigl			indom, 95% Cl	Α
/aurio et al 2011 (6-16yrs; GPT)	101.45	10.96	55	97.7 11	.45	55 100.0	% 0.33 [-0.04, 0.1	71]		•
			55			55 100.0	× 033100403	741		
fotal (95% CI) Heterogeneity: Not applicable			55			55 100.0	% 0.33 [-0.04, 0.7	/'J 		
est for overall effect: Z = 1.73 (P =	0.08)							-4 -2	Ó Ż	4 1
	,							Con	trol Confirmed	Unquantifiable
<u>Risk of bias legend</u>										
A) Overall RoB										
Confirmed PAE-Le	vel Unau	lantifia	ble a	nd Gro	oved	Pegbo	ard Test Domi	nant Hand (	>5 vears) (1	L studv)
	Confirmed			Con		-0	Std. Mean Differend		ean Difference	Risk of Bia
study or Subgroup	Mean	SD	Total			tal Weigl			ndom, 95% Cl	Α
1attson et al 2010 (7-21yrs; GPT)	0.62	1.14	38	-0.38 0	1.71	60 100.0	% 1.10 [0.67, 1.9	54]		•
						00 400		- 41		
Total (95% CI)			38			60 100.0	% 1.10 [0.67, 1.	54]	-	
leterogeneity: Not applicable Test for overall effect: Z = 4.96 (P ≤	0.000013							-4 -2	0 2	4
control overall eliett. Z = 4.90 (P S	0.00001)							Con	trol Confirmed	Unquantifiable
Risk of bias legend										
A) Overall RoB										
Confirmed PAE-Leve	l Unquar	ntifiabl	e and	Groov	ed Pe	egboar	d Test Non-Do	minant Han	d (>5 years	<b>)</b> (1 study)
	Confirmed			Con		-	Std. Mean Differend		ean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD To	tal Weig	ht IV, Random, 95%	CI IV, Ra	indom, <mark>95% Cl</mark>	Α
/lattson et al 2010 (7-21yrs; GPT)	0.93	1.8	38	-0.22 0	1.69	60 100.0 <sup>.</sup>	% 0.92 [0.49, 1.3	351		•
			50	0.22 0		· · -		•		
Total (0EW CI)							• •			
Fotal (95% CI)			38			60 100.0	• •		•	
leterogeneity: Not applicable							• •	35] -4 -2	• 0 2	4
							• •	35] -4 -2	trol Confirmed (	4 Unquantifiable

# Visual Motor Integration (> 5yrs)

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

	Confirmed	l Unquantif	iable	(	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.13; Chi <sup>2</sup> = 4.16, d Test for overall effect: $Z = 1.95$ (P = 0.05)	f=1 (P=0.0	4); I <sup>2</sup> = 76%							-4 -2 0 2	4
restion overall ellect. Z = 1.85 (F = 0.05)								Confirm	ed Unquantifiable Control	

Risk of bias legend (A) Overall RoB

## **DIAGNOSED STUDIES**

#### Total Motor Measures: Higher is Better FASD and Total Motor Measures (3 studies) FASD Control Std. Mean Difference Std. Mean Difference Risk of Bias Study or Subgroup Mean SD Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Total А 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 30 2.1 39 33.6% -1.50 [-2.04, -0.95] 1.4 1 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: Tau<sup>2</sup> = 0.14; Chi<sup>2</sup> = 5.52, df = 2 (P = 0.06); l<sup>2</sup> = 64% - 4 ń Δ Test for overall effect: Z = 3.60 (P = 0.0003) FASD Control

Risk of bias legend (A) Overall RoB

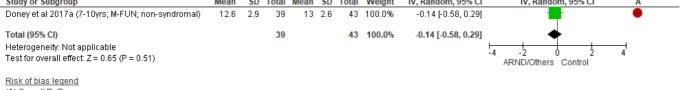
Note: Kooistra et al 2009 also reports M-ABC Ball Skills (m/SD). Jirikowic et al 2008a also reports BOTMP sensori-motor.

#### FAS and Total Motor Measures (1 study) Control Std. Mean Difference Std. Mean Difference **Risk of Bias** FAS Mean SD Total Weight IV, Random, 95% CI Study or Subgroup Mean SD Total IV, Random, 95% CI A Adnams et al 2001 (6-8yrs; GMDS Motor) 34 100.0% 102.13 1.45 34 104.93 1.3 -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) FAS Control 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

	FA	SD	and	Total	Mo	otor:	M-FUN	I Draw-a-kid (1 st	udy)	
	F	ASD		Co	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 = 0.2	29)							H -	4 -2 0 2 FASD Control	4
<u>Risk of bias legend</u> (A) Overall RoB										
ŀ		/Ot	hers	and T	ota	l Mo	tor: M	-FUN Draw-a-kid	(1 study)	
			ARND/	Others		Cont	rol	Std. Mean Differen	ce Std. Mean Difference	Risk of Bias
Study or Subgroup			Mean	SD Tot	tal N	lean S	D Total	Weight IV, Random, 95%	CI IV, Random, 95% CI	A



(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 <5<sup>th</sup> percentile (M-ABC)

	FASI	)	Cont	rol		Odds Ratio	Odds Ratio Risk of Bia
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl 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)							0.01 0.1 1 10 100 Control FASD

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

#### Gross Motor <2SD (BOT-2)

F	ASD an	d Fre	quenc	y of G	Gross N	lotor <2SD (BOT	Γ <b>-2)</b> (1 study)
	FAS	D	Cont	rol		Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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 Heterogeneity: Not applicable Test for overall effect: Z = 1.18 (P =	2 0.24)		1				0.001 0.1 1 10 1000 Control FASD
<u>Risk of bias legend</u> (A) Overall RoB							
			Gros	s Mo	otor <2	LSD (BOT-2)	

#### FASD and Frequency of Gross Motor <1SD (BOT-2) (1 study) FASD Control Odds Ratio Odds Ratio Risk of Bias Study or Subgroup Events Total Events Total Weight IV, Random, 95% CI IV, Random, 95% CI Α 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 0.01 0.1 10 100 Test for overall effect: Z = 0.48 (P = 0.63) Control FASD

Risk of bias legend

(A) Overall RoB

#### Fine Motor (BOT-2)

	F	ASD		Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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	2)								-4 -2 U 2 FASD Control	4

(A) Overall RoB

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

	ARND	/Othe	rs	Co	ontro	l i		Std. Mean Difference	Std. Mean Difference Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)									-4 -2 0 2 4 ARND/Others Control

# Fine Motor <2SD (BOT-2)

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

	FAS	D	Contr	ol		Odds Ratio	Odds Ratio	Risk of Bias	
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α	
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								<u>_</u>	
Test for overall effect: Z = 1.12 (P = 0.26	6)						0.001 0.1 1 10 100 FASD Control	10	
Pick of higs legend									

Risk of bias legend (A) Overall RoB

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

	ARND/O	thers	Cont	rol		Odds Ratio		Odds	Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% CI	Α
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 Heterogeneity: Not applicable Test for overall effect: Not applicable	0		0					0.1 1 RND/Others	10 Control	1000
Pick of bioc logond										

Risk of bias legend (A) Overall RoB

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

## Fine Motor (GPT completion time)

FASD	and F	ine N	lotor	<sup>.</sup> (Gro	oved	Peg	board 1	<b>Test Completion</b>	Time	<b>e)</b> (1 st	tudy)		
		FASD		C	ontrol			Std. Mean Difference		Std. Me	an Difference		<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Ran	idom, 95% Cl		Α
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	0.4.03								-4	-2	0 2	4	1
Test for overall effect: Z = 1.31 (P =	0.19)									Cont	rol FASD		

Risk of bias legend (A) Overall RoB

# Fine Motor (GPT dominant hand completion time)

FASD and Fine	e Mote	or (	Groo	ved P	egb	oard	Test –	DH Completion	Time) (z-score) (1 study)	
	E	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									-4 -2 0 2	4
Test for overall effect: Z = 0.07 (P = 0	1.94)								Control FASD	-
Risk of bias legend										

(A) Overall RoB

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

	FA		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	D Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
Aragon et al 2008b (7-17yrs; GPT)	0.43 1.	1 10	0.15	1.07	32	43.1%	0.25 [-0.46, 0.97]		?
Mattson et al 2010 (7-21yrs; GPT)	0.56 1.	2 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: Tau <sup>2</sup> = 0.20; Chi <sup>2</sup> = 3. Test for overall effect: Z = 1.82 (P = 0		= 0.08);	I² = 68%					-4 -2 0 2 Control FAS	4

#### pFAS and Fine Motor (Grooved Pegboard Test – DH Completion Time) (z-score) (2 studies) Std. Mean Difference Std. Mean Difference pFAS Control Risk of Bias Total Weight IV, Random, 95% CI SD Total Mean SD IV, Random, 95% CI Study or Subgroup Mean A Aragon et al 2008b (7-17yrs; GPT) 0.35 14 0.15 1.07 0.17 [-0.46, 0.80] 51.2% 1.3 32 Candelaria-Cook et al 2021 (8-12yrs; GPT;FAS/pFAS) 0.69 1.3555 15 -0.17 0.5609 0.91 [0.24, 1.58] -26 48.8% Total (95% CI) 29 58 100.0% 0.53 [-0.19, 1.25] Heterogeneity: Tau<sup>2</sup> = 0.16; Chi<sup>2</sup> = 2.48, df = 1 (P = 0.12); l<sup>2</sup> = 60% -4 4 Test for overall effect: Z = 1.44 (P = 0.15) Control pFAS

Risk of bias legend (A) Overall RoB

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

	10101	1010	0.00		, NOUI !	u ic.		in completion		• y )
	AR	ND/Other	S		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable			10			26	100.0%	1.96 [1.09, 2.84]		
Test for overall effect: $Z = 4.41$ (P < 0.0001)									-4 -2 0 2 Control ARND/Others	4
Risk of bias legend										

(A) Overall RoB

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

FASD and Fine N	Notor	(Gro	oove	d Peg	boaı	d Te	st – noi	n-DH Completio	<b>n Time) (z-score)</b> (1 study)
	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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 = 1	0.05)								-4 -2 0 2 4 Control FASD
Risk of bias legend									

(A) Overall RoB

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

	FA	AS	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
Aragon et al 2008b (7-17yrs; GPT)	0.54 0	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	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 Test for overall effect: Z = 3.81 (P = 0	•	(P = 0.63);	I <sup>2</sup> = 0%				-4	-2 0 2 Control FAS	4

Risk of bias legend (A) Overall RoB

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

			-0					eenipienen in	
		pFAS		С	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)									-10 -5 0 5 10 Control pFAS
Pick of bios logged									Control privio

Risk of bias legend (A) Overall RoB

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

	ARI	D/Other	S		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									-4 -2 0 2 Control ARND/Others	4

# Visual Motor Integration (Beery) (Standard Scores)

#### FASD and Beery VMI (Standard Score) (4 studies) FASD Control Std. Mean Difference Std. Mean Difference **Risk of Bias** Study or Subgroup Mean SD SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Total Mean 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 97.9 7.1 273 26.6% -0.75 [-1.10, -0.41] 38 May et al 2020b (6-7yrs; Beery VMI) -0.17 [-0.47, 0.12] ē 93.6 7.6 49 95.4 10.6 444 30.1% 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) 1091 100.0% 145 -0.46 [-0.73, -0.19] Heterogeneity: Tau<sup>2</sup> = 0.04; Chi<sup>2</sup> = 6.46, df = 3 (P = 0.09); l<sup>2</sup> = 54% -4 -2 Ó Ż 4 Test for overall effect: Z = 3.37 (P = 0.0007) FASD Control

Risk of bias legend (A) Overall RoB

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

	-	FAS		•	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.26, c Test for overall effect: Z = 4.38 (P < 0.000	`	0.61); I² =	= 0%					-4	I -2 0 2 FAS Control	4

Risk of bias legend (A) Overall RoB

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

	1	FAS		. 0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.59; Chi <sup>2</sup> = 5.49, df = 1 (P =	0.02); <b>i²</b> =	82%								
Test for overall effect: Z = 2.31 (P = 0.02)									pFAS Control	4

Risk of bias legend (A) Overall RoB

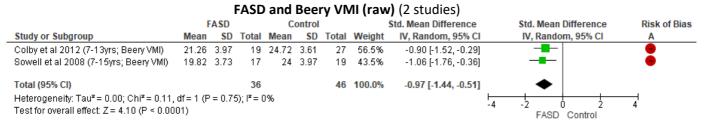
## ARND/Others and Beery VMI (Standard Score) (3 studies)

	ARM	ID/Othe	rs	C	ontrol	-		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> = 2.53, df = 2 (P = 0.2	28); <b>Iz</b> = 2	1%								
Test for overall effect: Z = 2.97 (P = 0.003)									ARND/Others Control	4

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)



# Visual Motor Integration (Beery) (Percentile)

	F	ASD		C	ontrol			Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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									<b>—</b>		
Test for overall effect: Z = 2.75 (P = 1	0.006)								-4	FASD Control	4

Risk of bias legend (A) Overall RoB

# Visual Motor Integration <5<sup>th</sup> percentile (Beery)

	FA	SD a	nd Bee	ery VI	<b>∕∕II &lt;5</b> <sup>th</sup>	percentile (1 st	udy)	
	FASI	D	Contr	ol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								100
Test for overall effect: Z = 1.84 (P = 0.07	7)						Control FASD	100

#### Risk of bias legend

(A) Overall RoB

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

	•				•			
	Experim	ental	Contr	ol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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 Heterogeneity: Not applicable	17		18					-
Test for overall effect: Z = 0.16 (P = 0.87	")						0.1 0.2 0.5 1 2 5 1 Control ARND/Others	U

Risk of bias legend (A) Overall RoB

# Summary of available outcomes for **memory**

	Memo	ry	
Study type	Measures	Data	# studies
Exposure	Verbal 'Short Delay': RAVLT, NEPSY Word list	mean/SD	3 studies: 1 light, 1 moderate, 1
Studies	interference		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	<b>4 studies:</b> 1 light, 1 moderate, 1 confirmed unquantifiable, 2 Any PAE
	Verbal 'Long Delay': CVLT-C	z-score	<b>1 studies:</b> 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	Verbal- 'Short Delay': WRAML-Verbal	mean/SD	7 studies: 4 FASD, 1 FAS, 1 pFAS, 2
Studies	Memory Index, Story memory, CMS-Stories,		ARND/Others
	CVLT-C, VSRT-mean		
	Verbal- 'Short Delay': CVLT-C	T-score	1 study: 1 pFAS, 1 ARND/Others
	Verbal- 'Long Delay': CVLT-C, VSRT, CMS-	mean/SD	6 studies: 3 FASD, 1 FAS, 1
	stories		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	mean/SD	5 studies: 5 FASD, 1 ARND/Others
Stem Completion Target, NEPSY-II memory for		
names, Memory of 16 objects		
Visual/Verbal- 'Short Delay': NEPSY-II	OR/Frequency	1 study: 1 FASD
memory for names		
Visual/Verbal- 'Long Delay': NEPSY-II memory	OR/Frequency	1 study: 1 FASD
for names		
Visual/Verbal- 'Long Delay': Memory of 16	mean/SD	2 study: 2 FASD
objects, NEPSY-II Memory for Names		
Non-Verbal- 'Short Delay': WRAML-Visual	mean/SD	<b>3 studies:</b> 1 FASD, 1 FAS, 1
memory index, NVSRT, TOMAL		ARND/Other
Non-Verbal- 'Short Delay': RCFT	T-score	3 studies: 2 FASD, 1 pFAS, 1
		ARND/Others
Non-Verbal- 'Short Delay': CANTAB Pattern	OR/Frequency	1 study: 1 FASD
Recognition		
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**

		Certainty	assessment			Nº of ∣	patients		Effect	Certainty
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% Cl)	Absolute (95% Cl)	
EXPOSU	RE STUDIE	S								
Verbal 's	hort delay	' (RAVLT, NEPSY	' Word list inte	rference)						
Light										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	93	6669	-	<b>SMD 0.00</b> (0.2 lower to 0.2 higher)	⊕⊕⊖⊖ Low
Moderat	te									
1	serious <sup>a</sup>	not serious	not serious	not serious	none	755	6669	-	<b>SMD 0.10</b> (0.03 higher to 0.18 higher)	⊕⊕⊕⊖ Moderate
Confirm	ed unquar	ntifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	49	47	-	SMD 1.12 lower (1.55 lower to 0.69 lower)	⊕⊕⊖⊖ Low
Any leve	el									
2	serious <sup>a</sup>	not serious	not serious	not serious	none	2546	7229	-	<b>SMD 0.14</b> (0.09 higher to 0.18 higher)	⊕⊕⊕⊖ Moderate
0 studies	s for heavy	or very heavy			1				0,	
Verbal 's	hort delay	' z-score (CVLT-	C)							
Confirm	ed unquar	ntifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	81	81	-	<b>SMD 0.8 lower</b> (1.12 lower to 0.48 lower)	⊕⊕⊖⊖ Low
0 studies	s for light,	moderate, heav	y & very heavy							
Verbal 'l	ong delay'	(CVLT-C, RAVLT	)							
Light										

1										
1	seriousª	not serious	not serious	not serious	none	755	6669	-	<b>SMD 0.10</b> (0.03 higher to 0.18 higher)	⊕⊕⊕⊖ Moderate
Modera	te							<u> </u>	iligher)	
1	serious <sup>a</sup>	not serious	not serious	not serious	none	755	6669	-	SMD 0.16 (0.08 higher to 0.23 higher)	⊕⊕⊕⊖ Moderate
Confirm	ied unquar	ntifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	81	81	-	<b>SMD 1.75 lower</b> (2.12 lower to 1.39 lower)	⊕○○○ Very Low
Any lev	el									
2	serious <sup>a</sup>	not serious	not serious	not serious	none	2546	7529	-	SMD 0.16 higher (0.11 higher to 0.20 higher)	⊕⊕⊕⊖ Moderate
0 studie	s for heavy	or very heavy	•	•					•	
Verbal '	long delay'	z-score (CVLT-C	C)							
Confirm	ed unquar	tifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	81	81	-	<b>SMD 0.96 lower</b> (1.29 lower to 0.64 lower)	⊕⊕⊖⊖ Low
0 studie	s for light,	moderate, heav	y & very heavy	,						
Visual/V	erbal 'shoi	rt delay' (K-ABC)								
Heavy										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	25	21	-	SMD 0.61 lower (1.21 lower to 0.02 lower)	⊕⊕⊖⊖ Low
0 studie	s for light,	moderate, very	heavy & unqua	antified				<u>.</u>	/	
Non-ver	bal 'short o	delay' (RCFT)								
Confirm	ed unquar	ntifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e, f</sup>	none	28	28	-	SMD 0.67 lower (1.21 lower to 0.13 lower)	⊕⊕⊖⊖ Low
0 studie	s for light,	moderate, heav	y & very heavy							
Non-ver	bal 'long d	elay' (RCFT)								
Confirm	ed unquar	ntifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	28	28	-	SMD 0.86 lower (1.41 lower to 0.31 lower)	⊕⊕⊖⊖ Low
0 studie	s for light,	moderate, heav	y & very heavy	,						
DIAGNO	DSED STUD	IES								
Verbal '	short dela	y' (WRAML-stor	y memory, CN	1S-stories, Stor	y Memo	ry				
FASD										
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	100	90	-	<b>SMD 1.10 lower</b> (2.13 lower to 0.07 lower)	⊕○○○ Very Low
Verbal '	short dela	y' (CVLT-C Story	Memory)						· · · ·	
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	19	18	-	SMD 0.95 lower (1.63 lower to 0.26	⊕⊕⊖⊖ Low
									lower)	

FAS       (2.11) Giver to 0.38 lower)       Very Lot 0.38 lower)         fAS       1       serious*       not serious       serious**1       none       45       49       -       SMD 0.78 lower (1.2 lower to 0.38 lower)       GPOC Low lower)         pFAS       1       serious*       not serious       not serious       serious**1       none       36       60       -       SMD 0.92 lower (1.36 lower to 0.39 lower)       GPOC         aRND/Other       2       serious*       not serious       serious**1       none       73       77       -       SMD 0.61 lower (1.36 lower to 0.32 lower)       GPOC         1       serious*       not serious       serious**1       none       73       77       -       SMD 2.06 lower (1.46 lower to 0.32 lower)       GPOC         1       serious*       not serious       serious**1       none       20       16       -       SMD 2.06 lower (1.2 lower to 1.68 lower)       GPOC         1       serious*       not serious       serious**1       none       24       16       -       SMD 2.06 lower (1.2 lower to 1.68 lower)       GPOC         3       serious*       not serious       serious**1       none       90       94       -       SMD 0.89 lower (1.9 lower to 1.68 lower)	FASD										
1       serious*       not serious       serious*       none       45       49       -       (1.2 lower to 0.36 lower)       (1.2 lower to 0.36 lower)         pFAS       1       serious*       not serious       not serious*       none       36       60       -       (1.2 lower to 0.36 lower)       (1.3 lower)       00000         ARND/Other       2       serious*       not serious       serious*.1       none       73       77       -       SMD 0.51 lower to 0.49 lower)       0.49 lower)         Verbal 'short delay' (CVLT-C) T-score       pFAS       1       serious*       not serious       serious*.1       none       20       16       -       SMD 2.06 lower (2.89 lower to 1.24 lower)       0.000         ARND/Other       1       serious*       not serious       serious*.1       none       20       16       -       SMD 2.06 lower (2.89 lower to 1.24 lower)       0.000         1       serious*       not serious       serious*.1       none       20       16       -       SMD 2.54 lower to 0.26 lower (2.89 lower to 1.68 lower)       0.000         1       serious*       not serious       serious*.1       none       24       16       -       SMD 2.54 lower to 0.60 lower       0.000       0.000       0.000 <th></th> <th>serious<sup>a</sup></th> <th>serious<sup>b</sup></th> <th>not serious</th> <th>serious<sup>e,f</sup></th> <th>none</th> <th>124</th> <th>121</th> <th>-</th> <th>(2.11 lower to</th> <th>⊕○○○ Very Low</th>		serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	124	121	-	(2.11 lower to	⊕○○○ Very Low
pFAS       (1.2 lower to 0.36 lower)       Low         1       serious <sup>a</sup> not serious       serious <sup>a</sup> ()       none       36       60       -       SMD 0.92 lower ()       0.49 lower)         2       serious <sup>a</sup> not serious       serious <sup>a</sup> ()       none       36       60       -       SMD 0.61 lower ()       0.49 lower)         2       serious <sup>a</sup> serious <sup>a</sup> not serious       serious <sup>a</sup> ()       none       73       77       -       SMD 0.61 lower ()       0.49 lower)         Verbal 'short delay' (CVLT-C) T-score       pFAS       -       SMD 2.06 lower ()       0.32 lower)       0.32 lower)       0.32 lower)       0.20 lower ()       0.00 low						1	•				
1       serious*       not serious       serious*-1       none       36       60       -       SMD 0.92 lower (1.36 lower to 0.49 lower)       0.49 lower)         2       serious*       serious*       not serious       serious*-1       none       73       77       -       SMD 0.51 lower to 0.32 lower)       0.49 lower to 0.32 lower)       0.40 lower to 1.24 lower)       0.40 lower to 0.58 lower)       0.40 lower)       0.40 lower to 0.58 lower)       0.40 lower to 0.58 lower)       0.40 lower to 0.39 lower)       0.40	1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	45	49	-	(1.2 lower to 0.36	⊕⊕⊖⊖ Low
ARND/Other       (1.36 lower to 0.49 lower)       Low         2       serious <sup>a</sup> not serious       serious <sup>a,t</sup> none       73       77       -       SMD 0.61 lower (1.54 lower to 0.32 lower)       0000 Very Lov         verbal 'short delay' (CVLT-C) T-score       pFAS       -       SMD 2.06 lower (2.89 lower to 1.24 lower)       0000 (2.89 lower to 1.24 lower)       0000 (2.89 lower to 1.24 lower)       0000 (2.89 lower to 1.24 lower)       0000 (2.89 lower to 1.24 lower)         4RND/Other       -       SMD 2.61 lower (2.89 lower to 1.24 lower)       0000 (2.89 lower to 1.24 lower)       0000 (2.89 lower to 1.24 lower)       0000 (2.80 lower)         4RND/Other       -       SMD 2.54 lower (3.4 lower to 1.68 lower)       00000 (2.80 lower)       00000 (2.90 lower)       00000 (2.90 lower)         3       serious <sup>a</sup> not serious       not serious       serious <sup>a,t</sup> none       none       90       94       -       SMD 0.89 lower (1.19 lower to 0.58 lower)       00000 (0.00 lower)         FAS       -       serious <sup>a,t</sup> not serious       not serious       serious <sup>a,t</sup> none       none       36       60       -       SMD 0.79 lower (1.19 lower to 0.38 lower)       00000 (0.00 lower)         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,t</sup> none       none       73       77       -       SMD 0.78	pFAS										
2       serious <sup>a</sup> serious <sup>a</sup> not serious       serious <sup>a,t</sup> none       73       77       -       SMD 0.61 lower (1.54 lower to 0.32 lower)       OCOC Very Lot 0.32 lower)         Verbal 'short delay' (CVLT-C) T-score       pFAS         1       serious <sup>a</sup> not serious       serious <sup>a,t</sup> none       20       16       -       SMD 2.66 lower (2.89 lower to 1.24 lower)       0.20       0.00       -       SMD 2.54 lower (2.89 lower to 1.24 lower)       0.00 </td <td></td> <td></td> <td>not serious</td> <td>not serious</td> <td>serious<sup>e,f</sup></td> <td>none</td> <td>36</td> <td>60</td> <td>-</td> <td>(1.36 lower to</td> <td>⊕⊕⊖⊖ Low</td>			not serious	not serious	serious <sup>e,f</sup>	none	36	60	-	(1.36 lower to	⊕⊕⊖⊖ Low
Verbal 'short delay' (CVLT-C) T-scorepFAS1serious*not seriousserious*!none2016-SMD 2.06 lower (2.89 lower to 1.24 lower)000000000000000000000000000000000	ARND/0	Other									
pFAS       Image: Serious <sup>a</sup> not serious not serious not serious serious <sup>e,f</sup> none       20       16       -       SMD 2.06 lower (2.89 lower to 1.24 low)         ARND/Other       1       serious <sup>a</sup> not serious not serious not serious serious <sup>e,f</sup> none       24       16       -       SMD 2.34 lower (2.89 lower to 1.68 lower) (2.89 lower to 1.68 lower)         Verbal 'long delay' (CVLT-C, VSRT, CMS-stories)       mone       24       16       -       SMD 0.89 lower (3.4 lower to 1.68 lower) (3.4 lower to 1.68 lower)       ⊕⊕○○○         ASD       serious <sup>a</sup> not serious not serious serious <sup>e,f</sup> none       90       94       -       SMD 0.89 lower (1.19 lower to 0.58 lower) (1.90 lower) (2.91 low)       ⊕⊕○○○         FAS       1       serious <sup>a</sup> not serious not serious serious <sup>e,f</sup> none       45       59       -       SMD 0.79 lower (1.19 lower to 0.58 lower) (1.90 lower) (2.91 lower) (2.91 lower) (2.91 lower) (2.91 lower)         pFAS (1x FAS/pFAS)       1       serious <sup>a</sup> not serious not serious serious <sup>e,f</sup> none       36       60       -       SMD 0.78 lower (2.59 lower) (2.91 lower)         ARND/Other       2       serious <sup>b</sup> not serious serious <sup>e,f,f</sup> none       73       77       -       SMD 0.83 lower (2.91 lower) (2.91 lower	2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	73	77	-	(1.54 lower to	⊕○○○ Very Low
ARND/OtherClassical and a serious a	Verbal '	short delay	' (CVLT-C) T-sco	ore	<u>.</u>						
ARND/OtherComparisonComparisonLowLow1serious*not seriousnot seriousserious*.fnone2416- $SMD 2.54$ lower (3.4 lower to 1.68 lower) $\oplus \bigcirc \bigcirc \bigcirc$ (3.4 lower to 1.68 lower)74 Diamondgelay' (CVLT-C, VSRT, CMS-stories)FASD-SMD 0.89 lower (1.19 lower to 0.58 lower) $\oplus \bigcirc \bigcirc \bigcirc$ Low3serious*not seriousnot seriousserious*.fnone9094-SMD 0.89 lower (1.19 lower to 0.38 lower) $\oplus \bigcirc \bigcirc \bigcirc$ Low7AS-serious*not seriousserious*.fnone4559-SMD 0.79 lower (1.19 lower to 0.39 lower) $\oplus \bigcirc \bigcirc \bigcirc$ Low1serious*not seriousserious*.fnone3660-SMD 0.78 lower (1.21 lower to 0.35 lower) $\oplus \bigcirc \bigcirc \bigcirc$ Low2serious*not seriousserious*.fnone7377-SMD 0.83 lower (2.59 lower to 0.35 lower) $\oplus \bigcirc \bigcirc \bigcirc$ Low4serious*serious*serious*.fnone7377-SMD 0.83 lower (2.59 lower to 0.94 lower) $\oplus \bigcirc \bigcirc \bigcirc$ Low4serious*not seriousserious*.fnone7377-SMD 0.83 lower (2.59 lower to 0.94 lower) $\oplus \bigcirc \bigcirc \bigcirc$ Very Lov 3.09)4serious*not seriousnot seriousserious*.fnone7377-SMD 0.79 lower (2.59 lower to 0.94 lower) $\oplus \bigcirc \bigcirc \bigcirc \bigcirc$ Low4seriou	pFAS										
1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       24       16       -       SMD 2.54 lower (3.4 lower to 1.68 lower)       methods         3       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       90       94       -       SMD 0.54 lower (3.4 lower to 1.68 lower)       methods         3       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       90       94       -       SMD 0.79 lower (1.19 lower to 0.58 lower)       methods         7AS       1       serious <sup>a</sup> not serious       serious <sup>e,f</sup> none       45       59       -       SMD 0.79 lower (1.19 lower to 0.58 lower)       methods       Low         pFAS (1x FAS/pFAS)       1       serious <sup>a</sup> not serious       serious <sup>e,f</sup> none       36       60       -       SMD 0.78 lower (1.21 lower to 0.35 lower)       methods         ARND/Other       2       serious <sup>b</sup> not serious       serious <sup>e,f</sup> none       73       77       -       SMD 0.83 lower (2.59 lower to 0.94 lower)       Methods         1       serious <sup>a</sup> not serious       serious <sup>e,f</sup> none       73       77       -       SMD 0.83 lower (2.59 lower to 0.94 lower)			not serious	not serious	serious <sup>e,f</sup>	none	20	16	-	(2.89 lower to	⊕⊕⊖⊖ Low
Verbal 'long delay' (CVLT-C, VSRT, CMS-stories)         FASD         3       serious <sup>a</sup> not serious       not serious <sup>e,f</sup> none       90       94       -       SMD 0.89 lower       ⊕⊕⊖○C         FAS         1       serious <sup>a</sup> not serious       not serious <sup>e,f</sup> none       45       59       -       SMD 0.79 lower       ⊕⊕○○C         pFAS (1x FAS/pFAS)       not serious       not serious <sup>e,f</sup> none       45       59       -       SMD 0.78 lower       ⊕⊕○○C         1       serious <sup>a</sup> not serious       not serious <sup>e,f</sup> none       36       60       -       SMD 0.78 lower       Low         1       serious <sup>a</sup> not serious       not serious <sup>e,f</sup> none       36       60       -       SMD 0.78 lower       Low       Low         0.33 lower)       not serious       serious <sup>e,f</sup> none       73       77       -       SMD 0.83 lower       Low       Very Low         2       serious <sup>a</sup> serious       serious <sup>e,f</sup> none       73       77       -       SMD 0.83 lower       Very Low         1       serious <sup>a</sup> not serious       serious <sup>e,f</sup> none       73       7	ARND/0	Other									
FASD       Serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       90       94       -       SMD 0.89 lower (1.19 lower to 0.58 lower)       ⊕⊕⊖⊖ Low         FAS       1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       45       59       -       SMD 0.79 lower (1.19 lower to 0.39 lower)       ⊕⊕⊖⊖ Low         pFAS (1x FAS/pFAS)       not serious       not serious       serious <sup>e,f</sup> none       36       60       -       SMD 0.78 lower (1.21 lower to 0.39 lower)       ⊕⊕⊖⊖ Low         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       36       60       -       SMD 0.78 lower (1.21 lower to 0.39 lower)       Low         1       serious <sup>a</sup> not serious       serious <sup>e,f</sup> none       36       60       -       SMD 0.78 lower (1.21 lower to 0.35 lower)       Low         2       serious <sup>a</sup> not serious       serious <sup>e,f</sup> none       73       77       -       SMD 0.83 lower (2.59 lower to 0.94 lower)       ⊕⊖⊖⊖         Verbal 'long delay' (CVLT-C) Frequency (Cut-offs unclear)       serious <sup>d,e,f</sup> 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)	1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	24	16	-	(3.4 lower to 1.68	⊕⊕⊖⊖ Low
3       serious <sup>a</sup> not serious       not serious       serious <sup>a</sup> ,f       none       90       94       -       SMD 0.89 lower (1.19 lower to 0.58 lower)       ⊕⊕⊖⊖ Low         FAS       1       serious <sup>a</sup> not serious       not serious       serious <sup>a</sup> ,f       none       45       59       -       SMD 0.79 lower (1.19 lower to 0.39 lower)       ⊕⊕⊖⊖ Low         pFAS (1x FAS/pFAS)       not serious       not serious       serious <sup>a</sup> ,f       none       36       60       -       SMD 0.78 lower (1.21 lower to 0.39 lower)       ⊕⊕⊖⊖ Low         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       36       60       -       SMD 0.78 lower (1.21 lower to 0.35 lower)       ⊕⊕⊖⊖⊖ Low         ARND/Other       2       serious <sup>a</sup> serious <sup>b</sup> not serious       serious <sup>a,f</sup> none       73       77       -       SMD 0.83 lower (2.59 lower to 0.94 lower)       ⊕⊖⊖⊖ Very Low 0.94 lower)         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> (68.6%)       none       23/35 (65.7%)       OR 1.14 (0.42 to 3.09)       29 more per 1,000 (from 211 fewer to 198 more)       ⊕⊖⊖⊖       ↓	Verbal '	long delay'	(CVLT-C, VSRT,	CMS-stories)			•			• • • • • • • • • • • • • • • • • • •	
FAS1Serious®not seriousnot seriousserious®fnone4559-SMD 0.79 lower (1.19 lower to 0.39 lower)⊕⊕⊖⊖ LowpFAS (1x FAS/pFAS)1serious®not seriousnot seriousserious®fnone3660-SMD 0.78 lower (1.21 lower to 0.35 lower)⊕⊕⊖⊖⊖ Low1serious®not seriousnot seriousserious®fnone3660-SMD 0.78 lower (1.21 lower to 0.35 lower)⊕⊕⊖⊖⊖ Low2serious®serious®not seriousserious®fnone7377-SMD 0.83 lower (2.59 lower to 0.94 lower)⊕⊖⊖⊖⊖ Very Low 0.94 lower)Verbal 'long delay' (CVLT-C) Frequency (Cut-offs unclear)none7377-SMD 0.83 lower (0.94 lower)⊕⊖⊖⊖⊖ Very Low 0.94 lower)1serious®not seriousvery serious <sup>d.ef</sup> none24/3523/35OR 1.14 (0.42 to 3.09)29 more per 1,000 (from 211 fewer to 198 more)⊕⊖⊖⊖ Very Low Very Low	FASD										
1seriousnot seriousnot seriousseriousseriousnone4559-SMD 0.79 lower (1.19 lower to 0.39 lower) $\oplus \oplus \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc$ LowpFAS (1x FAS/pFAS)1seriousnot seriousnot seriousseriousserious60-SMD 0.78 lower (1.21 lower to 0.35 lower) $\oplus \oplus \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc$ Low1seriousnot seriousnot seriousseriousserious60-SMD 0.78 lower (1.21 lower to 0.35 lower) $\oplus \oplus \bigcirc \bigcirc$	3	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	90	94	-	(1.19 lower to	⊕⊕⊖⊖ Low
pFAS (1x FAS/pFAS)         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       36       60       -       SMD 0.78 lower (1.21 lower to 0.35 lower)       ⊕⊕○○ Low         ARND/Other       2       serious <sup>a</sup> serious <sup>b</sup> not serious       serious <sup>e,f</sup> 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)       very serious <sup>d,e,f</sup> none       24/35       23/35       OR 1.14 (0.42 to 3.09)       29 more per 1,000 (from 211 fewer to 198 more)       ⊕○○○○	FAS										
1seriousnot seriousnot seriousseriousserious $serious^{e,f}$ none $36$ $60$ $-$ SMD 0.78 lower (1.21 lower to 0.35 lower) $\oplus \bigcirc \bigcirc$ ARND/Other2seriousseriousnot seriousseriousserious $73$ $77$ $-$ SMD 0.83 lower (2.59 lower to 0.94 lower) $\oplus \bigcirc \bigcirc$	1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	45	59	-	(1.19 lower to	⊕⊕⊖⊖ Low
ARND/Other         2       serious <sup>a</sup> serious <sup>b</sup> not serious       serious <sup>e,f</sup> none       73       77       -       SMD 0.83 lower (2.59 lower to 0.94 lower)       ⊕○○○ Very Low 0.94 lower)         Verbal 'long delay' (CVLT-C) Frequency (Cut-offs unclear)         FASD         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       24/35       23/35       OR 1.14 (0.42 to 3.09)       29 more per 1,000 (from 211 fewer to 198 more)       ⊕○○○	pFAS (1	x FAS/pFAS	5)								
2       serious <sup>a</sup> serious <sup>b</sup> not serious       serious <sup>e,f</sup> none       73       77       -       SMD 0.83 lower (2.59 lower to 0.94 lower)	1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	36	60	-	(1.21 lower to	⊕⊕⊖⊖ Low
Image: Second	ARND/0	Other									
Verbal 'long delay' (CVLT-C) Frequency (Cut-offs unclear)         FASD         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       24/35       23/35       OR 1.14       29 more per       #OOOC         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       24/35       23/35       OR 1.14       29 more per       #OOOC         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       24/35       68.6%)       (65.7%)       OR 1.14       29 more per       #OOOC         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       24/35       68.6%)       (65.7%)       0.4       1,000       (from 211)       Very Low         1       more)       more)       more)       1<	2	serious <sup>a</sup>	serious⁵	not serious	serious <sup>e,f</sup>	none	73	77	-	(2.59 lower to	⊕○○○ Very Low
1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       24/35       23/35       OR 1.14       29 more per       0000         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       24/35       23/35       OR 1.14       29 more per       0000         1       0.42 to       1,000 (from 211)       Very Low       1,000       fewer to 198       0000       0000       0000         1       0.00 (from 211)       0.000       0.000       0.000       0.000       0.000       0.000       0.000         1       0.000       0.000       0.000       0.000       0.000       0.000       0.000       0.000       0.000         1       0.000       <	Verbal '	long delay'	(CVLT-C) Freque	ency (Cut-offs	unclear)						
(68.6%)       (65.7%)       (0.42 to <b>1,000</b> (from 211       Very Low         3.09)       fewer to 198       more)       more)	FASD										
Verbal 'long delay' (CVLT-C) z-score	1	seriousª	not serious	not serious	very serious <sup>d,e,f</sup>	none	-	-	(0.42 to	<b>1,000</b> (from 211 fewer to 198	⊕○○○ Very Low
	Verbal '	long delay'	(CVLT-C) z-scor	e							
FASD	FASD										
	1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	21	7	-	(1.52 lower to	⊕○○○ Very Low
Visual/Verbal 'short delay' (K-ABC, Word Stem Completion Target, NEPSY-II memory for names, Memory of 16 objects)	Visual/\	/erbal <sup>(</sup> shoi	rt delay' (K-ABC,	Word Stem C	Completion Targe	et, NEPS	SY-II men	nory for n	ames, Mem	ory of 16 objects)	

FASD										
5	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,</sup>	none	228	275	-	SMD 0.44 lower (0.87 lower to 0.01 lower)	⊕○○○ Very Low
ARND/0						1			1	
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	62	35	-	SMD 0.09 lower (0.51 lower to 0.32 higher)	⊕○○○ Very Low
Visual/\	/erbal 'shor	rt delay' (NEPSY	-II memory fo	r names) (Freque	ency of	children	<1SD belo	ow normativ		
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none		8/30 (26.7%)	<b>OR 5.25</b> (1.77 to 15.61)	<b>390 more per</b> <b>1,000</b> (from 125 more to 584 more)	⊕⊕⊖⊖ Low
Visual/\	/erbal 'long	delay' (NEPSY-	II memory for	names) (Freque	ncy of c	hildren <	1SD belov	w normative	e mean)	
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	- / -	12/30 (40.0%)	<b>OR 5.36</b> (1.76 to 16.28)	<b>381 more per</b> <b>1,000</b> (from 140 more to 516 more)	⊕⊕⊖⊖ Low
Visual/\	/erbal 'long	; delay' (16 obje	cts, NEPSY-II N	Memory for Nam	ies)					
FASD										
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	79	84	-	SMD 0.79 lower (1.11 lower to 0.47 lower)	⊕⊕⊖⊖ Low
Non-vei	rbal 'short o	delay' (various r	neasures)							
FASD (V	VRAML-VM	II)								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	20	20	-	SMD 7.25 lower (9.04 lower to 5.47 lower)	⊕⊕⊖⊖ Low
FAS (NV	/RST)			• •						
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	47	58	-	SMD 0.58 lower (0.97 lower to 0.18 lower)	⊕⊕⊖⊖ Low
ARND/0	Other (TON	1AL)								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	19	21	-	SMD 1.00 lower (1.66 lower to 0.34 lower)	⊕⊕⊖⊖ Low
Non-vei	rbal 'short o	delay' (RCFT) (T·	-score)							
FASD										
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	67	106	-	SMD 0.78 lower (1.10 lower to 0.45 lower)	⊕⊕⊖⊖ Low
pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	20	16	-	<b>SMD 1.60 lower</b> (2.37 lower to 0.84 lower)	⊕⊕⊖⊖ Low
ARND/0	Other									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	22	16	-	<b>SMD 1.72 lower</b> (2.49 lower to 0.96 lower)	⊕⊕⊖⊖ Low
Non-vei	rbal 'short o	delay' (CANTAB	) Frequency (C	ut-offs unclear)						
FASD										

1	coriousa	not corious	not corious	serious <sup>d,f</sup>	nono	18/24	22/26	OR 0.55	95 fewer per	
1	serious <sup>a</sup>	not serious	not serious	serious	none	-	(84.6%)		<b>1,000</b> (from 429	$\oplus \oplus \bigcirc \bigcirc$
						(75.0%)	(84.0%)	(0.13 to	fewer to 78 more)	Low
NI	ula al (la va a al							2.23)	lewer to 78 more)	
	rbal long d	elay' (NVRST &	TOMAL)							
FAS	-									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	47	58	-	SMD 0.50 lower	$\Theta \Theta \bigcirc \bigcirc$
									(0.89 lower to	Low
									0.11 lower)	
ARND/	Other									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	19	21	-	SMD 1.04 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.70 lower to	Low
									0.37 lower)	
Non-ve	rbal 'long d	elay' (RCFT) (T-s	score)							
FASD										
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	67	106	-	SMD 0.77 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.09 lower to	Low
									0.45 lower)	
pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	20	16	-	SMD 2.28 lower	$\oplus \oplus \bigcirc \bigcirc$
									(3.14 lower to	Low
									1.42 lower)	
ARND/	Other									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	21	16	-	SMD 2.20 lower	$\oplus \oplus \bigcirc \bigcirc$
									(3.04 lower to	Low
									1.36 lower)	
Non-ve	rbal 'long d	elay' (BFLT) Fre	quency (Cut-ol	fs unclear)		•				
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	none	26/35	28/35	OR 0.72	58 fewer per	$\oplus \oplus \bigcirc \bigcirc$
						-	(80.0%)	(0.24 to	<b>1,000</b> (from 310	Low
						` '	、 ,	2.22)	fewer to 99 more)	
Self-rep	ort (Everyd	lay memory que	estionnaire – S	patial Memory)				,		
FASD				.,						
1	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	41	64	-	SMD 1.71 higher	$\oplus \oplus \bigcirc \bigcirc$
-	3011003	100 3011003	100 5011003	501005	lione		07		(1.25 higher to	Low
									2.17 higher)	LOW
N		dence interval <sup>.</sup> SI				L			2.17 (1161)	

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

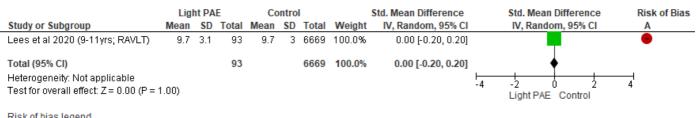
**Explanations:** a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity (I<sup>2</sup> >50% and significant chi-square for heterogeneity); c) >50% of studies had a sample not representative of the Australian populations; d) 95% CIs for overall estimate crossed the line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



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

	Moder	rate P	AE	Co	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									-4 -2 0 2	
Test for overall effect: Z = 2.61 (P = 1	0.009)								Moderate PAE Control	-
Risk of bias legend										

(A) Overall RoB

Note: Lees et al 2020 also reports RAVLT learning.

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

	Confirmed	unquanti	fiable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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)							Confirm	red unquantifiable Control	4
Risk of bias legend										
(A) Overall RoB										

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

	Ar	IY PAE		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	<u>+-</u>	•
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.13,	df = 1 (i	<sup>o</sup> = 0.7	2); l² =	0%					+ + + + + + + + + + + + + + + + + + +	
Test for overall effect: Z = 5.86 (P < 0.00	001)								Any PAE Control	4

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	l unquanti	fiable	0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
Fross 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]		•
otal (95% CI)			81			81	100.0%	-0.80 [-1.12, -0.48]	•	
leterogeneity: Not applicable								⊢ ⊢	<u> </u>	
Fest for overall effect: Z = 4.88 (P ≤ 0.00	0001)							Confirmed	Lunguantifiable Control	4

(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)

							•	<b>y' (mean/SD)</b> (1 s	stud	,,	
	Ligi	it PA	E	Co	ntro			Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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								ł	<u> </u>		
Test for overall effect: Z = 2.61 (P = 1	0.009)							-	-4	Light PAE Control	4

Risk of bias legend (A) Overall RoB

Note: Lees et al 2020 also reports RAVLT learning.

	Mode	rate P	AE	Co	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									+ + + + + + + + + + + + + + + + + + +	4
Test for overall effect: Z = 4.08 (P <	0.0001)								Moderate PAE Control	
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)

	Confirmed	unquanti	fiable	C	ontrol			Std. Mean Difference	St	d. Mean	Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IN	, Rando	om, 95% Cl	Α
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]	1			•
Total (95% CI)			81			81	100.0%	-1.75 [-2.12, -1.39]	•	•		
Heterogeneity: Not applicable												
Test for overall effect: Z = 9.45 (P < 0.0)	0001)							Confirm	ned unqua	ntifiable	Control	4
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).

		V PAE			ontrol	•	elay	(mean/SD) (2 Stud Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD		Mean			Weight		IV, Random, 95% CI	A
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]	<u>+</u>	•
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]	<b>–</b>	•
Total (95% CI)			2546			7529	100.0%	0.16 [0.11, 0.20]		
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.08 Test for overall effect: Z = 6.88 (P < 0.00		? = 0.7	'8); I² =	0%					-4 -2 0 2 Any PAE Control	4

#### 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)

	Confirmed	d unquantif	fiable	C	Control		:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 < 0.00	0001)							Confirm	-4 -2 0 2 ed unguantifiable Control	4

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)

	Very	Heavy F	PAE	C	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)								-4 -2 0 2 Very Heavy PAE Control	4

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)

	Confirmed	l unquantif	fiable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									4 -2 0 2	4
Test for overall effect: Z = 2.43 (P = 0.01)								Confirm	ed unquantifiable Control	

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 U	nquan	tifiab	le PA	E an	d No	n-Ver	bal 'Long Delay'	(mean/SD) (1 study)	
	Confirmed	unquantif	ïable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								ŀ	4 -2 0 2	4
Test for overall effect: Z = 3.08 (P = 0.002	2)							Confirme	ed unquantifiable Control	
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)

		ANU ASD	ven		Control	uela		an/SD) (3 studies Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 (6-8yrs; 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: Tau <sup>2</sup> = 0.73; Chi <sup>2</sup> = 17.42, df = 1 Test for overall effect: $Z = 2.09$ (P = 0.04)	2 (P = 0.0	002); I	²= 89%	ò				⊢ -4	4 -2 0 2 FASD Control	4

#### 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)

	F	ASD		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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) Heterogeneity: Not applicable			19			18	100.0%	-0.95 [-1.63, -0.26]	-4 -2 0 2	
Test for overall effect: Z = 2.71 (P = 0.007)									FASD Control	4

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			Control	,	(	an/SD) (4 studies Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight		IV, Random, 95% CI	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]	_ <b>-</b> _	?
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: Tau <sup>2</sup> = 0.67; Chi <sup>2</sup> = 25.24, df = 3 Test for overall effect: $Z = 2.83$ (P = 0.005)	} (P < 0.0	1001); I <sup>z</sup> = 8	8%					H	4 -2 0 2 FASD Control	4

#### 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)

		FAS		C	ontrol		•	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable			45			49	100.0%	-0.78 [-1.20, -0.36]	-2 0 2	4
Test for overall effect: Z = 3.65 (P = 0.0003)									FAS Control	

#### Risk of bias legend (A) Overall RoB

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

	. р	FAS		Co	ontro			Std. Mean Difference	Std. Mean	Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rando	m, 95% Cl	Α
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)								-4	4 -2 I pFAS	) 2 Control	4

#### 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)

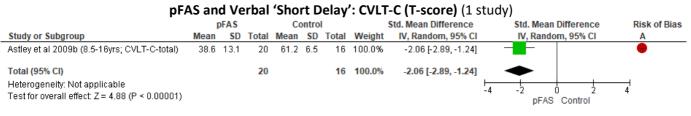
								(		
	ARN	D/Oth	er	Co	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
Dudek et al 2014 (11-14 yrs; CMS-stories; ARND)	9.3	3.2	18	12.6	2.4	17	44.5%	-1.14 [-1.86, -0.41]		•
Lewis et 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: Tau <sup>2</sup> = 0.37; Chi <sup>2</sup> = 5.35, df = 1 (P = 0	.02); I <sup>z</sup> =	81%						H		
Test for overall effect: Z = 1.28 (P = 0.20)								-	ARND/Other Control	4

#### 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)



#### Risk of bias legend

(A) Overall RoB

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

	ARN	D/Oth	ег	C	ontro	1		Std. Mean Difference		Std. Me	an Differenc	e	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% Cl		IV, Ran	dom, 95% C	1	Α
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 ARND/Oth	er Control	2	4

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) Std. Mean Difference FASD Control Std. Mean Difference **Risk of Bias** Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Study or Subgroup Α Crocker et al 2011 (7-14yrs; CVLT-C) -0.91 [-1.53, -0.28] 8.36 4.12 22 11 41 22 22 23.8% Gautam et al 2014 (6-17yrs; CVLT-C) 2 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] 94 100.0% Total (95% CI) 90 -0.89 [-1.19, -0.58] Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.02, df = 2 (P = 0.99); l<sup>2</sup> = 0% -4 ΰ 4 Test for overall effect: Z = 5.71 (P < 0.00001) 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)

		FAS		Co	ontro			Std. Mean Difference	Ste	d. Mean Diffe	rence	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD.	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV	/, Random, 95	5% CI	Α
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									<u> </u>		1	<u> </u>
Test for overall effect: Z = 3.83 (P = 0.0001)									-4 -2	FAS Con	trol	4
Risk of bias legend												
(A) Overall RoB												

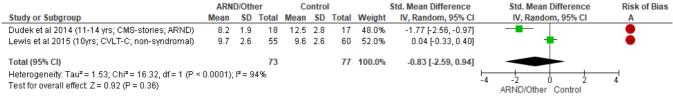
Note: Coles et al 2010 VSRT learning slope, recall 8th, NVSRT learning slope etc.

	pFAS a	and	l Ver	bal '	Lon	g De	lay' (n	nean/SD) (1 stud	y)	
	pl	FAS		Co	ontro	l i		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 3.57 (P = 0.0004)			36			60	100.0%	-0.78 [-1.21, -0.35] 	4 -2 0 2 pFAS Control	4

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)



#### 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.



Total events 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)

0.01

n'1

Control FASD

	E E	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
ryer 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]		•
otal (95% CI)			21			7	100.0%	-0.64 [-1.52, 0.23]	-	
leterogeneity: Not applicable								۲.		

#### 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)

		FASD		0	Control			Std. Mean Difference	5	td. Mean Differer	ice Risk	k of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95%	CI 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: Tau <sup>2</sup> = 0.18; Chi <sup>2</sup> = 18.59, df = 4 (P = 0.0	009); l <sup>2</sup> =	= 78%							<u> </u>	t l	<u> </u>	
Test for overall effect: Z = 1.99 (P = 0.05)									-4 ·	-2 U EASD Contro	2 4	

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)

	ARI	D/Othe	er	0	Control			Std. Mean Difference		Std. Mea	an Differenc	e	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Ran	dom, 95% C	1	Α
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)									-4	-2 ARND/Oth	er Control	2	4

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)

	FAS	D	Cont	rol	-	Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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							0.01 0.1 1 10 100	
Test for overall effect: Z = 2.98 (P = 0.003)							Control FASD	
Dials of high lange d								

Risk of bias legend (A) Overall RoB

Note: NEPSY-II MfN is Memory for Names.

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

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

	FAS	D	Cont	rol	-	Odds Ratio	Odds Ratio Risk of
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl 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 Heterogeneity: Not applicable Test for overall effect: Z = 2.96 (P = 0.003)	25		12				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 ar	nd Vis	ual	/Ver	bal 'l	.ong	g Del	ay' (m	iean/SD) (2 stu	ıdies)	
	F	ASD		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.01, df = 1 (P = 0.94	); I <sup>z</sup> = 0%	5								<u> </u>
Test for overall effect: Z = 4.85 (P < 0.00001)									-4 -2 0 2 FASD Control	4
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)

		ASD			ontrol			(mean/SD) (1 stu Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									FASD Control	
Risk of bias legend										
(A) Overall RoB										

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

		FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								Ŀ,	<u> </u>	-
Test for overall effect: Z = 2.88 (P = 0.004)								-4	FAS Control	4

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) ARND/Other Control Std. Mean Difference Std. Mean Difference Risk of Bias Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% Cl IV, Random, 95% CI Α 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 -4 -'r Ó ż 4 Test for overall effect: Z = 2.96 (P = 0.003) 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).

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

Control Total Mean SD		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Total Mean SD				
	) Total Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
34 42.4 13.64	35 43.9%	-0.67 [-1.15, -0.18]	-8-	•
33 47 12	? 71 56.1%	-0.86 [-1.29, -0.43]	-	•
67	106 100.0%	-0.78 [-1.10, -0.45]	•	
= 0.55); I² = 0%		-4		
		-4	FASD Graph	4
			-4	-4 -2 0 2 FASD Graph

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)

	pFA	S	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD Tota	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
Astley et al 2009b (8.5-16yrs; RCFT; FAS/pFAS)	30.1 10	1.3 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)								PFAS Control	4
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) ARND/Other Control Std. Mean Difference Std. Mean Difference **Risk of Bias** Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI -1.72 [-2.49, -0.96] Astley et al 2009b (8.5-16yrs; RCFT; SE/AE) 287 104 22 498 139 16 100.0% Total (95% CI) 16 100.0% -1.72 [-2.49, -0.96] 22 Heterogeneity: Not applicable 7 2 ò 2 4 Test for overall effect: Z = 4.43 (P < 0.00001) 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).

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

FASD and Non-Verbal 'Short Delay' (mean/SD) (1 study)												
	FAS	D	Cont	rol	-	Odds Ratio	Odds Ratio Risk of Bias					
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A					
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)							0.01 0.1 1 10 100 Control FASD					
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)												
		FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias		
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α		
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]		•		
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 2.50 (P = 0.0	1)		47			58	100.0%	-0.50 [-0.89, -0.11]	-4 -2 0 2 FAS Control	I		

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)

	ARND	)/Othe	ег	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 3.06 (P = 0.002)			19			21	100.0%	-1.04 [-1.70, -0.37]	-4 -2 0 2 ARND/Other Control	

Risk of bias legend (A) Overall RoB

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

	FA	SD a	and N	lon-V	'erba	l 'Lon	ig Dela	<b>y' (mean/SD)</b> (2	studies)		
	F	ASD		0	Control			Std. Mean Difference	Std. Mea	n Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Rand	om, 95% Cl	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = Test for overall effect: Z = 4.70 (P			= 0.45	i); I² = 09	%				-4 -2 FASE	0 2 Control	4

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)

	pl	FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	<b>•</b>	
Heterogeneity: Not applicable								ŀ	4 -2 0 2	
Test for overall effect: Z = 5.18 (P < 0.00001)								-	pFAS Control	4
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) ARND/Other Control Std. Mean Difference Std. Mean Difference **Risk of Bias** Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Study or Subaroup Α 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 -4 4 ò

ARND/Other Control

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)

FAS	D and I	Non-	Verba	l 'Lon	ig Dela	y' (mean/SD) (	(1 study)
	FAS	D	Cont	rol		Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)							0.01 0.1 1 10 100 Control FASD
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)

		FA	SD a	ind Se	elf-re	eport	t (meai	n/SD) (1 study)			
	F	ASD		C	ontrol			Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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 < 0.000	101)								-4	FASD Control	4
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		
	<b>TOVA:</b> 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	<b>1 study:</b> 1 light, 1 moderate, 1 heavy		
	Selective/ Sustained Attention: TEACh-5 Selective	OR/Frequency	<b>1 study:</b> 1 light, 1 moderate, 1 heavy		
	Selective/ Sustained Attention: TEACh-5 Sustained	OR/Frequency	<b>1 study:</b> 1 light, 1 moderate, 1 heavy		
	Other Attention Measures: NES3, D2 test of attention	mean/SD	<b>2 studies:</b> 1 confirmed unquantifiable, 1 any PAE (different measures)		
	Ext: Attention – Caregiver Report: CBCL	T-score	<b>6 studies:</b> 1 very heavy, 4 confirmed unquantifiable, 1 Any		
	Ext: Attention – Caregiver Report: CBCL	OR/Frequency	<b>2 studies:</b> 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	<b>2 studies:</b> 1 FASD, 1 ARND/Others (different measures)		
	Other Attention Measures: IVA CPT	Frequency	<b>1 study:</b> 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	<b>10 studies:</b> 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

TOVA omission errors (ss), commission errors (ss), omission errors block 1, and commission errors block 1       (0.44 lower to 0.05 higher)       (0.05 higher)         TOVA omission errors (ss), commission errors (ss), omission errors block 1, and commission errors block 1       Confirmed unquantifiable         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.68       lower (1.20)         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57 lower       (1.09 lower to 0.16)         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57 lower       (1.09 lower to 0.06)         1       serious <sup>a</sup> not serious       not serious       very       none       55       55       -       SMD 0.18 lower       (0.55 lower to 0.20)       0.20 higher         1       serious <sup>a</sup> not serious       not serious       very       none       54       54       -       SMD 0.11       (0.48 lower to 0.20)         1       serious <sup>a</sup> not serious       serious <sup>d,e,f</sup> none       109       168       -       SMD 0.22 lower (0.48 lower to 0.20)	
EXPOSURE STUDIES         NEPSY-II: Visual attention         Heavy       1       serious <sup>a</sup> not serious       serious <sup>c</sup> serious <sup>d,f</sup> none       108       165       -       SMD 0.2 lower       Q         TOVA omission errors (ss), commission errors (ss), omission errors block 1, and commission errors block 1       Confirmed unquantifiable       1       Serious <sup>a</sup> not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.68       G         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.68       G         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.68       G         1       serious <sup>a</sup> not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57       lower (1.20)         1       serious <sup>a</sup> not serious       not serious       serious <sup>6,f</sup> none       55       55       -       SMD 0.18       lower to       0.20       higher (0.27)       lower to 0.48       higher (0.27)       lower to 0.48       higher (0.27)       lower to 0.48       high	
NEPSY-II: Visual attention         Heavy       1       serious <sup>a</sup> not serious       serious <sup>a</sup> none       108       165       -       SMD 0.2 lower       Q         1       serious <sup>a</sup> not serious       serious <sup>a</sup> none       108       165       -       SMD 0.2 lower       Q         1       serious <sup>a</sup> not serious       serious <sup>a,f</sup> none       108       165       -       SMD 0.61 lower to       0.05 higher)         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       30       30       -       SMD 0.68 lower (1.20 lower to 0.16 lower)         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       30       30       -       SMD 0.78 lower (1.20 lower to 0.16 lower)         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f,f</sup> none       30       30       -       SMD 0.78 lower (1.20 lower to 0.16 lower)         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f,f</sup> none       30       30       -       SMD 0.78 lower (2.0 S) lower to 0.26 lower)       0.20 higher)       1         1       serious <sup>a</sup> not se	
Heavy         1       serious*       not serious       serious*       serious*       none       108       165       -       SMD 0.2 lower       0.05 higher)         TOVA omission errors (ss), commission errors (ss), commission errors (ss), omission errors block 1, and commission errors block 1         Confirmed unquantifiable         1       serious*       not serious       not serious       serious*.f       none       30       30       -       SMD 0.68       0wer (1.20)         1       serious*       not serious       not serious       serious*.f       none       30       30       -       SMD 0.70 lower (1.20)       lower to 0.16       lower (1.20)       lower to 0.16       lower)       lower to 0.26       lower to 0.26       lower)       lower to 0.26       lower)       lower to 0.26       lower V       0.20 higher       lower V       0.20 higher)       lower V       0.20 higher       lower V       0.20 higher       lower V       0.20 higher)       lower V       0.20 higher)       lower V       0.20 higher       lower V       0.20 higher)       lower V       0.20 higher)       lower V       0.20 higher) <td></td>	
1       serious <sup>a</sup> not serious       serious <sup>c</sup> serious <sup>a,f</sup> none       108       165       -       SMD 0.2 lower       6         TOVA omission errors (ss), commission errors block 1, and commission errors block 1         Confirmed unquantifiable         1       serious <sup>a</sup> not serious       not serious <sup>e,f</sup> none       30       30       -       SMD 0.68       6         1       serious <sup>a</sup> not serious       not serious <sup>e,f</sup> none       30       30       -       SMD 0.67       6       10wer (1.20)       10wer to 0.16       10wer to 0.20       100wer to 0.48       100	
TOVA omission errors (ss), commission errors (ss), omission errors block 1, and commission errors block 1       (0.44 lower to 0.05 higher)       (0.05 higher)         TOVA omission errors (ss), commission errors (ss), omission errors block 1, and commission errors block 1       Confirmed unquantifiable         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.68       lower (1.20)         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57 lower       (1.09 lower to 0.16)         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57 lower       (0.109 lower to 0.16)         1       serious <sup>a</sup> not serious       not serious       very       none       55       55       -       SMD 0.18 lower       (0.55 lower to 0.20 higher)         1       serious <sup>a</sup> not serious       not serious       very       none       54       54       -       SMD 0.11       (0.27)         1       serious <sup>a</sup> not serious       serious <sup>d,e,f</sup> none       109       168       -       SMD 0.22 lower       (0.46 lower to 0.020 higher)	
TOVA omission errors (ss), commission errors (ss), omission errors block 1, and commission errors block 1         Confirmed unquantifiable         1       serious <sup>a</sup> not serious       serious <sup>a,f</sup> none       30       30       -       SMD 0.68       €         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       30       30       -       SMD 0.68       €         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       30       30       -       SMD 0.75 lower (1.20)       Iower (0.20)	$\Theta O O O$
TOVA omission errors (ss), commission errors (ss), omission errors block 1, and commission errors block 1         Confirmed unquantifiable       1       serious <sup>a</sup> not serious       not serious <sup>e,f</sup> none       30       30       -       SMD 0.68       Generation         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.68       lower (1.20         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57       lower (1.20)         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57       lower (1.09)       lower to       0.06       lower)       1       serious <sup>a</sup> not serious       very       none       55       55       -       SMD 0.18       lower       60       (0.55)       lower to       0.020       higher (0.27)       No       0.20 higher       No       No       1       serious <sup>a</sup> not serious       very       serious <sup>d,e,f</sup> none       54       54       -       SMD 0.22       lower to       0.02 higher)       No       1       higher (0.27)	Very Low
Confirmed unquantifiable         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.68       (d)         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57       lower (1.20)       lower to 0.16       lower)         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57       lower (1.20)       lower to 0.16       lower)       (1.09)       lower to       0.06       lower)       (0.55)       lower to       0.06       lower       (0.55)       lower to       0.06       lower       (0.55)       lower to       0.20       higher       lower to       0.20       higher       lower to       0.20       higher       lower to       0.20       lower to       <	
1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.68       (e)         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57 lower       (f)         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57 lower       (f)         1       serious <sup>a</sup> not serious       not serious       very       none       55       55       -       SMD 0.51 lower       (g)         1       serious <sup>a</sup> not serious       not serious       very       none       55       55       -       SMD 0.18 lower       (0)       0.00 higher         1       serious <sup>a</sup> not serious       not serious       very       none       54       54       -       SMD 0.11       (h)       higher (0.27)       Nower to 0.48       higher)       Nower to 0.48       higher)       Nower to 0.48       higher)       Nower to 0.48       higher)       Nower to 0.46       Nower to 0.46       Nower to 0.20 higher       Nower to 0.46       Nower to 0.46       Nower to 0.46       Nower to 0.46	
Image:	$\Theta \Theta O O$
Image: Serious and serious are and serious and serious are	Low
1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       30       30       -       SMD 0.57 lower       (1.09 lower to 0.06 lower)         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       55       55       -       SMD 0.18 lower       (0.55 lower to 0.20 higher         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       54       54       -       SMD 0.11       (0.27 lower to 0.27 lower to 0.48 higher)         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       54       54       -       SMD 0.11       (0.27 lower to 0.48 higher)       Not serious	
Image: serious and serious are represented attention.none5555-SMD 0.18 lower to 0.06 lower)SMD 0.18 lower to 0.06 lower)1serious and serious and serious and serious are represented attention.none5454-SMD 0.11SMD 0.11SMD 0.27None1serious and serious are represented attention.noneserious and serious are represented attention.serious and serious are represented attention.SMD 0.22 lower are represented attention.SMD 0.21 lower to 0.02 higher).SMD 0.22 lower are represented attention.SMD 0.21 lower to 0.02 higher.TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean)	
Image: constraint of the serious of the serie	$\Theta \Theta O O$
1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       55       55       -       SMD 0.18 lower (0.55 lower to 0.20 higher       No         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       54       54       -       SMD 0.11 (0.55 lower to 0.20 higher       No         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       54       54       -       SMD 0.11 (0.27 lower to 0.48 higher)       No         Leiter sustained attention       -       Heavy       -       -       SMD 0.22 lower to 0.48 higher)       No         1       serious <sup>a</sup> not serious       serious <sup>c</sup> serious <sup>d,f</sup> none       109       168       -       SMD 0.22 lower (0.46 lower to 0.02 higher)       0.02 higher)         TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean)	Low
1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       54       54       -       SMD 0.11       4         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       54       54       -       SMD 0.11       4         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       54       54       -       SMD 0.27       None       None         Leiter sustained attention       Heavy       -       109       168       -       SMD 0.22 lower       4       4         1       serious <sup>a</sup> not serious       serious <sup>c</sup> serious <sup>d,f</sup> none       109       168       -       SMD 0.22 lower       4         1       serious <sup>a</sup> not serious       serious <sup>c</sup> serious <sup>d,f</sup> none       109       168       -       SMD 0.22 lower       4         1       serious <sup>a</sup> Not serious       serious <sup>c</sup> serious <sup>d,f</sup> none       109       168       -       SMD 0.22 lower       4         1       selective/sustained attention (OR/frequency) (<1SD below the mean)	
Image: constrained attentionImage: constrained attentionImage: constrained attentionImage: constrained attentionImage: constrained attention1serious <sup>a</sup> not seriousnot seriousvery serious <sup>d,e,f</sup> none5454-SMD 0.11 higher (0.27 lower to 0.48 higher)4Leiter sustained attentionLeiter sustained attentionserious <sup>a</sup> not seriousserious <sup>c</sup> serious <sup>d,f</sup> none109168-SMD 0.22 lower (0.46 lower to 0.02 higher)41serious <sup>a</sup> not seriousserious <sup>c</sup> serious <sup>d,f</sup> none109168-SMD 0.22 lower (0.46 lower to 0.02 higher)4TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean)	$\oplus 000$
1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       54       54       -       SMD 0.11 higher (0.27 lower to 0.48 higher)       None       None       1       Serious and attention         Leiter sustained attention       Heavy       -       SMD 0.22 lower (0.46 lower to 0.02 higher)       -       SMD 0.22 lower (0.46 lower to 0.02 higher)       -       SMD 0.22 lower (0.46 lower to 0.02 higher)       -       -       SMD 0.22 lower (0.46 lower to 0.02 higher)       -	Very Low
serious <sup>d,e,f</sup> higher (0.27 lower to 0.48 higher)       higher (0.27 lower to 0.48 higher)       higher (0.27 lower to 0.48 higher)         Leiter sustained attention       -       -       SMD 0.22 lower (0.46 lower to 0.02 higher)       -         1       serious <sup>a</sup> not serious       serious <sup>c</sup> serious <sup>d,f</sup> none       109       168       -       SMD 0.22 lower (0.46 lower to 0.02 higher)       -         TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean)	<u>*</u>
Leiter sustained attention       Iower to 0.48 higher)         Leiter sustained attention       Heavy         1       serious <sup>a</sup> not serious       serious <sup>c</sup> serious <sup>d,f</sup> none       109       168       -       SMD 0.22 lower (0.46 lower to 0.48 higher)         1       serious <sup>a</sup> not serious       serious <sup>c</sup> serious <sup>d,f</sup> none       109       168       -       SMD 0.22 lower (0.46 lower to 0.02 higher)       4         TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean)	⊕○○○ Very Low
Image: Leiter sustained attention       higher)       higher)         Heavy       Image: Leiter sustained attention       Serious <sup>c</sup> serious <sup>d,f</sup> none       109       168       -       SMD 0.22 lower (0.46 lower to 0.02 higher)       Image: Comparison of the description of the desc	Very LOW
Leiter sustained attention         Heavy         1       serious <sup>a</sup> not serious       serious <sup>c</sup> serious <sup>d,f</sup> none       109       168       -       SMD 0.22 lower       (0.46 lower to 0.02 higher)         TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean)	
1       serious <sup>a</sup> not serious       serious <sup>c</sup> serious <sup>d,f</sup> none       109       168       -       SMD 0.22 lower       (0.46 lower to 0.02 higher)         TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean)	
TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean)	
TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean)	$\Theta \Theta O O$
TEACH-5 selective/sustained attention (OR/frequency) (<1SD below the mean) Light	Low
Light	
1 1 not not serious not serious serious serious <sup>d, f</sup> inone 1,675 1,758 1 <b>208 1 17</b> 1 A	
	$\Theta \oplus \Theta \bigcirc$
	Moderate
1.81	
Moderate	
	$\oplus \oplus \oplus \bigcirc$
	Moderate
(0.63 to 2.97)	
Heavy	
	$\oplus \oplus \oplus \bigcirc$
	Moderate

	]							(1.08 to		
ТЕЛСН	elective (<19	D below the mea	n)					9.53)	l	l
Light		below the mea								
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	675	758	<b>aOR</b> <b>0.97</b> (0.61 to 1.54)		⊕⊕⊕⊖ Moderate
Modera	te		•							
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	175	758	<b>aOR 0.94</b> (0.45 to 1.95)		⊕⊕⊕⊖ Moderate
Heavy				•				•	•	
1	not serious	not serious	not serious	very serious <sup>d,e,f</sup>	none	20	758	<b>aOR 3.22</b> (0.94 to 11.05)		⊕⊕⊖⊖ Low
TEACH s	sustained (<1	SD below the me	an)	•				•	•	
Light										
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	675	758	<b>aOR 1.17</b> (0.75 to 1.81)		⊕⊕⊕⊖ Moderate
Modera	te		-							
1	not serious	not serious	not serious	very serious <sup>d,e,f</sup>	none	175	758	<b>aOR 2.05</b> (0.95 to 4.41)		⊕⊕⊖⊖ Low
Heavy				•				•	•	
1	not serious	not serious	not serious	serious <sup>e,f</sup>	none	20	758	<b>aOR 4.19</b> (1.17 to 14.96)		⊕⊕⊕⊖ Moderate
NES3 – A	Animal Follov	ving (number cor	rect)							
Confirm	ed unquantif	iable		-	-	-	-	-		-
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	38	60	-	<b>SMD 0.95 lower</b> (1.38 lower to 0.52 lower)	⊕⊕⊖C Low
D2 Test	of Attention									
Any PAE				-	-	-	-	-		
1	seriousª	not serious	serious <sup>c</sup>	serious <sup>d,f</sup>	none	28	28	-	SMD 0.39 higher (0.14 lower to 0.92 higher)	⊕○○C Very Low
CBCL Att	ention Careg	iver Report (T-sco	ore)		-	-			• •	
Very hea	avy									
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	20	19	-	SMD 1.22 higher (0.53 higher to 1.91 higher)	⊕⊕⊖C Low
Confirm	ed unquantif	iable	-						·	-
4	seriousª	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	179	276	-	SMD 1.95 higher (0.61 higher to 3.29 higher)	⊕○○C Very Low
Any PAE										
1	serious <sup>a</sup>	not serious	not serious	not serious	none	2518	7201	-	SMD 0.10 higher (0.05	⊕⊕⊕⊖ Moderate

	]								higher to 0.15 higher)	
CBCL Att	tention Caregi	iver Report (OR)	(Cut-offs uncle	ar)					8,	
Light	-		•							
1	not serious	not serious	not serious	serious <sup>d,e</sup>	none	208	690	<b>OR 1.68</b> (0.77, 3.68)		⊕⊕⊕⊖ Moderate
Modera	te							•		
1	serious	not serious	not serious	serious <sup>d</sup>	none	194	3609	<b>OR 0.6</b> (0.3, 1.2)	-	⊕⊕⊕⊖ Moderate
Heavy	<u> </u>									
2	seriousª	not serious	not serious	serious <sup>d</sup>	none	164	4299	<b>OR 2.04</b> (0.73, 5.71)	-	⊕⊕⊖⊖ Low
0 studies	s for very hea	vy PAE					-		• •	
YSR Atte	ntion Self-Re	port (OR) (Cut-of	fs unclear)							
Modera	te									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	194	3609	<b>OR 0.7</b> (0.3, 1.6)	-	⊕⊕⊖⊖ Low
Heavy										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	107	3609	<b>OR 1.1</b> (0.4, 3.0)	-	⊕⊕⊖⊖ Low
		ery heavy PAE								
DIAGNO	SED STUDIES									
NEPSY A	uditory Atten	tion								
FASD	<u> </u>									
6	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	330	444	-	<b>SMD 0.81 lower</b> (1.07 lower to 0.55 lower)	⊕○○C Very Low
NEPSY R	esponse Set		<u>.</u>		1	1			· · ·	
FASD										
6	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	328	448	-	SMD 0.64 lower (0.90 lower to 0.37 lower)	⊕○○○ Very Low
	ttention Meas	sures (VIGIL/W: V	visual Total Erro	ors, Auditory I	otal Erro	ors)				
FASD 1	serious <sup>a</sup>	not serious	not serious	serious <sup>e, f</sup>	none	46	53	-	<b>SMD 0.50</b> higher (0.10	⊕⊕⊖⊖ Low
									higher to 0.90 higher)	
1	seriousª	not serious	not serious	very serious <sup>d,e,f</sup>	none	46	53	-	<b>SMD 0.02 lower</b> (0.37 lower to 0.42 higher)	⊕○○○ Very Low
Other At	ttention Meas	sures (CPT-II Omi	ssion Errors)							
ARND/C	Others									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	22	21	-	SMD 1.29 higher (0.63 higher to 1.95	⊕⊕⊖⊖ Low
									higher)	
Other At	ttention Meas	ures: IVA CPT Fu	ll Response Qu	iotient (<2SD l	below po	pulation	mean)		nigner)	

1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	15/20	2/16	<b>OR 21.0</b> (3.49 to 126.3)	-	⊕⊕⊖⊖ Low
ARND/C	Others			•	•					•
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	13/24	2/16	<b>OR 8.27</b> (1.53 to 44.62)	-	⊕⊕⊖⊖ Low
Other Se	elective/Susta	ined Attention N	leasures (TEAC	Ch-Map Missio	n, NES A	nimal Fol	lowing (r	no. correct))		
FASD										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	55	60	-	SMD 0.19 higher (1.17 lower to 1.55 higher)	⊕○○○ Very Low
	ention – Careg	giver Report: CBC	L-C, CBRS (T-so	core)						
FASD	-		1			1	1			
6	seriousª	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	189	1132	-	SMD 1.01 higher (0.54 higher to 1.48 higher)	⊕○○○ Very Low
FAS				-		-	-			
2	seriousª	not serious	not serious	serious <sup>e</sup>	none	30	796	-	SMD 0.62 higher (0.17 higher to 1.07 higher)	⊕⊕⊖⊖ Low
pFAS						-	-			
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>d.e</sup>	none	73	777	-	SMD 1.17 higher (0.62 lower to 2.95 higher)	⊕○○○ Very Low
ARND/C	Others					1				
4	seriousª	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	152	833	-	SMD 1.46 higher (0.61 higher to 2.31 higher)	⊕○○○ Very Low
Ext: Atte	ention – Careg	giver Report: CBC	L-C (Attention	Problems T-so	ore >65	or ADHD	T-score >	>65)		
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	173/ 223	14/78	<b>OR 15.82</b> (8.19 to 30.55)	-	⊕⊕⊖⊖ Low
Ext: Atte	ention – Careg	giver Report: DBD	)							
pFAS										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	45	117	-	SMD 1.06 higher (0.23 lower to 2.36 higher)	⊕○○○ Very Low
Ext: Atte	ention – Teach	ner Report: TRF ( <sup>-</sup>	T-score)							
FASD										
3	serious <sup>a</sup>	not serious	not serious	not serious	none	124	1048	-	SMD 0.78 higher (0.59 higher to 0.97 higher)	⊕⊕⊕⊖ Moderate
FAS										
2	serious <sup>a</sup>	not serious	not serious	not serious	none	74	967	-	SMD 0.62 higher (0.36	⊕⊕⊕⊖ Moderate

	-	1	i i	1					1	1
									higher to 0.89 higher)	
pFAS										
2	serious <sup>a</sup>	not serious	not serious	not serious	none	132	967	-	SMD 0.38 higher (0.11 higher to 0.66 higher)	⊕⊕⊕⊖ Moderate
ARND/C	Others									
2	seriousª	not serious	not serious	not serious	none	83	967	-	SMD 0.91 higher (0.68 higher to 1.14 higher)	⊕⊕⊕⊖ Moderate
Ext: Atte	ention – Teacl	her Report: DBD								
pFAS										
2	seriousª	not serious	not serious	serious <sup>e</sup>	none	45	117	-	SMD 0.84 higher (0.48 higher to 1.19 higher)	⊕⊕⊖⊖ Low
Ext: Atte	ention – Self F	Report: YSR								
pFAS										
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	47	58	-	SMD 1.98 higher (1.51 higher to 2.45 higher)	⊕⊕⊖⊖ Low
ARND/C	others									
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	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 (l<sup>2</sup> >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)												
	Hea	vy PA	E	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias		
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α		
Coles et al 2021 (3.5-4.5yrs; NEPSY-VA)	10.98	2.55	108	11.47	2.43	165	100.0%	-0.20 [-0.44, 0.05]		•		
Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 1.59 (P = 0.11)			108			165	100.0%	-0.20 [-0.44, 0.05]  -  -	4 -2 0 2 Control Heavy PAE			

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



	Confirmed Unquantifiable		0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								H	4 -2 0 2	4
Test for overall effect: Z = 2.56 (P	= 0.01)							Confirme	d Unquantifiable Control	-
Risk of bias legend										

(A) Overall RoB

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

	Confirmed Unquantifiable			0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								l	-4 -2 0 2	4
Test for overall effect: Z = 2.18 (P	= 0.03)								Control Confirmed Un	quantifiable
Risk of bias legend										
(A) Overall RoB										

#### TOVA Omission Errors Block 1 (mean/SD)

#### **Confirmed Unguantifiable PAE and TOVA Omission Errors Block 1 (mean/SD)** (1 study)

	Confirme	d Unquantif	fiable	0	Control			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD.	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
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) Confirmed Unquantifiable Control Std. Mean Difference Std. Mean Difference Ri											
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl A	4	
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)								-4 -2 0 2 4 Control Confirmed Unguantif	ïable	

(A) Overall RoB

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

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

	Hea	avy PA	E	C	ontrol		:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
tudy or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
oles 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]		•
otal (95% CI)			109			168	100.0%	-0.22 [-0.46, 0.02]	•	
eterogeneity: Not applicable								-4		

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)

Ū			-	Odds Ratio	Odds Ratio Risk of Bi
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)					0.01 0.1 1 10 100 Control Light PAE
Risk of bias legend					

(A) Overall RoB

Study of Subgroup	learOdde Datial	65	Maight	Odds Ratio	Odds Ratio Risk o
Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5)	log[Odds Ratio] 0.3133	0.3956	-	IV, Random, 95% Cl 1.37 [0.63, 2.97]	IV, Random, 95% CI A
	0.0100	0.0000	100.0 %	1.01 [0.00, 2.01]	
Total (95% CI)			100.0%	1.37 [0.63, 2.97]	🕈
Heterogeneity: Not applicable					0.01 0.1 1 10 100
Test for overall effect: Z = 0.79 (P = 0.43)					Control Moderate PAE
Risk of bias legend					
(A) Overall RoB					
	and TEACh-5	Solart	ivo/Su	stained Attentio	on (aOR) (1 study)
neavy FAL		Jelett	ive/ Su	Odds Ratio	Odds Ratio Risk o
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	
Underbjerg et al 2012 (~5yrs; TEACh-5)	1.1657	0.5555	100.0%	3.21 [1.08, 9.53]	- <b>-</b>
Total (95% CI)			100.0%	3.21 [1.08, 9.53]	
Heterogeneity: Not applicable			100.0%	5.21 [1.00, 5.55]	
Test for overall effect: Z = 2.10 (P = 0.04)					0.01 0.1 1 10 100 Control Heavy PAE
<u>Risk of bias legend</u> ( <b>A</b> ) Overall RoB					
.,,					
	ective Attenti	ion: TE	ACh-5	Selective Atter	ntion (OR)
Sel				Selective Atter	
Sel				Selective Atter e Attention (aOl Odds Ratio	
Selo Ligh Study or Subgroup		Ch-5 S	electiv	e Attention (aO	R) (1 study) Odds Ratio Risk o
Selo Ligh	t PAE and TEA	Ch-5 S SE	electiv	e Attention (aO Odds Ratio	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A
Selo Ligh Study or Subgroup	t PAE and TEA	Ch-5 S SE	elective Weight	e Attention (aO Odds Ratio IV, Random, 95% CI	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5)	t PAE and TEA	Ch-5 S SE	elective Weight 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54]	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A
Selo Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI)	t PAE and TEA	Ch-5 S SE	elective Weight 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54]	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90)	t PAE and TEA	Ch-5 S SE	elective Weight 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54]	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable	t PAE and TEA	Ch-5 S SE	elective Weight 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54]	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) Risk of bias legend (A) Overall RoB	t PAE and TEA log[Odds Ratio] -0.0305	<b>SE</b> 0.2358	elective <u>Weight</u> 100.0% 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54]	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100 Control Light PAE
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) Risk of bias legend (A) Overall RoB	t PAE and TEA log[Odds Ratio] -0.0305	<b>SE</b> 0.2358	elective <u>Weight</u> 100.0% 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54]	R) (1 study) Odds Ratio IV, Random, 95% CI A 0.01 0.1 1 10 100 Control Light PAE A Control Light PAE
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) Risk of bias legend (A) Overall RoB Moder	t PAE and TEA log[Odds Ratio] -0.0305 ate PAE and T	Ch-5 S <u>se</u> 0.2358	elective <u>Weight</u> 100.0% 100.0% 5 Select	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] tive Attention (a Odds Ratio	R) (1 study) Odds Ratio IV, Random, 95% CI A Control Light PAE Risk o Risk o
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) Risk of bias legend (A) Overall RoB	t PAE and TEA log[Odds Ratio] -0.0305 ate PAE and T log[Odds Ratio]	Ch-5 S <u>se</u> 0.2358	elective Weight 100.0% 100.0% 5 Select Weight	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] tive Attention (a Odds Ratio IV, Random, 95% CI	R) (1 study) Odds Ratio IV, Random, 95% CI A Control Light PAE Risk o Risk o
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) Risk of bias legend (A) Overall RoB Moder Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5)	t PAE and TEA log[Odds Ratio] -0.0305 ate PAE and T log[Odds Ratio]	Ch-5 S <u>se</u> 0.2358 EACh-5 SE	elective <u>Weight</u> 100.0% 100.0% 5 Select <u>Weight</u> 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] tive Attention (a Odds Ratio IV, Random, 95% CI 0.94 [0.45, 1.95]	R) (1 study) Odds Ratio IV, Random, 95% CI A Control Light PAE Risk o Risk o
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) <u>Risk of bias legend</u> (A) Overall RoB Moder Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI)	t PAE and TEA log[Odds Ratio] -0.0305 ate PAE and T log[Odds Ratio]	Ch-5 S <u>se</u> 0.2358 EACh-5 SE	elective Weight 100.0% 100.0% 5 Select Weight	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] tive Attention (a Odds Ratio IV, Random, 95% CI	R) (1 study) Odds Ratio IV, Random, 95% CI 0.01 0.1 1 10 100 Control Light PAE A A A A A A A A A A A A A
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) <u>Risk of bias legend</u> (A) Overall RoB Moder Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable	t PAE and TEA log[Odds Ratio] -0.0305 ate PAE and T log[Odds Ratio]	Ch-5 S <u>se</u> 0.2358 EACh-5 SE	elective <u>Weight</u> 100.0% 100.0% 5 Select <u>Weight</u> 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] tive Attention (a Odds Ratio IV, Random, 95% CI 0.94 [0.45, 1.95]	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100 Control Light PAE R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) <u>Risk of bias legend</u> (A) Overall RoB Moder Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI)	t PAE and TEA log[Odds Ratio] -0.0305 ate PAE and T log[Odds Ratio]	Ch-5 S <u>se</u> 0.2358 EACh-5 SE	elective <u>Weight</u> 100.0% 100.0% 5 Select <u>Weight</u> 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] tive Attention (a Odds Ratio IV, Random, 95% CI 0.94 [0.45, 1.95]	R) (1 study) Odds Ratio IV, Random, 95% CI 0.01 0.1 1 10 100 Control Light PAE A A A A A A A A A A A A A
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) <u>Risk of bias legend</u> (A) Overall RoB Moder Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable	t PAE and TEA log[Odds Ratio] -0.0305 ate PAE and T log[Odds Ratio]	Ch-5 S <u>se</u> 0.2358 EACh-5 SE	elective <u>Weight</u> 100.0% 100.0% 5 Select <u>Weight</u> 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] tive Attention (a Odds Ratio IV, Random, 95% CI 0.94 [0.45, 1.95]	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100 Control Light PAE R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) Risk of bias legend (A) Overall RoB Moder Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.17 (P = 0.87)	t PAE and TEA log[Odds Ratio] -0.0305 ate PAE and T log[Odds Ratio]	Ch-5 S <u>se</u> 0.2358 EACh-5 SE	elective <u>Weight</u> 100.0% 100.0% 5 Select <u>Weight</u> 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] tive Attention (a Odds Ratio IV, Random, 95% CI 0.94 [0.45, 1.95]	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100 Control Light PAE R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) Risk of bias legend (A) Overall RoB Moder Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.17 (P = 0.87) Risk of bias legend	t PAE and TEA log[Odds Ratio] -0.0305 ate PAE and T log[Odds Ratio]	Ch-5 S <u>se</u> 0.2358 EACh-5 SE	elective <u>Weight</u> 100.0% 100.0% 5 Select <u>Weight</u> 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] tive Attention (a Odds Ratio IV, Random, 95% CI 0.94 [0.45, 1.95]	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100 Control Light PAE R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100
Sele Ligh Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.90) Risk of bias legend (A) Overall RoB Moder Study or Subgroup Underbjerg et al 2012 (~5yrs; TEACh-5) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.17 (P = 0.87) Risk of bias legend	t PAE and TEA log[Odds Ratio] -0.0305 ate PAE and T log[Odds Ratio]	Ch-5 S <u>se</u> 0.2358 EACh-5 SE	elective <u>Weight</u> 100.0% 100.0% 5 Select <u>Weight</u> 100.0%	e Attention (aOl Odds Ratio IV, Random, 95% CI 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] 0.97 [0.61, 1.54] tive Attention (a Odds Ratio IV, Random, 95% CI 0.94 [0.45, 1.95]	R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100 Control Light PAE R) (1 study) Odds Ratio Risk o IV, Random, 95% CI A 0.01 0.1 1 10 100

				Odds Ratio		Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
Underbjerg et al 2012 (~5yrs; TEACh-5)	1.1694	0.6291	100.0%	3.22 [0.94, 11.05]			•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.86 (P = 0.06)			100.0%	3.22 [0.94, 11.05]	L	0.1 1 10 Control Heavy PAE	100 E

Risk of bias legend (A) Overall RoB

### Sustained Attention: TEACh-5 Selective Attention (OR)

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

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

				Odds Ratio		Odd	s Ratio		Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Rand	om, 95% CI		Α
Underbjerg et al 2012 (~5yrs; TEACh-5)	0.7178	0.3908	100.0%	2.05 [0.95, 4.41]					•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.84 (P = 0.07)			100.0%	2.05 [0.95, 4.41]	L 0.01	0.1 Contro	1 10 Moderate	100 PAE	I

Risk of bias legend (A) Overall RoB

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

			Odds Ratio	Odds Ratio Risk of Bias
og[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
1.4327	0.6493	100.0%	4.19 [1.17, 14.96]	
		100.0%	4.19 [1.17, 14.96]	
				0.01 0.1 1 10 100 Control Heavy PAE
			1.4327 0.6493 100.0%	1.4327 0.6493 100.0% 4.19 [1.17, 14.96]

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)

	Confirme	d Unquanti	ifiable	Co	ontro	I		Std. Mean Difference		Std. Mean	Difference	,	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Rando	om, 95% CI		Α
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									-4	-2		4	
Test for overall effect: Z = 4.35 (P < 0.0001	)							Confirm	ied (	Unquantifiable	Control		

Risk of bias legend (A) Overall RoB

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

Risk of Bias

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

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

,,.,.,											
	Ar	IY PAE		С	ontrol			Std. Mean Difference	Std. Mean Differ	ence	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95	% CI	Α
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										<u> </u>	÷
Test for overall effect: Z = 1.45 (P = 0.15)									-4 -2 U Control Any F	PAE	+
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 F	PAE	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								_	-2 -1 0 1 2	
Test for overall effect: Z = 3.47 (P = 0.	.0005)								-2 -1 U 1 2 Control Very Heavy PAE	=

Risk of bias legend (A) Overall RoB

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

	Confirmed	Unquantif	iable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD		Mean	SD		Weight	IV, Random, 95% CI	IV, Random, 95% Cl	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: Tau <sup>2</sup> = 1.78; Chi <sup>2</sup> = 75.54, Test for overall effect: Z = 2.86 (P = 0.004	1	1.00001); I²	= 96%						-4 -2 0 2 Control Confirmed Ungu	⊣ 4 Jantifiable

#### Risk of bias legend

(A) Overall RoB

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

	An	y PA	E	Co	ontro	I	:	Std. Mean Difference	S	td. Mean Differenc	e I	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	I	V, Random, 95% C	I	Α
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)								-2 -	1 0 1 Control Any PAE	2	

Risk of bias legend (A) Overall RoB

#### Externalising Behaviour: CBCL Attention – Caregiver Report (OR)

Lig	ht PAE and CE	SCL Att	ention	– Caregiver (OR	) (1 study)	
				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
O'Leary et al 2009 (2, 5, 8yrs; CBCL-C)	0.5182	0.3997	100.0%	1.68 [0.77, 3.68]	-	•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.30 (P = 0.19)			100.0%	1.68 [0.77, 3.68]	<b>├ · · · · · · ·</b>	100

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

			Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio] S	E Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
O'Callaghan et al 2007 (~14yrs; CBCL-C)	-0.5093 0.352	9 100.0%	0.60 [0.30, 1.20]		?
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.44 (P = 0.15)		100.0%	0.60 [0.30, 1.20]		00
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) Odds Ratio Odds Ratio Risk of Bias Study or Subgroup log[Odds Ratio] SE Weight IV, Random, 95% CI IV, Random, 95% CI Α 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) 1.80 [0.40, 8.01] 0.5872 0.762 47.4% Total (95% CI) 100.0% 2.04 [0.73, 5.71] Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.05, df = 1 (P = 0.82); l<sup>2</sup> = 0% 0.01 100 0.1 10 Test for overall effect: Z = 1.36 (P = 0.17) Heavy PAF Control 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)

				Odds Ratio		Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
O'Callaghan et al 2007 (~14yrs; YSR)	-0.3567	0.4323	100.0%	0.70 [0.30, 1.63]			?
Total (95% CI) Heterogeneity: Not applicable			100.0%	0.70 [0.30, 1.63]	ı —	<b>•</b>	
Test for overall effect: Z = 0.83 (P = 0.41)					0.01	0.1 1 10 Control Moderate PAE	100 E

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) Odds Ratio Odds Ratio Risk of Bias Study or Subgroup log[Odds Ratio] SF Weight IV, Random, 95% CI IV, Random, 95% CI Α 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 ĥ Π1 0.1 10 100 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		0	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD.	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.06; Chi <sup>2</sup> = 13.19, df =	5 (P = 0	.02); I <sup>z</sup> = I	62%					F.	<u> </u>	<u> </u> .
Test for overall effect: Z = 6.15 (P < 0.00001)								-4	-2 0 2 FASD Control	4

(A) Overall RoB

#### NEPSY-II Response Set (mean/SD)

FASD and NEPSY Response Set (mean/SD) (6 studies)

								-1	
	FASD		0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
10	3	65	11.7	2.6	79	18.7%	-0.61 [-0.94, -0.27]		?
9.6	3.3941	72	11.4	2.846	90	19.3%	-0.58 [-0.89, -0.26]		•
7.22	7.5	21	11.13	5.88	80	14.0%	-0.62 [-1.11, -0.13]		•
8.28	1.15	32	10.42	1.58	30	11.9%	-1.54 [-2.11, -0.97]		•
8.9	3.9	101	10.1	3.5	129	21.1%	-0.32 [-0.59, -0.06]		•
11	2	37	12	2	40	15.0%	-0.49 [-0.95, -0.04]		•
		328			448	100.0%	-0.64 [-0.90, -0.37]	•	
5 (P = 0	.01); I² =	66%					H		<u> </u>
							-	FASD Control	4
	Mean 10 9.6 7.22 8.28 8.9 11	FASD           Mean         SD           10         3           9.6         3.3941           7.22         7.5           8.28         1.15           8.9         3.9           11         2	FASD           Mean         SD         Total           10         3         65           9.6         3.3941         72           7.22         7.5         21           8.28         1.15         32           8.9         3.9         101           11         2         37	FASD         Column 10           10         3         65         11.7           9.6         3.3941         72         11.4           7.22         7.5         21         11.3           8.28         1.15         32         10.42           8.9         3.9         101         101           11         2         37         12	FASD         Control           Mean         SD           10         3         65         11.7         2.6           9.6         3.3941         72         11.4         2.846           7.22         7.5         2.1         11.13         5.88           8.28         1.15         32         10.42         1.58           8.9         3.9         101         10.1         3.5           11         2         37         12         2	FASD         Control         Mean         SD         Total           10         3         65         11.7         2.6         79           9.6         3.3941         72         11.4         2.86         90           7.22         7.5         2.1         11.13         5.88         80           8.28         1.15         32         10.42         1.58         30           8.9         3.9         101         10.1         3.5         129           11         2         37         12         2.4         40	FASD         Control         Sontrol         Sontrol <thsontrol< th=""> <thsontrol< th=""> <thsont< td=""><td>FASD         Control         Std. Mean Difference           Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           10         3         65         11.7         2.6         79         18.7%         -0.61 [-0.94, -0.27]           9.6         3.3941         72         11.4         2.86         90         19.3%         -0.58 [-0.89, -0.26]           7.22         7.5         2.1         11.13         5.88         80         14.0%         -0.62 [-1.11, -0.13]           8.28         1.15         32         10.42         1.58         30         11.9%         -1.54 [-2.11, -0.97]           8.9         3.9         101         10.1         3.5         129         21.1%         -0.32 [-0.59, -0.06]           11         2         37         12         2         40         15.0%         -0.49 [-0.95, -0.04]           11         2         37         12         2         40         15.0%         -0.49 [-0.95, -0.04]</td><td>Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           10         3         65         11.7         2.6         79         18.7%         -0.61 [-0.94, -0.27]         -           9.6         3.3941         72         11.4         2.846         90         19.3%         -0.58 [-0.89, -0.26]         -           7.22         7.5         21         11.13         5.88         80         14.0%         -0.62 [-1.11, -0.13]         -           8.28         1.15         32         10.42         1.58         30         11.9%         -1.54 [-2.11, -0.97]         -           8.9         3.9         101         10.1         3.5         129         21.1%         -0.32 [-0.59, -0.06]         -           11         2         37         12         2         40         15.0%         -0.49 [-0.96, -0.04]         -           5 (P = 0.01); P = 66%         -         -         -         -         -         2         2         2</td></thsont<></thsontrol<></thsontrol<>	FASD         Control         Std. Mean Difference           Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           10         3         65         11.7         2.6         79         18.7%         -0.61 [-0.94, -0.27]           9.6         3.3941         72         11.4         2.86         90         19.3%         -0.58 [-0.89, -0.26]           7.22         7.5         2.1         11.13         5.88         80         14.0%         -0.62 [-1.11, -0.13]           8.28         1.15         32         10.42         1.58         30         11.9%         -1.54 [-2.11, -0.97]           8.9         3.9         101         10.1         3.5         129         21.1%         -0.32 [-0.59, -0.06]           11         2         37         12         2         40         15.0%         -0.49 [-0.95, -0.04]           11         2         37         12         2         40         15.0%         -0.49 [-0.95, -0.04]	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           10         3         65         11.7         2.6         79         18.7%         -0.61 [-0.94, -0.27]         -           9.6         3.3941         72         11.4         2.846         90         19.3%         -0.58 [-0.89, -0.26]         -           7.22         7.5         21         11.13         5.88         80         14.0%         -0.62 [-1.11, -0.13]         -           8.28         1.15         32         10.42         1.58         30         11.9%         -1.54 [-2.11, -0.97]         -           8.9         3.9         101         10.1         3.5         129         21.1%         -0.32 [-0.59, -0.06]         -           11         2         37         12         2         40         15.0%         -0.49 [-0.96, -0.04]         -           5 (P = 0.01); P = 66%         -         -         -         -         -         2         2         2

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)

		FASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total		SD	Total		IV, Random, 95% CI		Α
Coles et al 2002 (13-17yrs; VIGILW)	15.21	13.37	46	9.57	8.98	53	100.0%	0.50 [0.10, 0.90]	le l	•
Total (95% CI) Heterogeneity: Not applicable			46			53	100.0%	0.50 [0.10, 0.90]	-4 -2 0 2	
Test for overall effect: Z = 2.43 (P = 0.0	1)								Control FASD	
Risk of bias legend										

(A) Overall RoB

#### FASD and VIGIL/W: Auditory Total Errors (mean/SD) (1 study)

			_						( ····
		FASD		0	Control			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
Coles et al 2002 (13-17yrs; VIGILW)	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	)								-4 -2 0 2 4 Control FASD

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)

	ARNI	Co	Control			Std. Mean Difference	Std. Mean Difference Risk of B		
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
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)									Control ARND/Others
Risk of bias legend									

<sup>(</sup>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 IV	A CP	T Full	Resp	onse C	Quotient (%) (1	study)
-	pFA	S	Contr	ol		Odds Ratio	Odds Ratio Risk of Bia
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl A
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)							0.001 0.1 1 10 1000 Control pFAS
Risk of bias legend							

(A) Overall RoB

#### ARND/Others and IVA CPT Full Response Quotient (%) (1 study)

•					•	• •	
	ARND/Ot	thers	Contr	ol		Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
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 Heterogeneity: Not applicable Test for overall effect: Z = 2.46 (P = 0.01)	13		2				0.001 0.1 1 10 1000 Control ARND/Others

#### 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)

	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.86; Chi <sup>2</sup> = 9.25, df = 1 (P =	= 0.002):	<b> 2</b> = 89	1%					1		<u> </u>

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.

FAS	D and	I CBC	L/CB	RS A	ttent	ion -	Careg	(iver (T-score) (	(6 studies)
		FASD		0	Control		-	Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	I IV, Random, 95% CI 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]	ı <del>†</del> - ●
Total (95% CI)			189			1132	100.0%	1.01 [0.54, 1.48]	1 🔶
Heterogeneity: Tau² = 0.26; Chi² = 32.11, c	lf= 5 (P ·	< 0.000(	01); I <sup>z</sup> =	84%					
Test for overall effect: Z = 4.22 (P < 0.0001	)								Control FASD

#### Risk of bias legend

#### (A) Overall RoB

#### FAS and CBCL Attention - Caregiver (T-score) (2 studies)

		FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	- <b>+</b>	•
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.02, dt	í = 1 (P =	: 0.89)	; <b>I2</b> = 09	6				ŀ	<u>, t l t</u>	<u> </u>
Test for overall effect: Z = 2.70 (P = 0.007)								-	4 -2 U 2 Control FAS	4

Risk of bias legend (A) Overall RoB

#### pFAS and CBCL Attention - Caregiver (T-score) (2 studies)

	F	FAS		Co	ontro	1		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 1.57; Chi <sup>2</sup> = 18.92, df = 1 (P	< 0.0001	l);	95%						-4 -2 0 2	4
Test for overall effect: Z = 1.28 (P = 0.20)									Control pFAS	

<u>Risk of bias legend</u> (A) Overall RoB

#### ARND/Others and CBCL Attention (T-score) (4 studies)

									•/	
	ARN	D/Othe	rs	C	ontrol		Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	<b>_</b>	•
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: Tau <sup>2</sup> = 0.65; Chi <sup>2</sup> = 32.09, df = 3 (P Test for overall effect: Z = 3.37 (P = 0.0008)	< 0.0000	1); I²=	91%					H	4 -2 0 2 Control ARND/Others	4

<u>Risk of bias legend</u> (A) Overall RoB

### Externalising Behaviour: CBCL Attention – Caregiver Report (OR/Frequency)

0						0 1	
FASD and	Freque	ncy o	of Clini	cal Cl	BCL Att	ention Score - C	Caregiver (1 study)
	FAS	D	Contr	ol		Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl 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 Heterogeneity: Not applicable	173		14				
Test for overall effect: Z = 8.22 (P < 0.00	001)						Control FASD

#### pFAS and DBD Attention (mean/SD) (2 studies)

le.						·· • • · · ·		- / ( /		
		<b>pFAS</b>		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.80; Chi <sup>2</sup> = 12.19, df = 1 (P = 0.0	0005); I²	= 92%							-4 -2 0 2	4
Test for overall effect: Z = 1.61 (P = 0.11)									Control pFAS	

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)

	F	ASD		Co	ontro	I	:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	-	•
Fotal (95% CI)			124			1048	100.0%	0.78 [0.59, 0.97]	•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> =	= 1.03, df	f = 2 (	(P = 0.6	i0); I <sup>2</sup> = (	0%			H	. <u></u> .	-
Heterogeneity: Tau+= 0.00; Chi+= Test for overall effect: Z = 8.11 (P	•		,P = 0.6	iu); i= i	7%			-4	4 -2 0 2 Control FASD	4

#### Risk of bias legend (A) Overall RoB

#### FAS and CBCL Attention – Teacher (T-score) (2 studies)

		FAS		C	ontrol			Std. Mean Difference		Std. Mear	1 Difference	•	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rand	om, 95% Cl		Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.70 Test for overall effect: Z = 4.62 (P < 0.0		<sup>D</sup> = 0.4	0);   <b>2</b> =	0%					-4	-2 Contro	0 2 I FAS	4	1

Risk of bias legend (A) Overall RoB

#### pFAS and CBCL Attention – Teacher (T-score) (2 studies)

	p	FAS		C	ontrol		1	Std. Mean Difference		Std. Mear	n Difference	9	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Rand	om, 95% Cl		Α
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: Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> = 1.98, Test for overall effect: Z = 2.70 (P = 0.00		° = 0.1	6); I² = -	49%					-4	-2 Contro	 0 2   pFAS		4

<u>Risk of bias legend</u> (A) Overall RoB

#### ARND/Others and CBCL Attention (T-score) (2 studies)

	ARN	D/Othe	ers	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.24, df = 1 (	(P = 0.62	?); l² = l	0%							-
Test for overall effect: Z = 7.68 (P < 0.00001)									Control ARND/Others	4

#### Risk of bias legend (A) Overall RoB

82

#### Externalising Behaviour: DBD Attention – Teacher Report (mean/SD)

#### pFAS and DBD Attention – Teacher (mean/SD) (2 studies)

•							•		,	
	1	pFAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: $Tau^2 = 0.00$ ; $Chi^2 = 0.63$ , $df = 1$ (P = 0.4	3); I <sup>2</sup> = 0'	%								<u> </u>
Test for overall effect: Z = 4.60 (P < 0.00001)									Control pFAS	4

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)

	•		anu					eport (T-score) (1	••	D: 1 (D)
		DFAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								F	<u>, t l t</u>	<u> </u>
Test for overall effect: Z = 8.22 (F	° < 0.00	001)							Control pFAS	4

(A) Overall RoB

#### ARND/Others and YSR Attention – Self Report (T-score) (1 study)

	ARND/Others Control							Std. Mean Difference	Std. Mean Difference	Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α	
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 < 0.0	0001)							Control ARND/Others		

Risk of bias legend (A) Overall RoB

# Summary of available outcomes for executive functioning

	Executive F	unction	
Study type	Outcome	Data	# studies
Exposure Studies	NEPSY: Speeded Naming	mean/SD	<b>4 studies</b> : 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):	mean/SD	2 studies: 2 confirmed unquantifiable
	Composite		
	WCST: Total Errors (raw)	mean/SD	1 studies: 1 Any PAE
	NIH Toolbox: Dimensional Change Card	mean/SD	<b>1 study:</b> 1 light, 1 moderate, 1 any PAE
	Sort		
	Verbal Fluency: D-KEFS (total correct	mean/SD	3 studies: 3 confirmed unquantifiable
	letter)		
	Letter Fluency: F-A-S test (words/mins)	mean/SD	1 study: 1 confirmed unquantifiable
	Verbal Fluency: D-KEFS (Verbal Fluency	mean/SD	3 studies: 3 confirmed unquantifiable
	Switching)		
	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 KEES Multiple other subdomains	maan/SD	2 studios all different measures
	Other D-KEFS: Multiple other subdomains	mean/SD	3 studies, all different measures
	(colour inference, trail making, tower test).		
	BRIEF Global Executive Composite –		2 studies 1 light medewate heavy 1
	-	mean difference/	<b>2 studies:</b> 1 light, moderate, heavy, 1 confirmed unquantifiable
	Caregiver Report		commed unquantinable
	DDIEE Debenieur Desulation Indeu	mean/SD	2 studies 1 light medewate heavy 1
	BRIEF Behaviour Regulation Index –	mean difference/	<b>2 studies:</b> 1 light, moderate, heavy, 1
	Caregiver Reports		confirmed unquantifiable
	DDIES Dahariana Daardatian Indon	mean/SD	A studie liebt woods with basis
	BRIEF Behaviour Regulation Index –	mean	<b>1 study:</b> light, moderate, heavy
	Teacher Report	difference	2 studies 4 light medewate began 4
	BRIEF Metacognition Index – Caregiver	mean	<b>2 studies:</b> 1 light, moderate, heavy, 1
	Report	difference/	confirmed unquantifiable
	DDIES Matageneitien Inden. Tageben	mean/SD	1 studuu lisht woodowsto hoovu
	BRIEF Metacognition Index – Teacher	mean difference	<b>1 study:</b> light, moderate, heavy
	Report	mean/SD	2 studies 2 confirmed upquentificable
Diagnoord	BRIEF 8 Subdomains - Caregiver	· · ·	<b>2 studies:</b> 2 confirmed unquantifiable
Diagnosed Studies	NEPSY: Speeded Naming	mean/SD	<b>5 studies</b> : 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Other
	NEPSY: INN	mean/SD	<b>9 studies:</b> 8 FASD, 1 FAS, 1 pFAS, 2 ARND/Other
	NEPSY: INI	mean/SD	<b>10 studies:</b> 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	<b>5 studies:</b> 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Other
	NEPSY: Animal Sorting	mean/SD	6 studies: 6 FASD
	WCST: Multiple sub-domains	mean/SD	<b>4 studies:</b> 2 FASD, 2 pFAS, 2
		meany 3D	ARND/Other (all different measures)
	Letter Fluency: D-KEFS, NEPSY-II (total	mean/SD	4 studies: 3 FAS, 1 pFAS, 1
	correct)	meanyob	ARND/Others
	Letter Fluency: D-KEFS (speed)	mean/SD	<b>1 study:</b> 1 FAS, 1 ARND/Others
	Letter Fluency: F-A-S test (words/mins)	mean/SD	<b>1 study:</b> 1 FASD
	Verbal Fluency: D-KEFS (Verbal Fluency	mean/SD	<b>3 studies:</b> 1 FASD, 2 FAS, 1
	Switching)	meanyob	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-	mean/SD	2 studies: 2 FASD
	KEFS Tower Test (total)		
	Other D-KEFS Measures: Any age, incl:	mean/SD	<b>5 studies:</b> 2 FAS, 1 pFAS, 1
	Multiple other subdomains (colour		ARND/Others (all different
	inference, trail making, tower test)		measures/units)
	Other Measures: Trail Making Test Trial B,	mean/SD	3 studies: 3 FASD
	Test of Executive Function		
	BRIEF Global Executive Composite –	T-score	5 studies: 3 FASD, 2 pFAS, 2
	Caregiver Report		ARND/Others
	BRIEF Behaviour Regulation Index –	T-score	5 studies: 3 FASD, 2 pFAS, 2
	Caregiver Report		ARND/Others
	BRIEF Behaviour Regulation Index –	T-score	1 study: 1 FASD
	Teacher Report		
	BRIEF Metacognition Index – Caregiver	T-score	5 studies: 3 FASD, 2 pFAS, 2
	Report		ARND/Others
	BRIEF Metacognition Index – Teacher	T-score	1 study: 1 FASD

BRIEF Other Subdomains – Caregiver:	T-score	3 studies: 2 FASD (inhibit + shift), 1
Inhibit, Shift, Monitor, Plan/Organise,		FASD (all others), 1 ARND/Others
Working Memory		

# GRADE ratings for executive functioning

		Certainty	assessment			Nº of p	oatients		Effect	Certainty
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% CI)	
EXPOSU	RE STUDIE	S								
NEPSY S	peeded Na	aming								
Heavy										
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	serious <sup>e,f</sup>	none	82	132	-	SMD 0.64 lower (0.92 lower to 0.35 lower)	⊕○○○ Very Low
Confirm	ed unquar	ntifiable							•	
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	222	238	-	<b>SMD 0.57 lower</b> (0.96 lower to 0.17 lower)	⊕○○○ Very Low
NEPSY Ir	nhibition e	rrors (ss)								
Confirm	ed unquar	ntifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	142	160	-	SMD 0.68 lower (0.91 lower to 0.44 lower)	⊕⊕⊖⊖ Low
NEPSY Ir	nhibition e	rrors (raw)								
Confirm	ed unquar	ntifiable								
1	seriousª	not serious	not serious	very serious <sup>d,e,f</sup>	none	25	16	-	SMD 0.25 higher (0.38 lower to 0.88 higher)	⊕○○○ Very Low
Wiscons	in Card So	rting Test (WCS	r): Composite							
Confirm	ed unquar	ntifiable								
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	100	113	-	SMD 0.56 lower (0.95 lower to 0.17 lower)	⊕⊕⊖⊖ Low
Wiscons	in Card So	rting Test (WCS	F): Total Errors	(raw)						
Any PAE										
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	28	28	-	SMD 0.36 higher (0.17 lower to 0.89 higher)	⊕○○○ Very Low
NIH Tool	lbox: Dime	nsional Change	Card Sort							
Light PA	E									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	93	6669	-	SMD 0.18 higher (0.03 lower to 0.38 higher)	⊕⊕⊖⊖ Low
Moderat	te PAE									
1	serious <sup>a</sup>	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 <sup>a</sup>	not serious	not serious	not serious	none	2518	7501	-	SMD 0.13 higher	$\oplus \oplus \oplus \bigcirc$
									(0.08 higher to 0.17 higher)	Moderate
Verbal F	Fluency: D-	KEFS (total corre	ect letter)				I		0.17 Higher)	
	ed unquar	•	,							
3	serious <sup>a</sup>	not serious	not serious	not serious	none	388	314	_	SMD 0.90 lower	$\oplus \oplus \oplus \bigcirc$
Ū.	001100.0								(1.07 lower to 0.73	Moderate
									lower)	
Verbal F	luency: D-	KEFS (Verbal Flu	ency Switching	g)						
Confirm	ed unquar	ntifiable								
3	serious <sup>a</sup>	not serious	not serious	not serious	none	389	378	-	SMD 1.07 lower	$\oplus \oplus \oplus \bigcirc$
									(1.33 lower to 0.82	Moderate
Catagor		McCarthy, D-KE	EC						lower)	
-		-	гэ							
	ed unquan			· of			0.70	1		
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	84	273	-	SMD 0.61 lower (1.54 lower to 0.32	⊕○○○ Very Low
									lower)	Very LOW
D-KEFS:	Tower Tes	t (total achiever	nent)				•			
Confirm	ed unquar	ntifiable								
2	serious <sup>a</sup>	not serious	not serious	not serious	none	231	205	-	SMD 0.78 lower	$\oplus \oplus \oplus \bigcirc$
									(0.98 lower to 0.58	Moderate
									lower)	
	lobal Execu	itive Composite	– Caregiver Re	eport						
Light		-								
1	not	not serious	not serious	serious <sup>d</sup>	none	675	758	-	SMD 0.06 higher	$\oplus \oplus \oplus \bigcirc$
	serious								(0.04 lower to 0.17 higher)	Moderate
Modera	l								nigher)	
1	not	not serious	not serious	serious <sup>d</sup>	none	175	758	_	SMD 0.00 lower	$\oplus \oplus \oplus \bigcirc$
-	serious	not serious	not serious	Schous	none	1/5	/30		(0.17 lower to 0.16	Moderate
									higher)	
Heavy										
1	not	not serious	not serious	serious <sup>d,e</sup>	none	20	758	-	SMD 0.05 higher	$\oplus \oplus \oplus \bigcirc$
	serious								(0.39 lower to 0.5	Moderate
Confirm	l Ied Unguar								higher)	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	28	15	_	SMD 4.63 higher	<u></u>
Ŧ	serious	not serious	not senous	Serious	none	20	15	-	(3.43 higher to	⊕⊕⊖⊖ Low
									5.84 higher)	LOW
0 studie	s for very h	eavy or any pae	2						· · ·	
BRIEF Be	ehaviour Re	egulation Index	– Caregiver Re	ports						
Light										
1	not	not serious	not serious	serious <sup>d</sup>	none	675	758	-	SMD 0.07 higher	$\oplus \oplus \oplus \bigcirc$
	serious								(0.04 lower to 0.17	Moderate
									higher)	
Modera	1	1						1		
1	not	not serious	not serious	serious <sup>d</sup>	none	175	758	-	SMD 0.01 lower	$\oplus \oplus \oplus \bigcirc$
	serious								(0.18 lower to 0.15 higher)	Moderate
Heavy	1	1					1	1		
1	not	not serious	not serious	serious <sup>d,e</sup>	none	20	758	_	SMD 0.20 higher	$\oplus \oplus \oplus \bigcirc$
-	serious			0011000					(0.24 lower to 0.64	Moderate
									higher)	

Confirm	ed Unquar	ntifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	28	15	-	<b>SMD 3.00 higher</b> (2.09 higher to 3.92 higher)	⊕⊕⊖⊖ Low
) studie	s for very h	eavy, unquanti	fied or any pae							
BRIEF B	ehaviour Re	egulation Index	– Teacher Repo	ort						
Light										
1	not serious	not serious	not serious	serious <sup>d</sup>	none	675	758	-	<b>SMD 0.01 lower</b> (0.11 lower to 0.09 higher)	⊕⊕⊕⊖ Moderate
Modera	te									
1	not serious	not serious	not serious	serious <sup>d</sup>	none	175	758	-	<b>SMD 0.08 lower</b> (0.25 lower to 0.08 higher)	⊕⊕⊕⊖ Moderate
Heavy										
1	not serious	not serious	not serious	serious <sup>d,e</sup>	none	20	758	-	SMD 0.19 lower (0.63 lower to 0.26 higher)	⊕⊕⊕⊖ Moderate
0 studie	s for very h	eavy or any pae	5							
BRIEF M	letacognitio	on Index – Care	giver Report							
Light										
1	not serious	not serious	not serious	serious <sup>d</sup>	none	675	758	-	SMD 0.09 (0.01 lower to 0.20 higher)	⊕⊕⊕⊖ Moderate
Modera	te									
1	not serious	not serious	not serious	serious <sup>d,e</sup>	none	175	758	-	<b>SMD 0.01 higher</b> (0.16 lower to 0.17 higher)	⊕⊕⊕⊖ Moderate
Heavy			•				•			
1	not serious	not serious	not serious	serious <sup>d,e</sup>	none	20	758	-	SMD 0.38 higher (0.07 lower to 0.82 higher)	⊕⊕⊕⊖ Moderate
Confirm	ed Unquar	ntifiable	11				11		0-7	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	28	15	-	SMD 5.19 higher (3.88 higher to 6.50 higher)	⊕⊕⊖⊖ Low
0 studie	s for very h	eavy or any pae	5							
BRIEF M	letacognitio	on Index – Teac	her Report							
Light										
1	not serious	not serious	not serious	serious <sup>d</sup>	none	675	758	-	SMD 0.02 higher (0.08 lower to 0.12 higher)	⊕⊕⊕⊖ Moderate
Modera	te									
1	not serious	not serious	not serious	serious <sup>d</sup>	none	175	758	-	<b>SMD 0.02 lower</b> (0.18 lower to 0.15 higher)	⊕⊕⊕⊖ Moderate
Heavy	-								· 1	
1	not serious	not serious	not serious	serious <sup>d,e</sup>	none	20	758	-	<b>SMD 0.21 lower</b> (0.66 lower to 0.23 higher)	⊕⊕⊕⊖ Moderate
	-	eavy, unquanti								
BRIEF Su	ubdomains	– Caregiver Rep	ort: Inhibit							
Confirm	ed Unquar	ntifiable								

BRIEF Subdomains - Caregiver Report: Shift         2       Serious*       not serious       serious*       none       101       302       -       SMD 2.84 higher to       1         2       Serious*       not serious       serious*       none       101       302       -       SMD 2.84 higher to       3.13 higher         3       J.15 higher       (2.49 higher to)       3.13 higher       (9.4         2       Serious*       not serious       serious*       none       101       302       -       SMD 2.30 higher (1.97 higher to)       (9.6         2       Serious*       not serious       serious*       none       101       302       -       SMD 3.46 higher to)       (9.6         3BIEF Subdomains - Caregiver Report: Initiate       Confirmed Unquantifiable       -       SMD 4.71 higher to)       (9.6       (1.97 higher to)       (2.64 higher to)       (2.64 higher to)       (2.64 higher to)       (2.64 higher to)       (2.02 higher)	2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	101	302	-	SMD 2.94 higher (1.39 higher to	⊕○○○ Very Low
Confirmed Unquantifiable       not serious       serious*       none       101       302       -       SMD 2.84 higher (2.49 higher to 3.19 higher)       Geg         2       serious*       not serious       serious*       none       101       302       -       SMD 2.84 higher to 3.19 higher)       L         3.19 higher)       3.19 higher)       3.19 higher)       3.19 higher)       C.47 higher to 2.62 higher)       C       C.47 higher to 2.62 higher)       C       C       SMD 2.30 higher (1.97 higher to 2.62 higher)       C       C       C       SMD 2.30 higher (1.97 higher to 2.62 higher)       C       S       S       C										4.49 higher)	,
2       Serious*       not serious       serious*       none       101       302       -       SMD 2.84 higher to       L         BRIEF Subdomains - Caregiver Report: Emotional Control       Confirmed Unquantifiable       -       SMD 2.84 higher to       L         2       Serious*       not serious       not serious       serious*       none       101       302       -       SMD 2.84 higher to       L         2       Serious*       not serious       not serious*       serious*       none       101       302       -       SMD 2.84 higher to       L       Ver         SRIEF Subdomains - Caregiver Report: Initiate       -       SMD 3.46 higher to       2.62 higher)       Ver       L       2.62 higher)       Ver       2.62 higher)       Ver				oort: Shift							
BRIEF Subdomains - Caregiver Report: Emotional Control         Confirmed Unquantifiable         2       Serious*       not serious       serious*       none       101       302       -       (SMD 2.30 higher to 2.62 higher)       CV Ver         BRIEF Subdomains - Caregiver Report: Initiate       -       SMD 3.46 higher 2.62 higher)       CV Ver       CV 2.62 higher)       CV Ver         BRIEF Subdomains - Caregiver Report: Unitiate       -       SMD 3.46 higher 2.62 higher)       CV 4.28 higher)       CV	nfirmed	d Unquan	itifiable								
BRIEF Subdomains - Caregiver Report: Emotional Control         Confirmed Unquantifiable         2       serious <sup>3</sup> not serious       not serious'       none       101       302       -       SMD 2.30 higher (1.97 higher to 2.62 higher)       GC         BRIEF Subdomains - Caregiver Report: Initiate       Confirmed Unquantifiable       GC       SMD 3.46 higher (2.64 higher to 4.28 higher)       GC       GC       SMD 3.46 higher (2.64 higher to 4.28 higher)       GC	2 :	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	101	302	-	(2.49 higher to	⊕⊕⊖⊖ Low
2       serious <sup>a</sup> not serious       not serious       serious <sup>a</sup> none       101       302       -       SMD 2.30 higher (1.97 higher to 2.62 higher)       OVer (1.97 higher to 2.62 higher)       OVer (1.97 higher to 2.62 higher)       OVer (2.64 higher to 2.63 higher)       OVER (2.02 higher to 2.55 higher)       OVER (2.02 higher)       OVER (2	IEF Sub	domains	– Caregiver Rep	oort: Emotional	Control						
RILEF Subdomains - Caregiver Report: Initiate       Image: SMD 3.46 higher (2.62 higher)       Ver         2       serious <sup>a</sup> not serious       serious <sup>a</sup> none       101       302       -       SMD 4.71 higher       QC       Ver         BRIEF Subdomains - Caregiver Report: Plan/Organise       serious <sup>a</sup> not serious       serious <sup>a</sup> none       101       302       -       SMD 4.14 higher       QC       L	nfirmed	d Unquan	ıtifiable								
Confirmed Unquantifiable       not serious       not serious       serious*       none       101       302       -       SMD 3.46 higher (2.64 higher to 4.28 higher)       Confirmed L         BRIEF Subdomains - Caregiver Report: Working Memory         Confirmed Unquantifiable         2       serious*       serious*       not serious       serious*       none       101       302       -       SMD 4.71 higher (2.02 higher to Ver       CO         2       serious*       serious*       not serious       serious*       none       101       302       -       SMD 4.71 higher (2.02 higher to Ver       CO         BRIEF Subdomains - Caregiver Report: Plan/Organise       mone       101       302       -       SMD 4.14 higher (3.70 higher to 4.58 higher)       CO         2       serious*       not serious       serious*       none       101       302       -       SMD 4.14 higher (3.70 higher to 4.58 higher)       CO         2       serious*       not serious       serious*       none       101       302       -       SMD 3.95 higher (3.52 higher to 4.58 higher)       CO         2       serious*       not serious       serious*       none       101       302       -       SMD 2.18 higher (1.82 higher to 2.55 higher)       CO	2 :	seriousª	not serious	not serious	serious <sup>e</sup>	none	101	302	-	(1.97 higher to	⊕○○○ Very Low
2       serious®       not serious       not serious       serious®       none       101       302       -       SMD 3.46 higher (2.64 higher to 4.28 higher)          BRIEF Subdomains – Caregiver Report: Working Memory         Confirmed Unquantifiable         2       serious®       not serious       serious®       none       101       302       -       SMD 4.71 higher (2.02 higher to 7.41 higher)          BRIEF Subdomains – Caregiver Report: Plan/Organise       none       101       302       -       SMD 4.14 higher (3.70 higher to 4.58 higher)          2       serious®       not serious       serious®       none       101       302       -       SMD 4.14 higher (3.70 higher to 4.58 higher)          2       serious®       not serious       serious®       none       101       302       -       SMD 3.95 higher (3.52 higher to 4.58 higher)          2       serious®       not serious       serious®       none       101       302       -       SMD 3.95 higher (3.52 higher to 3.52 higher)          2       serious®       not serious       serious®       none       101       302       -       SMD 3.95 higher (3.52 higher)          2       serious® <td>IEF Sub</td> <td>domains</td> <td><ul> <li>Caregiver Rep</li> </ul></td> <td>oort: Initiate</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	IEF Sub	domains	<ul> <li>Caregiver Rep</li> </ul>	oort: Initiate							
BRIEF Subdomains - Caregiver Report: Working Memory       (2.64 higher to       1         Confirmed Unquantifiable       2       serious <sup>a</sup> not serious       serious <sup>a</sup> not serious <sup>a</sup> 101       302       -       SMD 4.71 higher (2.02 higher to 7.41 higher)       ()         BRIEF Subdomains - Caregiver Report: Plan/Organise       -       SMD 4.14 higher (3.70 higher to 4.58 higher)       ()       ()       302       -       SMD 4.14 higher (3.70 higher to 4.58 higher)       ()       ()       ()       302       -       SMD 4.14 higher (3.70 higher to 4.58 higher)       ()<	nfirmeo	d Unquan	itifiable								
Confirmed Unquantifiable       SMD 4.71 higher       ⊕ (2.02 higher to (2.02 higher to 7.41 higher)       ⊕ (2.02 higher to 4.38 higher)       ⊕ (2.02 higher to 4.58 higher)       ⊕ (2.02 higher to 4.38 higher)	2 9	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	101	302	-	(2.64 higher to	⊕⊕⊖⊖ Low
2       serious <sup>b</sup> not serious       serious <sup>b</sup> not serious       serious <sup>b</sup> none       101       302       -       SMD 4.71 higher (2.02 higher to 7.41 higher)	IEF Sub	domains	– Caregiver Rep	ort: Working N	lemory						
BRIEF Subdomains - Caregiver Report: Plan/Organise       (2.02 higher to 7.41 higher)       Ver         BRIEF Subdomains - Caregiver Report: Plan/Organise       (2.02 higher to 7.41 higher)       (3.70 higher to 4.58 higher)       (4.58 higher)         2       serious <sup>a</sup> not serious       not serious <sup>a</sup> serious <sup>a</sup> none       101       302       -       SMD 4.14 higher (3.70 higher to 4.58 higher)       (1.10 higher to 4.38 higher)	nfirme	d Unquan	itifiable								
Confirmed Unquantifiable       SMD 4.14 higher (3.70 higher to 4.58 higher)       Confirmed Unquantifiable         2       serious <sup>a</sup> not serious       not serious <sup>a</sup> serious <sup>a</sup> not serious       serious <sup>a</sup> none       101       302       -       SMD 4.14 higher (3.70 higher to 4.58 higher)       L         BRIEF Subdomains – Caregiver Report: Monitor       -       Confirmed Unquantifiable       -       SMD 3.95 higher (3.52 higher to 4.38 higher)       +       +       +       +       -       SMD 3.95 higher (3.52 higher to 4.38 higher)       +       +       +       +       +       -       SMD 3.95 higher (3.52 higher to 4.38 higher)       +       +       +       +       +       +       -       SMD 3.95 higher (3.52 higher to 4.38 higher)       +       +       +       +       +       +       +       +       +       +       -       SMD 3.95 higher (3.52 higher to 4.38 higher)       +	2 :	seriousª	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	101	302	-	(2.02 higher to	⊕○○○ Very Low
2       serious <sup>a</sup> not serious       not serious       serious <sup>a</sup> none       101       302       -       SMD 4.14 higher (3.70 higher to 4.58 higher)	IEF Sub	domains	– Caregiver Rep	oort: Plan/Orga	nise						
Image: Section of Sectin of Sectin of Sectin of Section of Section of Section of Section o	nfirmed	d Unquan	ıtifiable								
Confirmed Unquantifiable         2       serious <sup>a</sup> not serious       not serious <sup>e</sup> none       101       302       -       SMD 3.95 higher (3.52 higher to 4.38 higher)       0         BRIEF Subdomains – Caregiver Report: Organisation of Materials         Confirmed Unquantifiable         2       serious <sup>a</sup> not serious       serious <sup>e</sup> none       101       302       -       SMD 2.18 higher (1.82 higher to 2.55 higher)       0         2       serious <sup>a</sup> not serious       serious <sup>e</sup> none       101       302       -       SMD 2.18 higher (1.82 higher to 2.55 higher)       0         DIAGNOSED STUDIES         V         A serious <sup>b</sup> not serious       serious <sup>e</sup> none       156       935       -       SMD 0.84 lower (1.33 lower to 0.34 lower)       0         FASD         FASD	2 9	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	101	302	-	(3.70 higher to	⊕⊕⊖⊖ Low
2       serious <sup>a</sup> not serious       not serious <sup>e</sup> none       101       302       -       SMD 3.95 higher (3.52 higher to 4.38 higher)       ⊕ ⊕ L         BRIEF Subdomains – Caregiver Report: Organisation of Materials       -       SMD 2.18 higher (1.82 higher to 2.55 higher)       ● ⊕ L         2       serious <sup>a</sup> not serious       serious <sup>e</sup> none       101       302       -       SMD 2.18 higher (1.82 higher to 2.55 higher)       ● ⊕ L         DIAGNOSED STUDIES       -       SMD 2.18 higher (1.82 higher to 2.55 higher)       ● ⊕ L         4       serious <sup>a</sup> serious <sup>b</sup> not serious       serious <sup>e</sup> none       156       935       -       SMD 0.84 lower (1.33 lower to 0.34 lower)       ⊕ ⊖ Ver         FAS       -       -       -       SMD 0.84 lower (1.33 lower to 0.34 lower)       +       -	IEF Sub	domains	– Caregiver Rep	ort: Monitor							
Image: Second	nfirmed	d Unquan	itifiable								
Confirmed Unquantifiable         2       serious <sup>a</sup> not serious       not serious <sup>e</sup> none       101       302       -       SMD 2.18 higher to (1.82 higher to 2.55 higher)       ①         DIAGNOSED STUDIES         NEPSY: Speeded Naming         FASD         4       serious <sup>b</sup> not serious       serious <sup>e</sup> none       156       935       -       SMD 0.84 lower (1.33 lower to 0.34 lower)       ①       ○       Ver         FASD	2 9	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	101	302	-	(3.52 higher to	⊕⊕⊖⊖ Low
2       serious³       not serious       not serious       serious°       none       101       302       -       SMD 2.18 higher (1.82 higher to 2.55 higher)       0         DIAGNOSED STUDIES       NEPSY: Speeded Naming         FASD       -       -       SMD 0.84 lower (1.33 lower to 0.34 lower)       0	IEF Sub	domains	– Caregiver Rep	oort: Organisati	on of Materia	ls					
Image: Second Studies       Image: Second Studies         DIAGNOSED STUDIES         NEPSY: Speeded Naming         FASD         4       serious <sup>a</sup> serious <sup>b</sup> not serious       serious <sup>a</sup> SMD 0.84 lower (1.33 lower to 0.34 lower)       C         FASD         FAS	nfirme	d Unquan	itifiable								
NEPSY: Speeded Naming         FASD         4       serious <sup>a</sup> serious <sup>b</sup> not serious       serious <sup>e</sup> none       156       935       -       SMD 0.84 lower (1.33 lower to 0.34 lower)       ⊕C         FAS       FAS       -	2 :	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	101	302	-	(1.82 higher to	⊕⊕⊖⊖ Low
FASD       4       serious <sup>a</sup> serious <sup>b</sup> not serious       serious <sup>e</sup> none       156       935       -       SMD 0.84 lower (1.33 lower to 0.34 lower)       ⊕C         FAS       -       -       SMD 0.84 lower (1.33 lower to 0.34 lower)       -	AGNOS	ED STUDI	ES								
4       serious <sup>a</sup> serious <sup>b</sup> not serious       serious <sup>e</sup> none       156       935       -       SMD 0.84 lower (1.33 lower to 0.34 lower)       ⊕C         FAS	PSY: Sp	beeded Na	aming								
FAS	SD										
	4 9	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	156	935	-	(1.33 lower to 0.34	⊕○○○ Very Low
	s										
	1 :	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	`	⊕⊕⊖⊖ Low
pFAS	AS										
	1 :	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	44	761	-	(0.71 lower to 0.1	⊕⊕⊖⊖ Low
ARND/Others	ND/Otl	hers									

4				· do			764			***
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	SMD 0.06 lower (0.37 lower to 0.24	⊕⊕⊖⊖ Low
									higher)	LOW
NEPSY:	INN						•			
FASD										
8	serious <sup>a</sup>	serious <sup>b</sup>	not serious	not serious	none	428	1258	-	SMD 0.78 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.02 lower to 0.53	Low
FAS									lower)	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	761		SMD 0.00 (0.88	$\Theta \Theta \bigcirc \bigcirc$
1	Serious	not senous	not serious	Serious	none	J	701	-	lower to 0.88	Low
									higher)	
pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	SMD 0.03 lower	$\oplus \oplus \bigcirc \bigcirc$
									(0.33 lower to 0.28	Low
ARND/	Others								higher)	
2	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	66	860		SMD 0.32 lower	00⊕⊕
2	Serious	not senous	not senious	Serious /	none	00	800	_	(0.65 lower to 0.01	Low
									higher)	2011
NEPSY:	INI									
FASD										
9	serious <sup>a</sup>	serious <sup>b</sup>	not serious	not serious	none	431	1336	-	SMD 0.81 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.00 lower to 0.61	Low
FAS									lower)	
				e e ui e u e d e		-	764			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	SMD 0.34 lower (1.22 lower to 0.54	⊕⊕⊖⊖ Low
									higher)	2011
pFAS					<u> </u>				• • • •	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	SMD 0.20 lower	$\oplus \oplus \bigcirc \bigcirc$
									(0.50 lower to 0.10	Low
ARND/	Othor								higher)	
	1	not conicus	nat agricus				051			
2	serious <sup>a</sup>	not serious	not serious	not serious	none	66	851	-	SMD 0.32 lower (0.58 lower to 0.07	⊕⊕⊕⊖ Moderate
									lower)	Woderate
NEPSY:	INS						•		· · · · ·	
FASD										
8	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	424	1262	-	SMD 0.85 lower	000
									(1.19 lower to 0.51	Very Low
FAS									lower)	
	corious?	not corious	not corious	coriousde	nono	Г	761		SMD 0 44 bishor	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	SMD 0.44 higher (0.44 lower to 1.32	⊕⊕⊖⊖ Low
									higher)	_0.0
pFAS	-	-	-	-			-	-		
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	SMD 0.16 lower	$\oplus \oplus \bigcirc \bigcirc$
									(0.46 lower to 0.15	Low
ADNO (	Oth cr								higher)	
ARND/		• L		ے ام	,	~~~	07.1			
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>d,e</sup>	none	66	851	-	SMD 0.34 lower (0.94 lower to 0.26	$\oplus \bigcirc \bigcirc \bigcirc$
									higher)	Very Low
	1						I		ingliet	

ASD       All serious*       not serious       not serious       not serious       none       129       987       -       SMD 0.32 lower (0.50 lower to 0.13)       Mode lower)         FAS       1       serious*       not serious       serious**       none       5       761       -       SMD 0.32 lower to 0.52 lower to 0.55 lower to 0.52 lower to 0.55 lower	NEPSY:	INN vs INI									
4       serious <sup>1</sup> not serious       not serious       none       129       987       -       SMD 0.32 lower (0.50 lower to 0.13)       Mode Mode         FAS       1       serious <sup>4</sup> not serious       not serious       serious <sup>4,e</sup> none       5       761       -       SMD 0.32 lower (1.24 lower to 0.52 higher)       0+00 (0.55 lower)         pFAS       1       serious <sup>4</sup> not serious       not serious       serious <sup>4,e</sup> none       44       761       -       SMD 0.24 lower (0.55 lower)       0+00 (0.50 lower to 0.05 lower)         ARND/Other       1       serious <sup>4</sup> not serious       not serious       serious <sup>4,e</sup> none       44       761       -       SMD 0.21 lower (0.51 lower)       0+00 (0+00 higher)         PKEPSY: Animal Sorting       Not serious       serious <sup>4,e</sup> none       330       407       -       Image       SMD 0.23 lower (0.20 lower to 0.55)       0+00 (0.24 higher to 1.00 lower)       0+00 (0.24 higher to 1.55 higher)         FASD       6       serious <sup>4</sup> not serious       serious <sup>5,f</sup> none       20       -       SMD 0.89 higher (0.24 higher to 1.55 higher)       0+00 (0.24 higher to 1.55 higher)       0+00 (0.24 higher to 1.55 higher)         1       serious <sup>4</sup> not serious											
FAS       Image: Serious*       not serious       serious*       none       44       761       -       SMD 0.21 lower       Getto       Low         1       serious*       not serious       not serious       serious*       none       44       761       -       SMD 0.21 lower       Getto       Low         1       serious*       not serious       not serious       serious*       none       44       761       -       SMD 0.21 lower       Getto       Low         NEPSY: Animal Sorting       mot serious       serious*       none       330       407       -       SMD 1.02 lower       Getto       Low         6       serious*       serious*       not serious       serious*       none       330       407       -       SMD 0.89 higher       Getto       Low         MCST: Perseverative Errors - ss)       1       serious*       not		serious <sup>a</sup>	not serious	not serious	not serious	none	129	987	-	(0.50 lower to 0.13	⊕⊕⊕⊖ Moderate
pFAS         1       serious*       not serious       serious <sup>6,#</sup> none       44       761       -       (0.55 lower to 0.06) (0.55 lower to 0.06) (0.55 lower to 0.06) (0.51 lower to 0.06) (0.51 lower to 0.06) (0.51 lower to 0.09) (0.51 lower to 0.05) (0.51 lower to 0.55) (0.51 lower to 0.55)	FAS										
1       serious <sup>a</sup> not serious       serious <sup>4,a</sup> none       44       761       -       SMD 0.24 lower (0.55 lower to 0.06 higher)         ARND/Other       1       serious <sup>a</sup> not serious       serious <sup>4,a</sup> none       44       761       -       SMD 0.21 lower (0.51 lower to 0.06 higher)       000 (0.51 lower to 0.06 higher)         NEPSY: Animal Sorting       FASD       -       SMD 1.02 lower (0.51 lower to 0.05 higher)       000 (0.57 higher)         6       serious <sup>a</sup> not serious       serious <sup>a</sup> none       330       407       -       SMD 1.02 lower (0.40 lower to 0.65 lower)       000 (0.57 lower)         6       serious <sup>a</sup> not serious       serious <sup>a</sup> none       330       407       -       SMD 0.89 higher (0.24 higher to 0.55 lower)       000 Low i.55 higher)         1       serious <sup>a</sup> not serious       not serious <sup>a,1</sup> none       20       20       -       SMD 0.89 higher (0.24 higher to 0.54 lower)       000 Low i.55 higher)         1       serious <sup>a</sup> not serious       not serious <sup>a,1</sup> none       18       16       -       SMD 1.42 lower (2.03 lower to 0.54 lower)       Low lower)         1       serious <sup>a</sup> not serious       serious <sup>a,4</sup> none       21	1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	(1.24 lower to 0.52	⊕⊕⊖⊖ Low
ARND/Other       (0.55 lower to 0.06 higher)       Low         1       serious*       not serious       serious4.*       none       44       761       -       (0.55 lower to 0.09 higher)       Low         NEPSY: Animal Sorting       NEPSY: Animal Sorting       FASD       SMD 1.02 lower       ⊕ ○(0.51 lower to 0.09 higher)       ⊕ ○(0.51 lower to 0.05 lower)       ⊕ ○(0.24 higher to 0.65 lower)       ⊕ ⊕ ○(0.24 higher to 0.54 lower)       ⊕ ⊕ ○(0.24 higher)       ⊕ ⊕ ○(0.20 lower to 0.54 lower)       ⊕ ⊕ ○(0.20 lower to 0.54 lower)       ⊕ ⊕ ○(0.24 higher)       ⊕ ⊕ ○(0.24 higher)       ⊕ ⊕ ○(0.20 lower)       ⊕ ⊕ ○(0.24 higher)       ⊕ ⊕ ○(0.20 lower)	pFAS										
1       serious <sup>a</sup> not serious       not serious       serious <sup>6,a</sup> none       44       761       -       SMD 0.21 lower (0.51 lower to 0.05)       tower bigher)         NEPSY: Animal Sorting         FASD       6       serious <sup>a</sup> not serious       serious <sup>a</sup> none       330       407       -       SMD 0.21 lower (1.40 lower to 0.05)       CVery I lower)         6       serious <sup>a</sup> not serious       serious <sup>a</sup> none       330       407       -       SMD 0.21 lower (1.40 lower to 0.65)       CVery I lower)         6       serious <sup>a</sup> not serious       serious <sup>a</sup> none       330       407       -       SMD 0.21 lower (1.40 lower to 0.65)       CVery I lower)         WCST: Perseverative Errors (ss), Total Errors (ss), Preservative responses (ss), Preservative responses (raw), No. of Categories       Completed (ss)       FASD (Preserverative Errors - ss)       1       serious <sup>a</sup> not serious       not serious <sup>a,I</sup> none       20       20       -       SMD 0.89 higher (0.24 higher)       Dette       Low         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,I</sup> none       18       16       -       SMD 1.42 lower (2.04 lower to 0.24 lower)       Low         1       serious <sup>a</sup>			not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	(0.55 lower to 0.06	⊕⊕⊖⊖ Low
NEPSY: Animal Sorting       (0.51 lower to 0.09 higher)       Low higher)         FASD       6       serious*       serious*       not serious	ARND/0	Other		•					•		
FASD       -       SMD 1.02 lower (1.40 lower to 0.65 lower)       ⊕○○ (1.40 lower to 0.65 lower)         6       serious <sup>a</sup> serious <sup>b</sup> not serious       serious <sup>e</sup> none       330       407       -       SMD 1.02 lower (1.40 lower to 0.65 lower)       ⊕○○ (1.40 lower to 0.64 lower)         WCST: Perseverative Errors (ss), Total Errors (ss), Preservative responses (ss), Preservative responses (raw), No. of Categories         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       20       20       -       SMD 0.89 higher (0.24 higher to 1.55 higher)       ⊕⊕○ Low         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       18       16       -       SMD 1.29 lower (2.03 lower to 0.54 lower)       Every (2.03 lower to 0.54 lower)         1       serious <sup>a</sup> not serious       serious <sup>a,f</sup> none       18       16       -       SMD 1.42 lower (2.03 lower to 0.54 lower)       Every (2.04 lower to 0.74 lower)         1       serious <sup>a</sup> not serious       serious <sup>a,f</sup> none       21       7       -       SMD 1.42 lower (2.07 lower to 0.74 lower)       Every (2.07 lower to 0.74 lower)         pFAS (Preservative responses – Raw)       1       serious <sup>a</sup> not serious       serious <sup>a,f,f</sup> none	1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	(0.51 lower to 0.09	⊕⊕⊖⊖ Low
Image: Completed (s)       Image: Completed (s)         FASD (Perseverative Errors (ss), Total Errors (ss), Preservative responses (ss), Preservative responses (raw), No. of Categories         I       serious <sup>a</sup> not serious       not serious <sup>a,f</sup> none       20       20       -       SMD 0.89 higher (0.24 higher to 1.55 higher)       Image: Completed (s)         pFAS (Total Errors - ss)       Image: Completed (sc)       serious <sup>a,f</sup> none       20       20       -       SMD 0.89 higher (0.24 higher to 1.55 higher)       Image: Completed (sc)         pFAS (Total Errors - ss)       Image: Completed (sc)       not serious       not serious <sup>a,f</sup> none       18       16       -       SMD 1.29 lower (2.03 lower to 0.54 lower)       Image: Completed (sc)         ARND/Others (Total Errors - ss)       Image: Completed (sc)       serious <sup>a,f</sup> none       24       16       -       SMD 1.42 lower (2.14 lower to 0.71 lower)       Image: Completed (sc)         fASD       Image: Completed (sc)       Image: Completed (sc)       serious <sup>a,f</sup> none       21       7       -       SMD 1.42 lower (2.07 lower to 0.24 lower)       Image: Completed (sc)       Image: Com	NEPSY:	Animal Sort	ting		-						
Image: Completed (s)       Image: Completed (s)         FASD (Perseverative Errors (ss), Total Errors (ss), Preservative responses (ss), Preservative responses (raw), No. of Categories         I       serious <sup>a</sup> not serious       not serious <sup>a,f</sup> none       20       20       -       SMD 0.89 higher (0.24 higher to 1.55 higher)       Image: Completed (s)         pFAS (Fotal Errors - ss)       Image: Completed (sc)       serious <sup>a,f</sup> none       20       20       -       SMD 0.89 higher (0.24 higher to 1.55 higher)       Image: Completed (sc)         pFAS (Total Errors - ss)       Image: Completed (sc)       not serious       not serious <sup>a,f</sup> none       18       16       -       SMD 1.29 lower (2.03 lower to 0.54 lower)       Image: Completed (sc)         ARND/Others (Total Errors - ss)       Image: Completed (sc)       serious <sup>a,f</sup> none       24       16       -       SMD 1.42 lower (2.14 lower to 0.71 lower)       Image: Completed (sc)         fASD       Image: Completed (sc)       Image: Completed (sc)       serious <sup>a,f</sup> none       21       7       -       SMD 1.42 lower (2.07 lower to 0.24 lower)       Image: Completed (sc)       Image: Com	FASD										
Completed (ss)         FASD (Perseverative Errors - ss)         1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       20       20       -       SMD 0.89 higher (0.24 higher to 1.55 higher)       Lov         pFAS (Total Errors - ss)       -       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       18       16       -       SMD 1.29 lower (2.03 lower to 0.54 lower)       ⊕⊕ ( Lov         ARND/Others (Total Errors - ss)       -       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       24       16       -       SMD 1.42 lower (2.14 lower to 0.74 lower)       ⊕⊕ ( Lov         ARND/Others (Total Errors - ss)       -       -       SMD 1.42 lower (2.14 lower to 0.74 lower)       ⊕⊕ ( Low       Low         1       serious <sup>a</sup> not serious       serious <sup>a,f</sup> none       21       7       -       SMD 1.16 lower (2.07 lower to 0.24 lower)       E         pFAS (Preservative responses – Raw)       -       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       25       14       -       SMD 0.59 higher (0.08 lower to 1.26 higher)       Very I higher)         1       serious <sup>a</sup> not serious       not serious       very serio	6	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	330	407	-	(1.40 lower to 0.65	⊕○○○ Very Low
FASD (Perseverative Errors - ss)       not serious       not serious       serious <sup>e,f</sup> none       20       20       -       SMD 0.89 higher (0.24 higher to 1.55 higher)       ⊕⊕⊕ Low         pFAS (Total Errors - ss)       1       serious <sup>a</sup> not serious       not serious <sup>e,f</sup> none       18       16       -       SMD 1.29 lower (2.03 lower to 0.54 lower)       ⊕⊕⊕ Lov         ARND/Others (Total Errors - ss)       1       serious <sup>a</sup> not serious       serious <sup>e,f</sup> none       24       16       -       SMD 1.42 lower (2.14 lower to 0.71 lower)       ⊕⊕⊕ Lov         1       serious <sup>a</sup> not serious       not serious <sup>e,f</sup> none       21       7       -       SMD 1.61 lower (2.07 lower to 0.24 lower)       ⊕⊕⊕ Lov         pFAS (Preservative responses – Raw)       1       serious <sup>a</sup> not serious       serious <sup>d,e,f</sup> none       25       14       -       SMD 0.59 higher (0.08 lower to 1.26 higher)       ⊕⊖⊖ Very I         ARND/Others (Preservative responses – Raw)       1       serious <sup>a</sup> not serious       Very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower (0.70 lower to 0.46 higher)       ⊕⊖⊖ Very I         ARND/Others       not serious       Not serious       Very serious <sup>d,e,f</sup> none       62			e Errors (ss), To	otal Errors (ss)	, Preservative re	esponse	s (ss), Pr	eservativ	ve responses	s (raw), No. of Catego	ories
1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       20       20       -       SMD 0.89 higher (0.24 higher to 1.55 higher)       Detection         pFAS (Total Errors - ss)       1       serious <sup>a</sup> not serious       not serious       serious <sup>a,f</sup> none       18       16       -       SMD 1.29 lower (2.03 lower to 0.54 lower)       Detection         ARND/Others (Total Errors - ss)       1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       24       16       -       SMD 1.42 lower (2.14 lower to 0.71 lower)       Detection         fASD       1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       24       16       -       SMD 1.42 lower (2.14 lower to 0.71 lower)       Detection         fASD       1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       21       7       -       SMD 1.16 lower (2.07 lower to 0.24 lower)       Detection         pFAS (Preservative responses – Raw)       1       serious <sup>a</sup> not serious       not serious <sup>d,e,f</sup> none       25       14       -       SMD 0.59 higher (0.08 lower to 1.26 higher)       Very I lower         1       serious <sup>a</sup> not serious </td <td></td>											
pFAS (Total Errors - ss)	-	-					20	20	I		
1       serious <sup>a</sup> not serious       not serious <sup>e,f</sup> none       18       16       -       SMD 1.29 lower (2.03 lower to 0.54 lower)       ⊕⊕ (2.03 lower to 0.54 lower)         ARND/Others (Total Errors - ss)       not serious       not serious       serious <sup>e,f</sup> none       24       16       -       SMD 1.42 lower (2.14 lower to 0.71 lower)       ⊕⊕ (2.07 lower to 0.24 lower)         FASD         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       21       7       -       SMD 1.16 lower (2.07 lower to 0.24 lower)       ⊕⊕ (2.07 lower to 0.24 lower)         pFAS (Preservative responses – Raw)       not serious       not serious       very serious <sup>d,e,f</sup> none       25       14       -       SMD 0.59 higher (0.08 lower to 1.26 higher)       ⊕○ (Very I higher)         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower (0.70 lower to 0.46 higher)       ⊕○ (Very I very I         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower (0.70 lower to 0.46 higher)       ⊕○ (Very I         Verbal Fluency: D-KEFS, NEPSY-II (total correct Letter)       FAS	T	serious	not serious	not serious	serious	none	20	20	-	(0.24 higher to	Low
ARND/Others (Total Errors - ss)       not serious       not serious       serious <sup>e,f</sup> none       24       16       -       SMD 1.42 lower (2.14 lower to 0.71 lower)       ⊕⊕⊕ Low Low         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       21       7       -       SMD 1.42 lower (2.14 lower to 0.71 lower)       ⊕⊕⊕⊕ Low         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       21       7       -       SMD 1.16 lower (2.07 lower to 0.24 lower)       ⊕⊕⊕⊕ Low         pFAS (Preservative responses – Raw)       1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       25       14       -       SMD 0.59 higher (0.08 lower to 1.26 higher)       ⊕⊖⊖( Very I higher)         1       serious <sup>a</sup> not serious       not serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower (0.70 lower to 0.46 higher)       ⊕⊖( Very I         1       serious <sup>a</sup> not serious       not serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower (0.70 lower to 0.46 higher)       ⊕○( Very I         Verbal Fluency: D-KEFS, NEPSY-II (total correct Letter)	pFAS (T	otal Errors -	- ss)								
ARND/Others (Total Errors - ss)       Image: serious a constraint of serious constrai	1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	18	16	-	(2.03 lower to 0.54	⊕⊕⊖⊖ Low
1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       24       16       -       SMD 1.42 lower       (2.14 lower to 0.71)       Low         FASD       1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       21       7       -       SMD 1.16 lower       (2.07 lower to 0.24)       Low         1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       21       7       -       SMD 1.16 lower       (2.07 lower to 0.24)       Low         pFAS (Preservative responses – Raw)       1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       25       14       -       SMD 0.59 higher       (0.02)       Very I         ARND/Others (Preservative responses – Raw)       1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower       (0.02)       Very I         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower       (0.02)       Very I         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       62       <	ARND/0	Others (Tota	al Errors - ss)							lowery	
FASD       1       serious <sup>a</sup> not serious       not serious       serious <sup>e,f</sup> none       21       7       -       SMD 1.16 lower (2.07 lower to 0.24 lower)       ⊕⊕C Low         pFAS (Preservative responses – Raw)       1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       25       14       -       SMD 0.59 higher (0.08 lower to 1.26 higher)       ⊕○C Very I         ARND/Others (Preservative responses – Raw)       1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower (0.70 lower to 0.46 higher)       ⊕○C Very I         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower (0.70 lower to 0.46 higher)       ⊕○C Very I         Verbal Fluency: D-KEFS, NEPSY-II (total correct Letter)       FAS	-	· · · ·		not serious	serious <sup>e,f</sup>	none	24	16	-	(2.14 lower to 0.71	⊕⊕⊖⊖ Low
Image: serious and serious are serious and serious and serious and serious are serious and serious and serious and serious are serious and serious and serious are serious and serious and serious are serious and serious are serious and serious are serious are serious and serious are serious and serious are serious and serious are ser	FASD									,	
1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       25       14       -       SMD 0.59 higher (0.08 lower to 1.26 higher)       ⊕ ○ ○ Very I         ARND/Others (Preservative responses – Raw)       1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower (0.70 lower to 0.46 higher)       ⊕ ○ ○ Very I         Verbal Fluency: D-KEFS, NEPSY-II (total correct Letter)       FAS	1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	21	7	-	(2.07 lower to 0.24	⊕⊕⊖⊖ Low
ARND/Others (Preservative responses – Raw)         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower (0.70 lower to 0.46 higher) $\oplus \bigcirc \bigcirc \bigcirc$ Very I       very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower (0.70 lower to 0.46 higher) $\oplus \bigcirc \bigcirc \bigcirc$ Verbal Fluency: D-KEFS, NEPSY-II (total correct Letter)       FAS       -	<b>pFAS</b> (P	reservative	responses – Ra	w)	•				-	. ,	
1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       62       14       -       SMD 0.12 lower       ⊕ ○ ○         Verbal Fluency: D-KEFS, NEPSY-II (total correct Letter)	1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	25	14	-	(0.08 lower to 1.26	⊕○○○ Very Low
Verbal Fluency: D-KEFS, NEPSY-II (total correct Letter) FAS	ARND/0	Others (Pres	servative respo	nses – Raw)	•				-		
FAS	1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	62	14	-	(0.70 lower to 0.46	⊕○○○ Very Low
	Verbal I	Fluency: D-I	KEFS, NEPSY-II (	total correct L	etter)						
2 corioural not corious not corious corious none 142 252 SMD 1 00 lower or of	FAS										
	3	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	143	252	-	•	⊕⊕⊖⊖ Low
pFAS	pFAS										

1										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	24	32	-	<b>SMD 0.80 lower</b> (1.35 lower to 0.25 lower)	⊕⊕⊖⊖ Low
ARND/0	Others								, ,	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	117	185	-	<b>SMD 0.83 lower</b> (1.07 lower to 0.59 lower)	⊕⊕⊖⊖ Low
Letter F	luency: D-k	(EFS (speed)								
FAS										
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	10	10	-	<b>SMD 0.85 lower</b> (1.77 lower to 0.08 higher)	⊕○○○ Very Low
ARND/0	Others									
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	8	10	-	SMD 0.74 lower (1.71 lower to 0.23 higher)	⊕○○○ Very Low
Letter F	luency: F-A	-S test (words/r	nins)	•						
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	21	21	-	<b>SMD 1.72 lower</b> (2.43 lower to 1.00 lower)	⊕⊕⊖⊖ Low
Verbal I	Fluency: D-I	KEFS (Verbal Flu	ency Switchin	g)					· · · · · ·	
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	47	46	-	<b>SMD 0.44 lower</b> (0.85 lower to 0.03 lower)	⊕⊕⊖⊖ Low
FAS										
2	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	120	231	-	<b>SMD 0.97 lower</b> (1.21 lower to 0.74 lower)	⊕⊕⊖⊖ Low
ARND/0	Others									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	117	185	-	<b>SMD 0.85 lower</b> (1.09 lower to 0.61 lower)	⊕⊕⊖⊖ Low
Categor	y Fluency:	D-KEFS (total co	rrect)	•						
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	73	47	-	<b>SMD 0.77 lower</b> (1.15 lower to 0.39 lower)	⊕⊕⊖⊖ Low
FAS										
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	64	67	-	<b>SMD 0.60 lower</b> (1.11 lower to 0.09 lower)	⊕⊕⊖⊖ Low
Categor	y Fluency:	F-A-S test (word	ls/min)							
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	21	21	-	SMD 0.94 lower (1.58 lower to 0.30 lower)	⊕⊕⊖⊖ Low
Other D	-KEFS Mea	sures: Tower Te	est (total achie	vement)						
FASD										
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	112	76	-	<b>SMD 0.94 lower</b> (1.24 lower to 0.63 lower)	⊕⊕⊖⊖ Low

pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	20	6	-	<b>SMD 1.37 lower</b> (2.37 lower to 0.37 lower)	⊕⊕⊖⊖ Low
ARND/0		<b>-</b>	1	-			1		1	
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	24	16	-	<b>SMD 1.04 lower</b> (1.72 lower to 0.37 lower)	⊕⊕⊖⊖ Low
Other N	/leasures: T	rail Making Tes	t Trial B							
FASD										
2	seriousª	not serious		very serious <sup>d,e,f</sup>		68	81	-	SMD 0.28 higher (0.07 lower to 0.63 higher)	⊕○○○ Very Low
Other N	/leasures: T	est of Executive	e Control - No	n-Inhibitory Cor	dition:	Incorrec	t			
FASD			-				_			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	26	19	-	SMD 2.36 higher (1.58 higher to 3.15 higher)	⊕⊕⊖⊖ Low
BRIEF G	lobal Execu	itive Composite	e – Caregiver R	eport						
FASD										
3	seriousª	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	177	201	-	<b>SMD 2.05 higher</b> (1.48 higher to 2.62 higher)	⊕○○○ Very Low
pFAS										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	35	42	-	<b>SMD 2.07 higher</b> (0.20 higher to 3.95 higher)	⊕○○○ Very Low
ARND/0	Other			•						
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	34	42	-	<b>SMD 2.78 higher</b> (1.67 higher to 3.88 higher)	⊕○○○ Very Low
BRIEF B	ehaviour Re	gulation Index	– Caregiver Re	port			1			
FASD										
3	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	304	227	-	SMD 2.14 higher (1.81 higher to 2.47 higher)	⊕⊕⊖⊖ Low
pFAS									0,	
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	35	42	-	SMD 1.72 higher (0.17 higher to 3.28 higher)	⊕○○○ Very Low
ARND/0	Other			•						
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	34	42	-	SMD 2.34 higher (1.72 higher to 2.96 higher)	⊕⊕⊖⊖ Low
BRIEF B	ehaviour Re	egulation Index	– Teacher Rep	ort						
FASD										
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	55	23	-	SMD 1.12 higher (0.60 higher to 1.64 higher)	⊕⊕⊖⊖ Low
BRIEF IV	letacognitic	on Index – Care	giver Report							
FASD										
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	304	226	-	SMD 1.46 higher (0.89 higher to 2.03 higher)	⊕○○○ Very Low

pFAS										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	35	42	-	SMD 1.93 higher (0.10 lower to 3.95 higher)	⊕○○○ Very Low
ARND/	Other			_						
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	34	42	-	<b>SMD 2.61 higher</b> (1.03 higher to 4.19 higher)	⊕○○○ Very Low
BRIEF N	1etacognitic	on Index – Teac	her Report	-						
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	55	23	-	SMD 0.69 higher (0.19 higher to 1.19 higher)	⊕⊕⊖⊖ Low
Other B	RIEF Measu	<b>ures:</b> Inhibit, Sh	ift, Plan/Orgar	nise, Monitor – C	Caregive	r Report	t			
FASD (I	nhibit)									
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	83	110	-	<b>SMD 2.22 higher</b> (1.32 higher to 3.12 higher)	⊕○○○ Very Low
FASD (S	hift)									
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	83	110	-	<b>SMD 1.77 higher</b> (1.43 higher to 2.11 higher)	⊕⊕⊖⊖ Low
FASD (N	/onitor)			<b>I</b>						
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	47	70	-	SMD 2.51 higher (2.02 higher to 3.00 higher)	⊕⊕⊖⊖ Low
FASD (P	lan/Organis	se)							0.0080	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	46	70	-	SMD 2.53 higher (2.03 higher to 3.03 higher)	⊕⊕⊖⊖ Low
FASD (V	Vorking Me	mory)					<u> </u>		<u> </u>	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e, f</sup>	none	46	70	-	SMD 2.95 higher (2.41 higher to 3.48 higher)	⊕⊕⊖⊖ Low
ARND/	Others (Wo	rking Memory)								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	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 (I<sup>2</sup> >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**

			NEP:	SY Sp	eed	ed N	laming	(mean/SD)		
н	eavy F	ΑΕ ά	and I	NEPS	Y Sp	eede	d Nam	ing (mean/SD)	(1 study)	
	Hea	avy PA	E	C	ontrol			Std. Mean Difference	Std. Mean Difference F	isk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		9
Total (95% CI)			82			132	100.0%	-0.64 [-0.92, -0.35]	◆	
Heterogeneity: Not applicable										
Test for overall effect: Z = 4.42 (P < 0.000	001)								-4 -2 0 2 4 Heavy PAE Control	
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) Confirmed Unquantifiable Std. Mean Difference Std. Mean Difference Risk of Bias Control Total Weight IV, Random, 95% CI Study or Subgroup Mean SD Total Mean SD IV. Random, 95% CI Doyle et al 2018 (10-16yrs; NEPSY-II) 82 278 142 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) 238 100.0% -0.57 [-0.96, -0.17] 222 Heterogeneity: Tau<sup>2</sup> = 0.08; Chi<sup>2</sup> = 6.59, df = 2 (P = 0.04); l<sup>2</sup> = 70% -4 -2 Ó 4 Test for overall effect: Z = 2.82 (P = 0.005) Confirmed Unquantifiable Control

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)

								· · ·		
	Confirmed	Unquanti	fiable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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	~~							H	4 -2 0 2	4
Test for overall effect: Z = 5.71 (P < 0.000	U1)							Confirme	ed Unquantifiable Control	
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) **Confirmed Unquantifiable** Control Std. Mean Difference Std. Mean Difference **Risk of Bias** Total Mean SD Total Weight IV. Random, 95% CI IV. Random, 95% CI Study or Subaroup Mean SD 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 -4 -2 ó 2 Л Test for overall effect: Z = 0.79 (P = 0.43) Confirmed Unguantifiable Control 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)

Confirme	d PAE L	evel Un	nquan	tifiab	le an	d W	CST C	omposite (mea	n/SD) (2 studies)	
	Confirmed	l Unquantif	iable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> = 2.02 Test for overall effect: Z = 2.79 (P = 0.00		0.15); I² = 5	1%					Confirm	-4 -2 0 2 ed Unguantifiable Control	4

Risk of bias legend (A) Overall RoB

Note: Vaurio et al 2011 also reports COWAT Letter Fluency and COWAT Category Fluency (mean/SD).

	A	ny PAE		0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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	)								-4 -2 U 2 Control Any PAE	4

<sup>(</sup>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 a	nd NI	Н То	olbo	x: Dii	men	siona	al Chan	ge Card Sort (m	ean	/SD) (1	. study)		
_	Lig	ht PA	E	C	ontrol			Std. Mean Difference		Std. Me	an Difference	Risk of	Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rar	idom, 95% Cl	Α	
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									-4	-1			
Test for overall effect: Z = 1.70 (P = 0.09)									-4	Cont	rol Light PAE	4	
Risk of bias legend													

(A) Overall RoB

#### Moderate PAE and NIH Toolbox: Dimensional Change Card Sort (mean/SD) (1 study)

	Mode	erate P	PAE	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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	n								-4 -2 0 2 4	
Disk of bios langed	· ·								Control Moderate PAE	

Risk of bias legend (A) Overall RoB

#### Any PAE and NIH Toolbox: Dimensional Change Card Sort (mean/SD) (1 study)

/			0.00				- Chian			
	Ar	IY PAE		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 5.44 (P < 0.000)	D1)		2518			7501	100.0%	0.13 [0.08, 0.17]	-4 -2 0 2 Control Any PAE	4
Disk of bigs legend										

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)

	Confirmed Ung	uantifiable	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	<b>•</b>	•
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.09, Test for overall effect: Z = 11.12 (P < 0.0		²=0%					⊢ -2 Confirme	4 -2 0 2 d Unquantifiable Control	4

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)

	Confirmed Unquantifiable			C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 4.70,	df = 2 (P = 0.	10); I <sup>z</sup> = 57	'%					F		
Test for overall effect: Z = 8.33 (P < 0.00	1001)							Confirme	d Unquantifiable Control	4
Dials of hims la sound										

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)

				-						/	
	Confirmed Unquantifiable			Control			Std. Mean Difference		Std. Mean Difference	Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α	
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: Tau <sup>2</sup> = 0.41; Chi <sup>2</sup> = 11.89	9, df = 1 (P = 1	0.0006); I <b>ž</b>	= 92%					H			
Test for overall effect: Z = 1.29 (P = 0.20	))							Confirme	d Unquantifiable Control	4	

#### 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)

	С	onfirm	ed PA	AE Le	vel	Unqu	uantifi	able (2 studies)		
	Confirmed	l Unquantif	iable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.18 Test for overall effect: Z = 7.54 (P < 0.00		.67); I² = 0%	6					Confirm	-4 -2 0 2 ed Unguantifiable Control	4

Risk of bias legend (A) Overall RoB

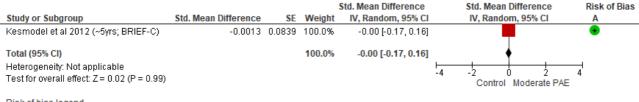
Note: Nguyen et al 2014 also reports D-KEFS Colour Interference and Trail Making Test (completion time and total errors).

#### BRIEF Global Executive Composite – Caregiver Report (SMD)

Light PAE and BRIEF Global Executive Composite – Caregiver (SMD) (1 study)										
				Std. Mean Difference	Std. Mean Difference	Risk of Bias				
Study or Subgroup	Std. Mean Difference	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α				
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				+	4 -2 0 2					
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)



					Std. Me	an Difference	Std. Mean D	ifference	Risk of Bia
Study or Subgroup	Std. M	ean Difference	SE	Weig	iht IV, R	andom, 95% Cl	IV, Random	n, 95% CI	Α
Kesmodel et al 2012 (~5yrs; BRIEF-C)	1	0.0522	0.2265	100.0	)% 0	.05 [-0.39, 0.50]			•
Fotal (95% CI)				100.	0% 0.	05 [-0.39, 0.50]	•		
Heterogeneity: Not applicable							<u>    t     t     t      t       t       </u>	<u> </u>	
Fest for overall effect: Z = 0.23 (P = 0.8	2)						-4 -2 0	2 4	
· · · · · · · · · · · · · · · · · · ·	-,						Control	Heavy PAE	
Risk of bias legend									
A) Overall RoB									
	ahlo DA	E and BRI		hal F	vocutiv	e Composite	- Caregiver	· (SMD) (1	(study)
Confirmed Unquantifi					xecutiv	•	-		
Confirmed Unquantifi	Confirmed	Unquantifiable	Co	ntrol		Std. Mean Difference	Std. Mean	n Difference	Risk of Bias
Confirmed Unquantific	Confirmed Mean	Unquantifiable SD Tota	Co Mean	ntrol SD To	otal Weight	Std. Mean Difference IV, Random, 95% C	Std. Mean		Risk of Bias A
Confirmed Unquantifi	Confirmed	Unquantifiable	Co Mean	ntrol		Std. Mean Difference IV, Random, 95% C	Std. Mean	n Difference	Risk of Bias
Confirmed Unquantifia Study or Subgroup McGee et al 2008a (13-18yrs; BRIEF-C)	Confirmed Mean	Unquantifiable SD Tota	Co Mean 47.6	ntrol SD To	otal Weight	Std. Mean Difference IV, Random, 95% C 4.63 [3.43, 5.84	Std. Mean IV, Rand	n Difference	Risk of Bias A
Confirmed Unquantific	Confirmed Mean	Unquantifiable SD Tota 8.28 28	Co Mean 47.6	ntrol SD To	otal Weight 15 100.0%	Std. Mean Difference IV, Random, 95% C 4.63 [3.43, 5.84	Std. Mean IV, Rand	n Difference	Risk of Bia A

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) Std. Mean Difference Std. Mean Difference **Risk of Bias** Study or Subgroup Std. Mean Difference SE Weight IV, Random, 95% CI IV, Random, 95% CI Α Skogerbo et al 2012 (~5yrs; BRIEF-C) 0.067 0.0529 100.0% 0.07 [-0.04, 0.17] Total (95% CI) 0.07 [-0.04, 0.17] 100.0% Heterogeneity: Not applicable ⊢ -4 -2 ó ż 4 Test for overall effect: Z = 1.27 (P = 0.21) Control Light PAE

Risk of bias legend (A) Overall RoB

Risk of bias legend (A) Overall RoB

#### Moderate PAE and BRIEF Behaviour Regulation Index - Caregiver (SMD) (1 study)

				Std. Mean Difference	5	Std. Mean Difference	Risk of Bias
Study or Subgroup	Std. Mean Difference	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
Skogerbo et al 2012 (~5yrs; BRIEF-C)	-0.0113	0.0839	100.0%	-0.01 [-0.18, 0.15]			•
Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.13 (P = 0.89)			100.0%	-0.01 [-0.18, 0.15]	-4	-2 0 2 Control Moderate PAE	4

Risk of bias legend (A) Overall RoB

#### Heavy PAE and BRIEF Behaviour Regulation Index - Caregiver (SMD) (1 study)

-			-	Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Std. Mean Difference	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl 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]	<b>•</b>
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)

	Confirmed	l Unquanti	fiable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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	)								-4 -2 0 2 Control Confirmed Unqu	4 uantifiable

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)

				Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Std. Mean Difference	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
Skogerbo et al 2012 (~5yrs; BRIEF-T)	-0.0098	0.0529	100.0%	-0.01 [-0.11, 0.09]		-	•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.19 (P = 0.85)	)		100.0%	-0.01 [-0.11, 0.09]	-4	-2 0 2 Control Light PAE	4
Risk of bias legend							

(A) Overall RoB

# Moderate PAE and BRIEF Behaviour Regulation Index – Teacher (SMD) (1 study)

				Std. Mean Difference		Std. Mean	Difference	е	Risk of Bias
Study or Subgroup	Std. Mean Difference	SE	Weight	IV, Random, 95% CI		IV, Rando	m, 95% Cl		Α
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]			<u>ا</u>		
Heterogeneity: Not applicable Test for overall effect: Z = 0.97 (P = 0.33)					-4	-2 Control	0 2 Moderate	4 PAE	1

Risk of bias legend (A) Overall RoB

#### Heavy PAE and BRIEF Behaviour Regulation Index - Teacher (SMD) (1 study)

-			-	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Std. Mean Difference	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
Skogerbo et al 2012 (~5yrs; BRIEF-T)	-0.1878	0.2266	100.0%	-0.19 [-0.63, 0.26]	-	•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.83 (P = 0.41)	)		100.0%	-0.19 [-0.63, 0.26]	-4 -2 0 2 Control Heavy PAE	
Risk of bias legend						

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) Std. Mean Difference Std. Mean Difference **Risk of Bias** Std. Mean Difference Study or Subgroup SE Weight IV, Random, 95% CI IV, Random, 95% CI Δ 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 -4 4 -2 ά Test for overall effect: Z = 1.76 (P = 0.08) Control Light PAE

Risk of bias legend (A) Overall RoB

#### Moderate PAE and BRIEF Metacognition Index - Caregiver (SMD) (1 study)

			0	Std. Mean Difference	•	Std. Mean Difference	Risk of Bias
Study or Subgroup	Std. Mean Difference	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
Skogerbo et al 2012 (~5yrs; BRIEF-C)	0.0933	0.053	100.0%	0.09 [-0.01, 0.20]		-	•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.76 (P = 0.08)			100.0%	0.09 [-0.01, 0.20]	-4	-2 0 2 Control Light PAE	] 4

Study or Subgroup	Std. Mea	an Difference	SE	Weight		Difference dom, 95% Cl	Std. Mean Difference IV, Random, 95% Cl	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				100.070	0.50		<b>\</b>	
Test for overall effect: Z = 1.67 (P = 0.0	9)					-4	-2 0 2 Control Heavy PAE	4
							Control Houty HAL	
<u>Risk of bias legend</u> (A) Overall RoB								
Confirmed Unqua	ntifiable	PAE and	BRIEF	Metao	cognitio	n Index – Ca	regiver (SMD) (1 stud	dy)
C Study or Subgroup	Confirmed Un Mean	nquantifiable SD Total	Co Mean	ntrol SD Tota	l Weight	Std. Mean Differenc IV, Random, 95%		Risk of I A
McGee et al 2008a (13-18yrs; BRIEF-C)	79.89		48.07		5 100.0%	5.19 [3.88, 6.5		- ?
		28		4	5 100.0%	E 40 [2 00 6 E	01	
Total (95% CI) Heterogeneity: Not applicable		28	•	1:	5 100.0%	5.19 [3.88, 6.5		
Test for overall effect: Z = 7.76 (P < 0.00001)							-4 -2 0 2 4 Control Confirme	d Unquantifiable
Diak of biog logand								
<u>Risk of bias legend</u> (A) Overall RoB								
				<b>.</b> .	, -			
ote: Skogerbo et al 2012 reports ad	justed m	ean differer	nce. SM	D autoge	enerated	by revman.		
	BRIEF N	/letacogn	ition I	ndex -	– Teach	er Report (S	SMD)	
Light P	AE and	BRIEF Me	tacogi	nition I	ndex –	Teacher (SM	ID) (1 studv)	
8						Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Std. Mea	an Difference	SE	Weight	IV, Ran	dom, 95% Cl	IV, Random, 95% CI	Α
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				100.070	0.02		<u>    t         t        t             </u>	
Test for overall effect: Z = 0.38 (P = 0.7	0)					-4	-2 0 2 Control Light PAE	4
Risk of bias legend								
(A) Overall RoB								
Moderate	e PAE ar	nd BRIEF I	Metac	ognitio	n Index	. – Teacher (	<b>SMD)</b> (1 study)	
				-	Std. Mear	Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Std. Mea	in Difference		Weight		idom, 95% Cl	IV, Random, 95% Cl	A
Skogerbo et al 2012 (~5yrs; BRIEF-T)		-0.018	0.0839	100.0%	-0.02	2 [-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	3)					-4	-2 0 2 Control Moderate PAB	4
Disk of hiss langes?								
Risk of bias legend (A) Overall RoB								
e., oronani tob								
Heavy F	PAE and	BRIEF Me	etacog	nition	Index -	Teacher (SN	<b>/ID)</b> (1 study)	
-			5		Std. Mean	Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Std. Mea	n Difference		Weight		dom, 95% Cl	IV, Random, 95% Cl	A
Skogerbo et al 2012 (~5yrs; BRIEF-T)		-0.2127	0.2266	100.0%	-0.21	[-0.66, 0.23]	=	•
				100.0%	-0.21	[-0.66, 0.23]		
Total (95% CI)							<u> </u>	
Total (95% CI) Heterogeneity: Not applicable						-4	-2 0 2 Control Heavy PAE	4
	5)						Control Hoday PAL	
Heterogeneity: Not applicable Test for overall effect: Z = 0.94 (P = 0.35	5)							
Heterogeneity: Not applicable Test for overall effect: Z = 0.94 (P = 0.35 <u>Risk of bias legend</u>	5)							
Heterogeneity: Not applicable Test for overall effect: Z = 0.94 (P = 0.35	5)							
Heterogeneity: Not applicable Test for overall effect: Z = 0.94 (P = 0.35 <u>Risk of bias legend</u>		ean differer	nce. SM	D autoge	enerated	by revman.		

### BRIEF Subdomains – Caregiver Report (mean/SD)

#### Confirmed PAE-Level Unquantifiable and BRIEF Inhibit – Caregiver (mean/SD) (2 studies)

	Confirmed	l Unquanti	fiable	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 1.15; Chi <sup>2</sup> = 11.86, d	f = 1 (P = 0.0	0006); I <sup>z</sup> = !	92%							-
Test for overall effect: Z = 3.72 (P = 0.0002	)								-4 -2 U 2 Control Confirmed Ur	1quantifiable
Disk of biss is sound										

Risk of bias legend (A) Overall RoB

#### Confirmed PAE-Level Unquantifiable and BRIEF Shift – Caregiver (mean/SD) (2 studies)

	Confirmed	l Unquanti	fiable	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.02, dt	= 1 (P = 0.90	); I <sup>z</sup> = 0%								-
Test for overall effect: Z = 15.74 (P < 0.000	101)								Control Confirmed Und	quantifiable

Risk of bias legend (A) Overall RoB

#### Confirmed PAE-Level Unquantifiable and BRIEF Emotional Control – Caregiver (mean/SD) (2 studies)

	Confirmed	l Unquantif	fiable	C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.09, df	= 1 (P = 0.77	7); I² = 0%							
Test for overall effect: Z = 13.94 (P < 0.000	01)								Control Confirmed Unquantifiable

#### Risk of bias legend

(A) Overall RoB

#### Confirmed PAE-Level Unquantifiable and BRIEF Initiate – Caregiver (mean/SD) (2 studies)

	Confirmed	Unquantif	iable	С	ontrol		:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.22; Chi <sup>2</sup> = 2.23, df	•	); l² = 55%							-10 -5 0 5	10
Test for overall effect: Z = 8.27 (P < 0.0000	1)							Confirm	ed Unquantifiable Control	

Risk of bias legend (A) Overall RoB

#### Confirmed PAE-Level Unquantifiable and BRIEF Working Memory – Caregiver (mean/SD) (2 studies)

	-						-		
	Confirme	d Unquanti	fiable	С	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl 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: Tau <sup>2</sup> = 3.60; Chi <sup>2</sup> = 21.78, Test for overall effect: Z = 3.43 (P = 0.0006		00001); I² =	95%						-10 -5 0 5 10 Control Confirmed Unquantifiable

Risk of bias legend

(A) Overall RoB

#### **Confirmed PAE-Level Unquantifiable and BRIEF Plan/Organise – Caregiver (mean/SD)** (2 studies)

	Confirmed	Unquanti	fiable	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.46, dt Test for overall effect: Z = 18.49 (P < $0.000$		); I² = 0%							-10 -5 0 5 Control Confirmed Un	10 Iquantifiable

#### Confirmed PAE-Level Unquantifiable and BRIEF Monitor - Caregiver (mean/SD) (2 studies)

	Confirmed	Unquantif	fiable	С	ontrol			Std. Mean Difference	Std. Me	an Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Ran	dom, 95% Cl	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.53, df	= 1 (P = 0.47)	); I² = 0%							-10 -5		10
Test for overall effect: Z = 18.19 (P < 0.000	01)								10 0	ol Confirmed U	10

Risk of bias legend

(A) Overall RoB

#### Confirmed PAE-Level Unquantifiable and BRIEF Organisation of Materials – Caregiver (mean/SD) (2 studies)

	Confirmed	Unquantif	iable	C	ontrol		1	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 1.61, df	= 1 (P = 0.20)	); <b>I<sup>z</sup> = 38%</b>								7
Test for overall effect: Z = 11.87 (P ≤ 0.000	01)								-4 -2 U 2 Control Confirmed Ung	4 uantifiable

<u>Risk of bias legend</u> (**A**) Overall RoB

#### **DIAGNOSED STUDIES**

		ſ	NEPS	SY: S	pe	edeo	d Na	aming	g (mean/SD)			
F	ASD a	and	NEP	SY: S	pe	edec	d Na	ming	(mean/SD) (4	stud	lies)	
		FAS	_			ontrol			Std. Mean Differenc	-	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mea		SD Tot					Weigh			IV, Random, 95% Cl	A
May et al 2020a (6-7yrs; NEPSY-II)		.8			9.2	3.1	302			-	-	
May et al 2020b (6-7yrs; NEPSY-II)				38	10	3	273					
May et al 2020c (6-7yrs; NEPSY-II)					9.3	2.7	330		• •	-		<b>—</b>
Rasmussen et al 2013 (6-16yrs; NEPSY-II)	) 7.3	38 1.3	31 3	32 10	.29	1.55	30	20.4%	-2.01 [-2.63, -1.3	39]		-
Total (95% CI)			1	56			935	100.0%	-0.84 [-1.33, -0.3	4]	•	
Heterogeneity: Tau <sup>2</sup> = 0.21; Chi <sup>2</sup> = 20.52, d Test for overall effect: Z = 3.33 (P = 0.0009)		= 0.00(	01); I²=	85%						-4	-2 0 2 FASD Control	4
Risk of bias legend (A) Overall RoB												
(),	FAS a	and	NEP	SY: S	pe	edec	d Na	ming	(mean/SD) (1	stud	v)	
	F	AS		C	ontr	ol		S	d. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SE	) Tota	al W	/eight	IV, Random, 95% CI		IV, Random, 95% CI	Α
Chambers et al 2019 (6-7yrs; NEPSY)	10.6	4.7	5	8.9	3.2	2 76	1 10	10.0%	0.53 [-0.35, 1.41]			•
Total (95% CI)			5			76	1 10	00.0%	0.53 [-0.35, 1.41]		-	
Heterogeneity: Not applicable										-	-2 0 2	<u> </u>
Test for overall effect: $Z = 1.18$ (P = 0.24)										-4	FAS Control	4
Risk of bias legend												
(A) Overall RoB					_				1 10-2 1			
	pFAS	and	NEP	SY:	Spe	ede	d Na	aming	<b>; (mean/SD)</b> (1	. stu	dy)	
	р	FAS		C	ontr	ol		St	d. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SE	) Tota	al W	/eight	IV, Random, 95% CI		IV, Random, 95% CI	Α
Chambers et al 2019 (6-7yrs; NEPSY)	7.6	3	44	8.9	3.2	2 76	1 10	0.0%	-0.41 [-0.71, -0.10]			•
Total (95% CI)			44			76	1 10	0.0%	-0.41 [-0.71, -0.10]		•	
Heterogeneity: Not applicable										<u> </u>	<u>t l</u>	<u> </u>
Test for overall effect: Z = 2.62 (P = 0.009	)									-4	-2 0 2 pFAS Control	4
Risk of bias legend (A) Overall RoB												
ARN	D/Ot	hers	and	NEP	PSY	: Spe	eede	ed Na	ming (mean/S	<b>D)</b> (1	studv)	
	-	)/Othe			Cont	•			td. Mean Difference	-, (-	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean		Total				tal W		IV, Random, 95% C	I	IV, Random, 95% Cl	A
Chambers et al 2019 (6-7yrs; NEPSY)	8.7	3.3	44	8.9	33.	2 76	61 10	00.0%	-0.06 [-0.37, 0.24]	]		•
Total (95% CI)			44			76	61 1	00.0%	-0.06 [-0.37, 0.24]	1	•	
Heterogeneity: Not applicable										<u>⊢</u>		— <u> </u>
Test for overall effect: $Z = 0.40$ (P = 0.69)										-4	-2 0 2 ARND/Others Control	4

# NEPSY: Inhibition – Naming (mean/SD)

FASD and NEPSY: Inhibition - Naming (mean/SD) (8 studies)

		FASD		0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	<b>—</b>	•
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: Tau <sup>2</sup> = 0.09; Chi <sup>2</sup> = 25.79, df =	7 (P = 0	.0005); I <sup>2</sup>	= 73%					ł		<u> </u>
Test for overall effect: Z = 6.25 (P < 0.00001)									4 -2 U 2 FASD Control	4

Risk of bias legend

(A) Overall RoB

Note: Paolozza et al 2014a also reports NEPSY-II Direction Errors and Timing Errors.

1	FAS a	nd I	NEPS	Y: Inł	nibit	tion -	- Nami	ng (mean/SD) (1	1 study)
	1	FAS		Co	ontro	I .		Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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]	<b>•</b>
Heterogeneity: Not applicable									
Test for overall effect: Z = 0.00 (P = 1.00)									FAS Control
Risk of bias legend (A) Overall RoB									

### pFAS and NEPSY: Inhibition – Naming (mean/SD) (1 study)

	p	FAS		Co	ontro	1		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	•	•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.18 (P = 0.86)			44			761	100.0%	-0.03 [-0.33, 0.28]	-4 -2 0 2 pFAS Control	<u>4</u>

Risk of bias legend (A) Overall RoB

#### ARND/Others and NEPSY: Inhibition – Naming (mean/SD) (1 study)

	AR	ND/Other	S	0	Control			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD.	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> = 1.49, df Test for overall effect: Z = 1.91 (P = 0.06)	= 1 (P =	0.22); I² =	33%						-4 -2 0 2 4 ARND/Others Control	

# NEPSY: Inhibition – Inhibition (mean/SD)

		FASD			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α		
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]		•		
Mayet 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: Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 18.20, df	= 8 (P = 0	.02); <b>I2</b> =	56%							<u> </u>		
Test for overall effect: Z = 8.20 (P < 0.00001			-						-4 -2 0 2	4		

Risk of bias legend (A) Overall RoB

Note: Paolozza et al 2014a also reports NEPSY-II Direction Errors and Timing Errors.

F7			EFJI					ion (mean/SD)	,,	
	I	FAS		Co	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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									-4 -2 0 2	
Test for overall effect: Z = 0.76 (P = 0.45)									FAS Control	4

Risk of bias legend (A) Overall RoB

#### pFAS and NEPSY: Inhibition – Inhibition (mean/SD) (1 study)

-	p	FAS		Co	ontro	I		Std. Mean Difference	Std. Mean	Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Rando	m, 95% Cl	Α
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)									-4 -2 pFAS	0 2 Control	4

Risk of bias legend (A) Overall RoB

#### ARND/Others and NEPSY: Inhibition – Inhibition (mean/SD) (2 studies)

	ARI	ND/Other	S	0	Control			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.18, df: Test for overall effect: Z = 2.46 (P = 0.01)	= 1 (P = I	0.67); I² =	:0%						-4 -2 0 2 ARND/Others Control	

NEPSY: Inhibition – Switc	hing (mean/SD)

FASD and NEPSY: Inhibition – Switching (mean/SD) (8 studies)

		FASD		0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bi
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.20; Chi <sup>2</sup> = 49.00, df =	7 (P < 0	.00001); (	<b>r</b> = 869	<b>X</b> 6						
Test for overall effect: Z = 4.94 (P < 0.00001)									-4 -2 U 2 FASD Control	4

Risk of bias legend

(A) Overall RoB

Note: Paolozza et al 2014a also reports NEPSY-II Direction Errors and Timing Errors.

		FAS		Control			:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
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 Fest for overall effect: Z = 0.97 (P = 0.33	)							-4	-2 0 2 FAS Control	4

#### pFAS and NEPSY: Inhibition - Switching (mean/SD) (1 study)

	p	FAS		Co	ontro	l i		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									-4 -2 0 2 pFAS Control	4

Risk of bias legend (A) Overall RoB

#### ARND/Others and NEPSY: Inhibition – Switching (mean/SD) (2 studies)

	ARI	ND/Other	S	0	Control		:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD.	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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: Tau <sup>2</sup> = 0.15; Chi <sup>2</sup> = 4.57, df =	= 1 (P = 1	0.03); I <b>²</b> =	78%						-10 -5 0 5	+
Test for overall effect: Z = 1.12 (P = 0.26)									ARND/Others Control	10

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 NE	PSA: I	nhi	bitio	n – N	amı	ing vs		-	nean/SD) (4 studies)	
	E.	ASD		Co	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
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]	-8-	•
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.	70, df = 3	3 (P =	= 0.64);	$ ^{2} = 0\%$				-4	<u> </u>	-
Test for overall effect: $Z = 3.39$ (P = 0	).0007)							-4	FASD Control	4

	1	FAS		C	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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										-j
Test for overall effect: Z = 0.81 (P = 0.42)									FAS Control	4
<u>Risk of bias legend</u>										
A) Overall RoB										
pFAS and NEP	SY: Ir	nhib	ition	– Na	mii	ng vs	Inhibit	tion – Inhibition	(mean/SD) (1 study)	
-	F	FAS		C	ontro	I T		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		•

Risk of bias legend

Heterogeneity: Not applicable

Test for overall effect: Z = 1.56 (P = 0.12)

(A) Overall RoB

Total (95% CI)

#### ARND/Others and NEPSY: Inhibition – Naming vs Inhibition – Inhibition (mean/SD) (1 study)

761 100.0%

44

-0.24 [-0.55, 0.06]

-4

	ARNE	ers	Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.36 (P = 0.17)			44			761	100.0%	-0.21 [-0.51, 0.09]	-4 -2 0 2 ARND/Others Control	4
Risk of bias legend										

(A) Overall RoB

### NEPSY: Animal Sorting (mean/SD)

FASD and NEPSY: Animal Sorting (mean/SD) (6 studies)

		FASD			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		•
McLachian 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]	- <b>-</b> -	•
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: Tau <sup>2</sup> = 0.17; Chi <sup>2</sup> = 26.74, df =	5 (P < 0	.0001); I <sup>z</sup>	= 81%					-4	-2 0 2	i
Test for overall effect: Z = 5.33 (P < 0.00001)								*	FASD Control	-

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)

		FAS		C	ontrol			Std. Mean Difference	Std. Mean Differe	nce Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95%	CI 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)									-4 -2 0 Control FAS	2 4

Risk of bias legend (A) Overall RoB

Note: Kodituwakku et al 2001 also reports WCST no. categories completed (ss) and response set loss.

4

pFAS Control

# WCST: Total Errors (ss)

### pFAS and WCST: Total Errors (ss) (1 study)

	p	FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)									-4 -2 0 2 4 pFAS Control
<u>Risk of bias legend</u> (A) Overall RoB									

#### ARND/Others and WCST: Total Errors (ss) (1 study)

	ARN	D/Oth	er	C	ontrol			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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% Cl) Heterogeneity: Not applicable Test for overall effect: Z = 3.91 (P < 0.0001)			24			16	100.0%	-1.42 [-2.14, -0.71]	-4 -2 0 2 ARND/Others Control	4

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)

		FASD		Co	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl 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)								-4 -2 U 2 4 FASD Control
<u>Risk of bias legend</u> ( <b>A</b> ) Overall RoB									

#### pFAS and WCST: Preservative responses (raw) (1 study)

	1	pFAS		C	Control			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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]	
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.74 (P = 0.08)			25			14	100.0%	0.59 [-0.08, 1.26]	-4 -2 0 2 4 Control pFAS

Risk of bias legend (A) Overall RoB

#### ARND/Others and WCST: Preservative responses (raw) (1 study)

	ARM	ID/Othe	rs	0	Control			Std. Mean Difference	Std. Mean Difference Ri	sk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	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)									-4 -2 0 2 4 Control ARND/Others	

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)

n <mark>SD</mark> 8 5.9	Total 23	Mean		Total	Weight	IV. Random, 95% CI	IV. Random, 95% CI	Α
	23	44.0					,	
		11.9	5.22	21	23.6%	-0.55 [-1.15, 0.06]		•
3 2.82	41	11.43	2.99	46	31.5%	-1.26 [-1.72, -0.80]		•
1 3.28	79	10.17	3.35	185	44.9%	-1.25 [-1.53, -0.96]	•	•
	143			252	100.0%	-1.09 [-1.46, -0.71]	•	
.11); I² =	= 55%					H		<u> </u>
						-4	FAS Control	4
)	01 3.28	01 3.28 79	01 3.28 79 10.17 143	01 3.28 79 10.17 3.35 <b>143</b>	01 3.28 79 10.17 3.35 185 143 252	01 3.28 79 10.17 3.35 185 44.9% 143 252 100.0%	01 3.28 79 10.17 3.35 185 44.9% -1.25 [-1.53, -0.96] 143 252 100.0% -1.09 [-1.46, -0.71] 0.11); I <sup>2</sup> = 55% ⊢	01 3.28 79 10.17 3.35 185 44.9% -1.25 [-1.53, -0.96] 143 252 100.0% -1.09 [-1.46, -0.71] 0.11); I <sup>2</sup> = 55%4 -2 0 2

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)

	1	pFAS		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									-4 -2 0 2 pFAS Control	4
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)

	ARN	D/Othe	ers	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		-
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)									-4 -2 0 2 ARND/Others Control	4
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)

	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		•
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)									-4 -2 0 2 FASD Control	4

Risk of bias legend (A) Overall RoB

#### Letter Fluency: D-KEFS (speed)

#### FAS and Letter Fluency: D-KEFS (speed) (1 study)

		FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		•
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)									Control FAS	4

	ARNE	D/Othe	ers	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 1.49 (P = 0.14)			8			10	100.0%	-0.74 [-1.71, 0.23]	-4 -2 0 2 ARND/Others Control	4
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)

		FASD			Control			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	\$D	Total	Mean	\$D	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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)								H-	4 -2 0 2 FASD Control	4
Risk of bias legend									1765 001101	

(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)



Risk of bias legend (A) Overall RoB

#### ARND/Others and Verbal Fluency (Switching): D-KEFS (1 study)

	ARN	D/Othe	ers	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 6.93 (P < 0.00001)			117			185	100.0%	-0.85 [-1.09, -0.61]	-100 -50 0 50 / ARND/Others Control	100

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)

	E	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl 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 < 0.00	001)								-4 -2 0 2 4 FASD Control

		FAS		Control				Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 1.95, df = 1	(P = 0.1	6); l² =	49%					I		
Test for overall effect: Z = 2.29 (P = 0.02)									FAS Control	4

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-9	5 Te	st Ca	tegoı	'y Fl	uenc	y (wor	ds/min) (mean/SI	<b>))</b> (1 study)	
	FASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias	
Study or Subgroup	Mean			Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)								-4	-2 0 2 FASD Control	4

Risk of bias legend (A) Overall RoB

### Other D-KEFS Measures: Tower Test (total achievement)

## FASD and Tower Test (total achievement) (2 studies)

	F	ASD		Control			Std. Mean Difference Std. Mean Diffe					ce	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% C	3	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.16, Test for overall effect: Z = 5.98 (P < 0.000		= 0.69	); I² = 0	%					-4	-2 FASD	Control	2	⊣ 4

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)

-										
	F	FAS		Co	ontro	1		Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								H H	<u> </u>	
Test for overall effect: Z = 2.69 (P = 0.007)								-4	pFAS Control	4
Disk of bios logand										

Risk of bias legend (A) Overall RoB

## ARND/Others and Tower Test (total achievement) (1 study)

	ARND	/Othe	ers	Co	ontro	1		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 3.02 (P = 0.003)			24			16	100.0%	-1.04 [-1.72, -0.37]	-4 -2 0 2 ARND/Others Control	4
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)

	F	ASD		Control				Std. Mean Difference		Std. Mean	Differen	се	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Rando	om, 95% (	1	Α
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]		_	<b>-</b>		•
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: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 1.10 Test for overall effect: Z = 1.59 (P = 0.1		P = 0.29	l); I² = 9	1%					-4	-2 Control	0 FASD	2	4

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)

	F	ASD		Control				Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
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 0000,	1\							-4 -2 0 2 4
restion overall ellect. Z = 5.32 (F <	0.0000	"							Control FASD

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)

		EF Global Executive Cor FASD Control				-		Std. Mean Difference			Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% Cl	Α
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: Tau <sup>2</sup> = 0.19; Chi <sup>2</sup> = 8.00, d	f = 2 (P =	0.02);	l² = 75	%					<u> </u>	- <u>t</u>	<u>l</u>	<u> </u>
Test for overall effect: Z = 7.04 (P < 0.000)							-4	Control	FASD	4		

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)

p								0	-, (=,	
		pFAS			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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]		<b>→</b> ●
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: Tau <sup>2</sup> = 1.64; Chi <sup>2</sup> = 9.56, df = 1 (P = 0.002	?); I² = 90	1%							-4 -2 0 2	4
Test for overall effect: Z = 2.17 (P = 0.03)									Control pFAS	

Risk of bias legend (A) Overall RoB

## ARND/Others and BRIEF Global Executive Composite - Caregiver (mean/SD) (2 studies)

	ARND/Others				Control			Std. Mean Difference	Std.	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV,	Random, 95% Cl	Α
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: Tau <sup>2</sup> = 0.40; Chi <sup>2</sup> = 2.67, df = 1 (P = 0.10);	; <b>I</b> ² = 639	6							H	<u> </u>	
Test for overall effect: Z = 4.92 (P < 0.00001)									-4 -2 C	ontrol ARND/Other	4 /S
									С	ontrol ARND/Other	S

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).

FASD and BRIEF Behaviour Regulation Index - Caregiver (mean/SD) (3 studies)

			-0		-			-0 - 1 /					
		FASD		C	Control			Std. Mean Difference		Std. Mea	n Difference	F	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rand	lom, 95% Cl		Α
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: Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 4.13, df = 2 (P = 0.13	i); l² = 52	%							H	<u> </u>	<u> </u>	— <u>-</u> -	
Test for overall effect: Z = 12.54 (P < 0.00001)									-4	Contro	DI FASD	4	

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)

			-0-		-	-					- /		
		pFAS			Control			Std. Mean Difference		Std. Mean	Difference		Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rand	om, 95% Cl		Α
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: Tau <sup>2</sup> = 1.09; Chi <sup>2</sup> = 7.58, df = 1 (P = 0.006	); l² = 87	%							-4	-1			
Test for overall effect: Z = 2.18 (P = 0.03)									-4	Control	pFAS	4	

Risk of bias legend (A) Overall RoB

#### ARND/Others and BRIEF Behaviour Regulation Index – Caregiver (mean/SD) (2 studies)

· · · · · · ·				-0-			-			- / .		/	
	ARI	ND/Other	s		Control			Std. Mean Difference		Std. Mea	n Differ	ence	Risk of B
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rand	dom, 95	% CI	Α
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]				٠	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.22, df = 1 (P = 0.64);	I² = 0%								-4	-2		2	4
Test for overall effect: Z = 7.42 (P < 0.00001)										Contro	ARN	ID/Others	\$

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	Beha	aviou	ır Re	egula	tion	Ind	ex – Te	eacher (mean/	'SD	<b>)</b> (1 stud	dy)	
		FASD		C	ontrol			Std. Mean Difference		Std. Mea	n Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rand	lom, 95% Cl	Α
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)									-4	-2 Contro	0 2 DI FASD	4

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)

	F	FASD		0	Control		-	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.22; Chi <sup>2</sup> = 14.66, df = 2 (P = 0.0	0007); I <sup>z</sup> :	= 86%						F		
Test for overall effect: $Z = 5.01$ (P < 0.00001)									Control FASD	4

Risk of bias legend (A) Overall RoB

Note: Quattlebaum and O'Connor 2013 also reports CCT Form 1 and Form 2.

		pFAS			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	— — I	- •
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: Tau <sup>2</sup> = 1.95; Chi <sup>2</sup> = 11.60, df = 1 (P = 0.00	007); I <sup>z</sup> =	91%								
Test for overall effect: Z = 1.86 (P = 0.06)									Control pFAS	4

Risk of bias legend (A) Overall RoB

#### ARND/Others and BRIEF Metacognition – Caregiver (mean/SD) (2 studies) ARND/Others Control Std. Mean Difference Std. Mean Difference

Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rando	om, 95% Cl	Α
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: Tau <sup>2</sup> = 1.07; Chi <sup>2</sup> = 5.68, df = 1 (P = 0.02); Test for overall effect: Z = 3.23 (P = 0.001)	l² = 82%	b							-4 -2 Control	0 2 ARND/Others	4
Rick of bias legend									Control	ARTEROTO	

(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		0	Control			Std. Mean Difference		Std. M	lean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Ra	andom, 95% Cl	Α
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									H	-		
Heterogeneity. Not applicable Test for overall effect: Z = 2.70 (P = 0.007)									-4	-2	o 2 ntrol FASD	4

(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)

	FASD		C	ontrol			Std. Mean Difference	St	d. Mean Diffe	erence	Risk of Bias
Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IN	V, Random, 9	5% CI	Α
70.8	13.49	46	45	5.73	70	50.3%	2.68 [2.17, 3.19]				•
69	13	37	50	8	40	49.7%	1.76 [1.23, 2.29]				•
		83			110	100.0%	2.22 [1.32, 3.12]			$\bullet$	
df = 1 (P	= 0.01)	; I <sup>z</sup> = 83	3%							<u> </u>	7
•	Mean 70.8 69	Mean         SD           70.8         13.49           69         13	Mean         SD         Total           70.8         13.49         46           69         13         37           83	Mean         SD         Total         Mean           70.8         13.49         46         45           69         13         37         50	Mean         SD         Total         Mean         SD           70.8         13.49         46         45         5.73           69         13         37         50         8           83         83         83         83         83	Mean         SD         Total         Mean         SD         Total           70.8         13.49         46         45         5.73         70           69         13         37         50         8         40           83         110	Mean         SD         Total         Mean         SD         Total         Weight           70.8         13.49         46         45         5.73         70         50.3%           69         13         37         50         8         40         49.7%           83         110         100.0%	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           70.8         13.49         46         45         5.73         70         50.3%         2.68 [2.17, 3.19]           69         13         37         50         8         40         49.7%         1.76 [1.23, 2.29]           83         110         100.0%         2.22 [1.32, 3.12]	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV           70.8         13.49         46         45         5.73         70         50.3%         2.68 [2.17, 3.19]         69         13         37         50         8         40         49.7%         1.76 [1.23, 2.29]         1.76 [1.23, 2.29]         1.76 [1.23, 3.12]         100.0%         2.22 [1.32, 3.12]         1.76 [1.23, 2.29]         1.76 [1.	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 9           70.8         13.49         46         45         5.73         70         50.3%         2.68 [2.17, 3.19]         IV         100         100         100.0%         2.22 [1.32, 3.22]         100         100         100.0%         2.22 [1.32, 3.12]         100	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           70.8         13.49         46         45         5.73         70         50.3%         2.68 [2.17, 3.19]            69         13         37         50         8         40         49.7%         1.76 [1.23, 2.29]            83         110         100.0%         2.22 [1.32, 3.12]

Risk of bias legend (A) Overall RoB

## Other BRIEF Measures: Shift - Caregiver Report (mean/SD)

## FASD and BRIEF: Shift – Caregiver (mean/SD) (2 studies)

		FASD		C	ontrol			Std. Mean Difference		Std. M	ean Dif	ference		Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Ra	ndom,	95% CI		Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.26, Test for overall effect: Z = 10.26 (P < 0.0		? = 0.61)	); I <sup>z</sup> = 0°	%					-4	-2 Con	0 trol F/	2 ASD	4	

Risk of bias legend (A) Overall RoB Risk of Rias

	FASD and BRIEF: Monitor – Caregiver (mean/SD) (1 study)											
		FASD		C	ontrol			Std. Mean Difference	Std. Me	an Difference	Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rai	ndom, 95% Cl	Α	
Bernes et al 2021 (5-18yrs; BRIEF-C)	66.6	10.89	47	42.4	8.59	70	100.0%	2.51 [2.02, 3.00]		-	•	
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 9.97 (P < 0.01	0001)		47			70	100.0%	2.51 [2.02, 3.00]	-4 -2	0 2 rol FASD	4	

Risk of bias legend (A) Overall RoB

## Other BRIEF Measures: Plan/Organise – Caregiver Report (mean/SD)

	I	FASD		C	ontrol			Std. Mean Difference		Std. Mean Di	ference	Risk of E
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random,	95% CI	Α
Bernes et al 2021 (5-18yrs; BRIEF-C)	67.7	10.43	46	44.7	7.98	70	100.0%	2.53 [2.03, 3.03]			-	- 🔴
Fotal (95% CI)			46			70	100.0%	2.53 [2.03, 3.03]			•	
Heterogeneity: Not applicable									-4	-2 0		4
Fest for overall effect: Z = 9.96 (P < 0.00	001)								•	Control F	ASD	·

(A) Overall RoB

## Other BRIEF Measures: Working Memory – Caregiver Report

	FAS	D and	BRI	EF: W	/orki	ing N	/lemor	y - Caregiver (1	study)	
		FASD		C	ontrol	-		Std. Mean Difference	Std. Mean Difference Ris	sk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl A	1
Bernes et al 2021 (5-18yrs; BRIEF-C)	70.3	11.11	46	44.6	6.59	70	100.0%	2.95 [2.41, 3.48]		•
Total (95% CI)			46			70	100.0%	2.95 [2.41, 3.48]	•	
Heterogeneity: Not applicable										
Test for overall effect: Z = 10.78 (P < 0.0	0001)								-4 -2 U 2 4 FASD Control	
Risk of bias legend (A) Overall RoB										

## ARND/Others and BRIEF: Working Memory - Caregiver (1 study)

	ARNI	)/Othe	rs	С	ontrol	-		Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
Malisza et al 2012 (10-14yrs; BRIEF-C; ARND)	75.5	9.09	22	50.38	9.96	21	100.0%	2.59 [1.76, 3.42]	
Total (95% CI)			22			21	100.0%	2.59 [1.76, 3.42]	•
Heterogeneity: Not applicable Test for overall effect: Z = 6.12 (P < 0.00001)									-4 -2 0 2 4
									Control FASD

Risk of bias legend (A) Overall RoB

Note: Bernes et al 2021 also reports Teacher Report and Self-Report measures.

	Working Me	emory	
Study type	Outcome	Data	# studies
Exposure	Working Memory Index	N/A	
•	Freedom From Distractibility Index:	mean/SD	2 studies: confirmed unquantifiable
	WISC-III		
	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	mean/SD	3 studies: confirmed unquantifiable
	span backwards		
	Spatial WM: CANTAB total errors, spatial	z-scores	2 studies: confirmed unquantifiable
	span length		
Diagnosed	Working Memory Index/ Freedom from	mean/SD	4 studies: 2 FASD, 1 pFAS, 2
	Distractibility Index: WISC-IV & WISC-III		ARND/Other
	Freedom from Distractibility Index: WISC-	Frequency	<b>1 study:</b> 1 pFAS, 1 ARND/Others
	III		
	Digit Span Total Scaled Score: WISC-III,	mean/SD	2 studies: 2 FAS, 2 pFAS, 2
	WISC-IV		ARND/Others
	Digit Span Total: WISC-III, WISC-IV, WISC-	mean/SD	<b>7 studies:</b> 4 FASD, 3 pFAS, 2
	V, JSAIS		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,	mean/SD	9 studies: 7 FASD, 1 pFAS, 1
	TOMAL, WMTB-C		ARND/Others
	Backwards Digit Span: WISC-IV, JSAIS	mean/SD	6 studies: 4 FASD, 1, pFAS, 1
			ARND/Others
	Other Spatial Working Memory	mean/SD	3 studies: 2 FASD, 1 ARND/Others
	Measures: spatial WM strategy		
	Other Spatial Working Memory	z-scores	2 studies: 2 FAS, 1 ARND/Others
	Measures: CANTAB — Spatial WM Total		
	Errors		
	Other Working Memory Measures: DAS	mean/SD	2 studies: 2 FASD (different measures)
	working memory percentile		

## Summary of available outcomes for **working memory**

## GRADE ratings for working memory

			assessment			Nº of	patients		Effect	Certainty
№ of tudies		Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% Cl)	Absolute (95% Cl)	
XPOSI	JRE STUD	IES								
reedo	m From D	istractibility Ind	dex: WISC-III							
onfirn	ned unqua	antifiable								
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	51	40	-	<b>SMD 1.65 lower</b> (2.14 lower to 1.16 lower)	⊕⊕⊖⊖ Low
igit Sp	oan: WISC	-111								
ny PA	E									
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	very serious <sup>d,e,f</sup>	none	28	28	-	SMD 0.22 higher (0.31 lower to 0.75 higher)	⊕○○○ Very Low
orwar	d Digit Sp	an: WISC-III								
Confirm	ned unqua	antifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e, f</sup>	none	29	27	-	<b>SMD 0.99 lower</b> (1.55 lower to 0.43 lower)	⊕⊕⊖⊖ Low
Backwa	ards Digit	Span: WISC-III								
onfirn	ned unqua	antifiable								
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	98	168	-	SMD 0.78 lower (1.04 lower to 0.52 lower)	⊕⊕⊖⊖ Low
Spatial	WM: CAN	ITAB/WISC-III sp	oatial span bac	kwards (mear	n/SD), (	CANTA	B total err	ors (z-score)		
Confirm	ned unqua	antifiable (SS ba	ackwards)							
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	261	323	-	<b>SMD 0.90 lower</b> (1.25 lower to 0.54 lower)	⊕○○○ Very Low
Confirn	ned unqua	antifiable (total	errors)							
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	247	245		<b>SMD 0.71 lower</b> (1.24 lower to 0.18 lower)	⊕⊕⊖⊖ Low
DIAGN	OSED STU	DIES								
Norkin	g Memor	y Index/ Freedo	om from Distra	actibility Index	k: WISC	-IV & V	VISC-III			
ASD										
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	54	99	-	<b>SMD 1.18 lower</b> (2.36 lower to 0.00 lower)	⊕⊕⊖⊖ Low
FAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	20	16	-	SMD 2.68 lower (3.61 lower to 1.75 lower)	⊕⊕⊖⊖ Low
ARND/	Other									
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e, f</sup>	none	46	37	-	<b>SMD 2.83 lower</b> (4.38 lower to	⊕⊖⊖⊖ Very Low
L									1.28 lower)	
	m from Di	istractibility Ind	lex: WISC-III						1.28 lower)	

				· of	1	0 /00	0/10			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	8/20	0/16	<b>OR 22.04</b> (1.18 to	-	$\oplus \oplus \bigcirc \bigcirc$
								426.72)		Low
ARND/	Others							120172)		
1	serious <sup>a</sup>	not serious	not serious	very	none	5/24	0/16	<b>OR 9.31</b> (0.48	-	000
-	00.100.0			serious <sup>d,e,f</sup>		0,	0, 20	to 181.13)		Very Low
Digit S	pan Scaled	Score: WISC-I\	/ & WISC-III					. · ·		- / -
AS										
2	serious <sup>a</sup>	not serious	serious <sup>c</sup>	not serious	none	135	293	-	SMD 0.86 lower	$\Theta \Theta \bigcirc \bigcirc$
_									(1.08 lower to	Low
									0.65 lower)	-
FAS										
2	serious <sup>a</sup>	not serious	serious <sup>c</sup>	not serious	none	139	293	-	SMD 0.43 lower	$\Theta \Theta O O$
									(0.63 lower to	Low
									0.22 lower)	
	'Other		<b>-</b>		1					
2	serious <sup>a</sup>	not serious	serious <sup>c</sup>	serious <sup>e,f</sup>	none	74	293	-	SMD 0.80 lower	$\oplus OOO$
									(1.09 lower to	Very Low
Jigit C	nan Totali	WISC-IV, WISC-			L				0.51 lower)	
	pan Tutal:		III, JSAIS							
					r –					
4	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	228	206	-	SMD 0.70 lower	000
									(1.05 lower to 0.35 lower)	Very Low
FAS	1								0.33 lower)	
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very	none	85	112	_	SMD 0.42 lower	000
5	Serious	senous	not senous	serious <sup>d,e,f</sup>	none	65	112	_	(1.01 lower to	Very Low
				0011000					0.17 higher)	
ARND/	Others									
2	serious <sup>a</sup>	not serious	not serious	very	none	96	80	-	SMD 0.04 lower	000
				serious <sup>d,e,f</sup>					(0.34 lower to	Very Low
									0.27 higher)	-
Block F	Recall: WⅣ	ITB-C (raw), WI	MTB-C (ss)							
ASD (	raw)									
3	serious <sup>a</sup>	not serious	not serious	not serious	none	241	298	-	SMD 0.80 lower	$\oplus \oplus \oplus \bigcirc$
									(0.98 lower to	Moderate
									0.63 lower)	
AS (ss	;)									
1	serious <sup>a</sup>	not serious	not serious	very	none	25	28	-	SMD 0.41 higher	$\oplus O O O$
				serious <sup>d,e,f</sup>					(0.14 lower to	Very Low
									0.95 higher)	
-	ecall: WM	IR-C								
ASD			<b>-</b>		1					
3	serious <sup>a</sup>	not serious	not serious	not serious	none	244	300	-	SMD 0.96 lower	$\oplus \oplus \oplus \bigcirc$
									(1.14 lower to	Moderate
									0.78 lower	
	rd Digit Spa	an: WISC-III, JSA	AIS, TOMAL, W	INT B-C						
ASD			•							
7	serious <sup>a</sup>	not serious	not serious	not serious	none	378	449	-	SMD 0.83 lower	$\oplus \oplus \oplus \bigcirc$
									(0.98 lower to	Moderate
			1		1				0.69 lower)	

			1	-	-			1	1	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e, f</sup>	none	24	32	-	SMD 0.90 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.45 lower to	Low
	/- ·								0.34 lower)	
RND/	/Other									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	18	17	-	SMD 1.01 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.72 lower to 0.3	Low
									lower)	
Backw	ards Digit	Span: WISC-IV,	JSAIS							
ASD										
4	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	177	199	-	SMD 0.60 lower	$\oplus \oplus \bigcirc \bigcirc$
									(0.81 lower to	Low
									0.39 lower)	
oFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e, f</sup>	none	24	32	-	SMD 0.82 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.37 lower to	Low
									0.26 lower)	
ARND,	/Other									
ARND, 1	<b>/Other</b> serious <sup>a</sup>	not serious	not serious	serious <sup>e, f</sup>	none	18	17	-	SMD 0.85 lower	$\oplus \oplus \bigcirc \bigcirc$
		not serious	not serious	serious <sup>e,f</sup>	none	18	17	-		
		not serious	not serious	serious <sup>e,f</sup>	none	18	17	-	SMD 0.85 lower (1.55 lower to 0.16 lower)	⊕⊕⊖⊖ Low
1	serious <sup>a</sup>	not serious orking Memory						- ategy	(1.55 lower to	
1 Other	serious <sup>a</sup> Spatial Wo		Measures: CA					- ategy	(1.55 lower to	
1 Other	serious <sup>a</sup> Spatial Wo	orking Memory	Measures: CA					- ategy -	(1.55 lower to 0.16 lower)	Low
1 Other FASD (	serious <sup>a</sup> Spatial Wo	orking Memory rking Memory	Measures: CA Strategy)	NTAB – Spatia	al Worki	ing Me	mory Stra	- ategy -	(1.55 lower to 0.16 lower) SMD 0.65 higher	Low $\oplus \oplus \bigcirc \bigcirc$
1 Other FASD (	serious <sup>a</sup> Spatial Wo	orking Memory rking Memory	Measures: CA Strategy)	NTAB – Spatia	al Worki	ing Me	mory Stra	- ategy -	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to	Low
1 Other FASD ( 2	serious <sup>a</sup> Spatial Wo Spatial Wo serious <sup>a</sup>	orking Memory rking Memory	Measures: CA Strategy) not serious	NTAB – Spatia serious <sup>e,f</sup>	al Worki	ing Mer 31	mory Stri 48	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher)	Low $\oplus \oplus \bigcirc \bigcirc$
1 Dther FASD ( 2 Dther	serious <sup>a</sup> Spatial Wo Spatial Wo serious <sup>a</sup>	rking Memory rking Memory not serious	Measures: CA Strategy) not serious	NTAB – Spatia serious <sup>e,f</sup>	al Worki	ing Mer 31	mory Stri 48	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher)	Low $\oplus \oplus \bigcirc \bigcirc$
1 Other FASD ( 2 Other FAS	serious <sup>a</sup> Spatial Wo Spatial Wo serious <sup>a</sup> Spatial Wo	rking Memory rking Memory not serious	Measures: CA Strategy) not serious	NTAB – Spatia serious <sup>e,f</sup>	al Worki	ng Mer 31 ng Mer	mory Stri 48	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores)	Low $\oplus \oplus \bigcirc \bigcirc$ Low
1 Other FASD ( 2 Other	serious <sup>a</sup> Spatial Wo Spatial Wo serious <sup>a</sup>	orking Memory rking Memory not serious orking Memory	Measures: CA Strategy) not serious Measures: CA	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia	al Worki none al Worki	ing Mer 31	mory Stra 48 mory Tot	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower	
1 Other FASD ( 2 Other FAS	serious <sup>a</sup> Spatial Wo Spatial Wo serious <sup>a</sup> Spatial Wo	orking Memory rking Memory not serious orking Memory	Measures: CA Strategy) not serious Measures: CA	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia	al Worki none al Worki	ng Mer 31 ng Mer	mory Stra 48 mory Tot	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower (1.30 lower to	Low $\oplus \oplus \bigcirc \bigcirc$ Low
1 FASD ( 2 Other FAS 2	serious <sup>a</sup> Spatial Wo Spatial Wo Serious <sup>a</sup> Spatial Wo Serious <sup>a</sup>	orking Memory rking Memory not serious orking Memory	Measures: CA Strategy) not serious Measures: CA	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia	al Worki none al Worki	ng Mer 31 ng Mer	mory Stra 48 mory Tot	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower	
1 FASD ( 2 Other FAS 2	serious <sup>a</sup> Spatial Wo Spatial Wo serious <sup>a</sup> Spatial Wo	orking Memory rking Memory not serious orking Memory not serious	Measures: CA Strategy) not serious Measures: CA not serious	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia serious <sup>e,f</sup>	al Worki none al Worki	31 ing Met	48 mory Tot 231	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower (1.30 lower to 0.83 lower)	
1 Other FASD ( 2 Other FAS 2 ARND,	serious <sup>a</sup> Spatial Wo Spatial Wo serious <sup>a</sup> Spatial Wo Serious <sup>a</sup> (others	orking Memory rking Memory not serious orking Memory	Measures: CA Strategy) not serious Measures: CA	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia	al Worki none al Worki	ng Mer 31 ng Mer	mory Stra 48 mory Tot	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower (1.30 lower to 0.83 lower) SMD 0.82 lower	Low ⊕⊕⊖⊖ Low €⊕⊕⊖⊖
1 Other FASD ( 2 Other FAS 2 ARND,	serious <sup>a</sup> Spatial Wo Spatial Wo serious <sup>a</sup> Spatial Wo Serious <sup>a</sup> (others	orking Memory rking Memory not serious orking Memory not serious	Measures: CA Strategy) not serious Measures: CA not serious	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia serious <sup>e,f</sup>	al Worki none al Worki	31 ing Met	48 mory Tot 231	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower (1.30 lower to 0.83 lower) SMD 0.82 lower (1.06 lower to	
1 FASD ( 2 Other FAS 2 ARND, 1	serious <sup>a</sup> Spatial Wo Spatial Wo Serious <sup>a</sup> Spatial Wo Serious <sup>a</sup> Spatial Wo Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup>	orking Memory rking Memory not serious orking Memory not serious	Measures: CA Strategy) not serious Measures: CA not serious not serious	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia serious <sup>e,f</sup>	al Worki none al Worki none	120	48 mory Tot 231 185	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower (1.30 lower to 0.83 lower) SMD 0.82 lower	Low ⊕⊕⊖⊖ Low €⊕⊕⊖⊖
1 Other FASD ( 2 Other FAS 2 ARND, 1 Other	serious <sup>a</sup> Spatial Wo Spatial Wo Serious <sup>a</sup> Spatial Wo Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup>	orking Memory rking Memory not serious orking Memory not serious	Measures: CA Strategy) not serious Measures: CA not serious not serious	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia serious <sup>e,f</sup>	al Worki none al Worki none	120	48 mory Tot 231 185	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower (1.30 lower to 0.83 lower) SMD 0.82 lower (1.06 lower to	Low ⊕⊕⊖⊖ Low €⊕⊕⊖⊖
1 FASD ( 2 Other FAS 2 ARND, 1 Other FASD (	serious <sup>a</sup> Spatial Wo Spatial Wo Serious <sup>a</sup> Spatial Wo Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup> DAS)	orking Memory rking Memory not serious orking Memory not serious not serious	Measures: CA Strategy) not serious Measures: CA not serious not serious Measures: DA	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia serious <sup>e,f</sup> serious <sup>f</sup>	al Worki none none none	ing Mer 31 ing Mer 120 117	48 mory Tot 231 185 ile	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower (1.30 lower to 0.83 lower) SMD 0.82 lower (1.06 lower to 0.58 lower)	
1 Other FASD ( 2 Other FAS 2 ARND, 1 Other	serious <sup>a</sup> Spatial Wo Spatial Wo Serious <sup>a</sup> Spatial Wo Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup>	orking Memory rking Memory not serious orking Memory not serious	Measures: CA Strategy) not serious Measures: CA not serious not serious	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia serious <sup>e,f</sup>	al Worki none al Worki none	120	48 mory Tot 231 185	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower (1.30 lower to 0.83 lower) SMD 0.82 lower (1.06 lower to 0.58 lower)	Low ⊕⊕⊖⊖ Low ⊕⊕⊖⊖ Low
1 Dther FASD ( 2 Dther FAS 2 ARND/ 1 Dther FASD (	serious <sup>a</sup> Spatial Wo Spatial Wo Serious <sup>a</sup> Spatial Wo Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup> Serious <sup>a</sup> DAS)	orking Memory rking Memory not serious orking Memory not serious not serious	Measures: CA Strategy) not serious Measures: CA not serious not serious Measures: DA	NTAB – Spatia serious <sup>e,f</sup> NTAB – Spatia serious <sup>e,f</sup> serious <sup>f</sup>	al Worki none none none	ing Mer 31 ing Mer 120 117	48 mory Tot 231 185 ile	-	(1.55 lower to 0.16 lower) SMD 0.65 higher (0.18 higher to 1.12 higher) cores) SMD 1.07 lower (1.30 lower to 0.83 lower) SMD 0.82 lower (1.06 lower to 0.58 lower)	

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 (l<sup>2</sup> >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) Confirmed Unquantifiable Std. Mean Difference Std. Mean Difference **Risk of Bias** Control Total Mean Total Weight Mean SD SD IV, Random, 95% CI IV, Random, 95% CI Study or Subgroup Δ Bjorkquist et al 2010 (8-16yrs; WISC-III FfD) 21 111.6 11.47 81.48 15.79 10 28.1% -2.01 [-2.94, -1.09] Lee et al 2004 (9-17yrs; WISC-III FfD) 30 71.9% -1.51 [-2.09, -0.93] 85.4 13.68 30 105.5 12.57 Total (95% CI) 51 40 100.0% -1.65 [-2.14, -1.16] ⊢ -4 Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.81, df = 1 (P = 0.37); l<sup>2</sup> = 0% -2 ή ż 4 Test for overall effect: Z = 6.60 (P < 0.00001) Confirmed Unquantifiable Control Risk of bias legend

(A) Overall RoB

## Digit Span: WISC-III (mean/SD)

	-					-	•	(mean/SD) (1 stu		Risk of Bias
Study or Subgroup	Mean	iy PAE SD		Mean	ontrol SD	Total	Weiaht	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% Cl	A
, ,									iv, Randolli, 95% Cl	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								ŀ		<u> </u>
Test for overall effect: Z = 0.82 (P = 0.41)								-	4 -2 U 2 Control Any PAE	4

Risk of bias legend (A) Overall RoB

## Forward Digit Span: WISC-III (mean/SD)

	Confirmed	Unquanti	fiable	C	ontrol			Std. Mean Difference	Std. Mean	Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rando	m, 95% Cl	Α
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									-4 -2		4
Test for overall effect: Z = 3.48 (P = 0.0005)								Confirm	ed Unquantifiable	Control	

(A) Overall RoB

## Backwards Digit Span: WISC-III (mean/SD)

Confirmed P	Confirmed	Unquantif	iable	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.42, Test for overall effect: $Z = 5.86$ (P < 0.00	•	52); I² = 0%	6					-4 Confirmed	-2 0 2 Unquantifiable Control	4

Risk of bias legend (A) Overall RoB

### Spatial Working Memory: CANTAB, WISC-III spatial span backwards (mean/SD)

Confirmed PAF Level Unquantifiable and SWM (mean/SD) (3 studies)

	Confirmed	Unquantif	ïable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.07; Chi <sup>2</sup> = 7.01, Test for overall effect: Z = 4.94 (P < 0.00	•	03); I² = 71	%					-4 Confirmed	-2 0 2 Unquantifiable Control	4

### Confirmed PAE Level Unquantifiable and Spatial Working Memory (total errors) (z-scores) (2 studies)

	Confirmed	Unquantif	fiable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.12; Chi <sup>2</sup> = 5.33,	•	02); I² = 81	%					F -	4 -2 0 2	4
Test for overall effect: Z = 2.62 (P = 0.00)	9)							Confirme	d Unquantifiable Control	
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)

		FAS	SD ar	nd WN	∕∕II/Ff	DI (n	nean/S	<b>5D)</b> (2 studies)		
		FASD		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.63; Chi <sup>2</sup> = 8.07, d	f=1 (P=	0.004)	; <b>i²</b> = 88	%				H		-,
Test for overall effect: $Z = 1.97$ (P = 0.05)								-2	FASD Control	4

Risk of bias legend (A) Overall RoB

## pFAS and WMI/FfDI (mean/SD) (1 study)

	- p	FAS		C	ontrol	•		Std. Mean Difference		Std. Mean	Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Rando	om, 95% Cl	Α
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)									-4	-2 pFAS	0 2 Control	4

Risk of bias legend (A) Overall RoB

## ARND/Others and WMI/FfDI (mean/SD) (2 studies)

ARN	D/Othe	rs	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
79	10.1	24	120.9	12.7	16	47.2%	-3.67 [-4.72, -2.61]	<b>-</b>	•
69.62	16.49	22	100.86	12.65	21	52.8%	-2.08 [-2.84, -1.32]		•
		46			37	100.0%	-2.83 [-4.38, -1.28]		
= 0.02);	<b> =</b> 83	%							-
								ARND/Others Control	4
	Mean 79 69.62	Mean         SD           79         10.1           69.62         16.49	79 10.1 24 69.62 16.49 22	Mean         SD         Total         Mean           79         10.1         24         120.9           69.62         16.49         22         100.86           46	Mean         SD         Total         Mean         SD           79         10.1         24         120.9         12.7           69.62         16.49         22         100.86         12.65           46	Mean         SD         Total         Mean         SD         Total           79         10.1         24         120.9         12.7         16           69.62         16.49         22         100.86         12.65         21           46         37	Mean         SD         Total         Mean         SD         Total         Weight           79         10.1         24         120.9         12.7         16         47.2%           69.62         16.49         22         100.86         12.65         21         52.8%           46         37         100.%	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           79         10.1         24         120.9         12.7         16         47.2%         -3.67 [-4.72, -2.61]           69.62         16.49         22         100.86         12.65         21         52.8%         -2.08 [-2.84, -1.32]           46         37         100.0%         -2.83 [-4.38, -1.28]	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           79         10.1         24         120.9         12.7         16         47.2%         -3.67 [-4.72, -2.61]           69.62         16.49         22         100.86         12.65         21         52.8%         -2.08 [-2.84, -1.32]           46         37         100.0%         -2.83 [-4.38, -1.28]

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 (%)

p	FAS an	d Fre	equen	cy of	FfDI <	<b>2SD (%)</b> (1 stud	y)	
	pFA	S	Contr	ol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								1
Test for overall effect: Z = 2.07 (P = 0.04)							0.001 0.1 1 10 10 Control pFAS	JU
Pick of bias legend								

## ARND/Others and Frequency of FfDI <2SD (%) (1 study)

				-	-			
	ARND/O	thers	Cont	rol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 Heterogeneity: Not applicable Test for overall effect: Z = 1.47 (P = 0.14)	5		0				0.001 0.1 1 10 100 ARND/Others Controls	
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)

	F	FAS		Co	ontro	I		Std. Mean Difference		Std. Mean Difference	e Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Random, 95% Cl	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0 Test for overall effect: Z = 7.84 (P <	•		= 0.42)	; I² = 0%	6				-4	-2 0 2 FAS Control	4

Risk of bias legend (A) Overall RoB

## pFAS and Digit Span (ss) (mean/SD) (2 studies)

pFA	S	Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Mean S	D Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
5.1 2.	8 51	6.7	3.3	87	33.9%	-0.51 [-0.86, -0.16]		•
4.9 2.	6 88	5.9	2.6	206	66.1%	-0.38 [-0.64, -0.13]		•
	139			293	100.0%	-0.43 [-0.63, -0.22]	•	
.32, df = 1 (	(P = 0.57)	); I <sup>z</sup> = 0%	6					
0.0001)							pFAS Control	4
	Mean S 5.1 2. 4.9 2.	5.1 2.8 51 4.9 2.6 88 <b>139</b> .32, df = 1 (P = 0.57)	Mean         SD         Total         Mean           5.1         2.8         51         6.7           4.9         2.6         88         5.9           139           .32, df = 1 (P = 0.57); I <sup>2</sup> = 0%	Mean         SD         Total         Mean         SD           5.1         2.8         51         6.7         3.3           4.9         2.6         88         5.9         2.6           139         .32, df = 1 (P = 0.57); P = 0%         P = 0%	Mean         SD         Total         Mean         SD         Total           5.1         2.8         51         6.7         3.3         87           4.9         2.6         88         5.9         2.6         206           139         293           .32, df = 1 (P = 0.57); I <sup>P</sup> = 0%         1         1         1         1         1         1         1         1         1         1         1         1         1         1         1         1         1         2         1	Mean         SD         Total         Mean         SD         Total         Weight           5.1         2.8         51         6.7         3.3         87         33.9%           4.9         2.6         88         5.9         2.6         206         66.1%           139         293         100.0%           .32, df = 1 (P = 0.57); P = 0%         5         5         100.0%	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           5.1         2.8         51         6.7         3.3         87         33.9%         -0.51 [-0.86, -0.16]           4.9         2.6         88         5.9         2.6         206         66.1%         -0.38 [-0.64, -0.13]           139         293         100.0%         -0.43 [-0.63, -0.22]           .32, df = 1 (P = 0.57); I <sup>2</sup> = 0%         - <td>Mean         SD         Total         Meight         IV, Random, 95% CI         IV, Random, 95% CI           5.1         2.8         51         6.7         3.3         87         33.9%         -0.51 [-0.86, -0.16]            4.9         2.6         88         5.9         2.6         206         66.1%         -0.38 [-0.64, -0.13]            139         293         100.0%         -0.43 [-0.63, -0.22]         ◆           .32, df = 1 (P = 0.57); P = 0%           </td>	Mean         SD         Total         Meight         IV, Random, 95% CI         IV, Random, 95% CI           5.1         2.8         51         6.7         3.3         87         33.9%         -0.51 [-0.86, -0.16]            4.9         2.6         88         5.9         2.6         206         66.1%         -0.38 [-0.64, -0.13]            139         293         100.0%         -0.43 [-0.63, -0.22]         ◆           .32, df = 1 (P = 0.57); P = 0%

Risk of bias legend (A) Overall RoB

## ARND/Others Digit Span (ss) (mean/SD) (2 studies)

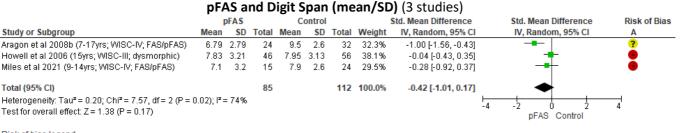
	ARNE	)/Othe	ers	Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
May et al 2013a (6-7yrs; WISC-IV)	4.7	2.7	35	6.7	3.3	87	44.7%	-0.63 [-1.03, -0.23]	-8-	•
May et al 2016 (6-7yrs; WISC-III)	3.5	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: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = $^{\circ}$ Test for overall effect: Z = 5.38 (P <	•		0.27);	l² = 17%	6				-4 -2 0 2 ARND/Others Control	4

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)

		_		-0				,		
	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.08; Chi <sup>2</sup> = 7.82, df = 3 (P = 0 Test for overall effect: Z = 3.95 (P < 0.0001)	.05); I² =	62%							-4 -2 0 2 FASD Control	4



Risk of bias legend

(A) Overall RoB

Note: Aragon et al 2008b also reports DRST Spatial measures and Lhermitte measures.

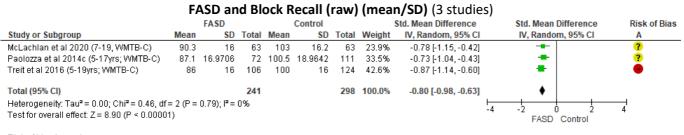
#### ARND/Others and Digit Span (mean/SD) (2 studies)

					D	<b>P</b>	1	., , (=	•/	
	ARN	D/Othe	rs	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.57, df = 1 (P = 0. Test for overall effect: Z = 0.23 (P = 0.81)	45); l² = l	0%							-4 -2 0 2 ARND/Others Control	4

#### Risk of bias legend

(A) Overall RoB

## Block Recall: WMTB-C (raw) (mean/SD)



Risk of bias legend (A) Overall RoB

#### Block Recall: WMTB-C (ss) (mean/SD)

	FA	SD a	nd B	lock	Reca	ll (ss	) (mea	n/SD) (1 study)	)		
		FASD		0	Control			Std. Mean Difference	Std. Me	an Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rai	ndom, 95% Cl	Α
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)									-4 -2 Cont	0 2 rol FASD	4

Risk of bias legend (A) Overall RoB

## Digit Recall: WMTB-C (mean/SD)

FASD and Digit Recall (mean/SD) (3 studies)

		-				•		1 (		
		FASD			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>z</sup> = 0.00; Chi <sup>z</sup> = 0.12, df Test for overall effect: Z = 10.52 (P < 0.000		0.94); l² =	0%					H -	4 -2 0 2 FASD Control	4

	· · ·
FASD and Forward Digit Span	(moon/SD) (7 studios)
FASD allu FUI walu Digil Suali	(IIIedil/JDI (/ Studies)

					0				/	
		FASD			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD.	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
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: $Tau^{2} = 0.00$ ; $Chi^{2} = 4.93$ , $df = 6$ (P =	0.55); l <sup>2</sup> :	= 0%								
Test for overall effect: Z = 11.40 (P < 0.00001)									-4 -2 U 2 FASD Control	4
									TASE CONTO	

Risk of bias legend (A) Overall RoB

## pFAS and Forward Digit Span (mean/SD) (1 study)

F F	FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of B
Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
6.29	1.79	24	8.25	2.39	32	100.0%	-0.90 [-1.45, -0.34]	
		24			32	100.0%	-0.90 [-1.45, -0.34]	•
								-4 -2 0 2 4
								pFAS Control
	Mean	pFAS <u>Mean SD</u> 6.29 1.79	Mean SD Total 6.29 1.79 24	Mean         SD         Total         Mean           6.29         1.79         24         8.25	Mean         SD         Total         Mean         SD           6.29         1.79         24         8.25         2.39	Mean         SD         Total         Mean         SD         Total           6.29         1.79         24         8.25         2.39         32	Mean         SD         Total         Mean         SD         Total         Weight           6.29         1.79         24         8.25         2.39         32         100.0%	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           6.29         1.79         24         8.25         2.39         32         100.0%         -0.90 [-1.45, -0.34]

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)

	ARND	)/Othe	ers	Co	ontro	1		Std. Mean Difference	Std. Mean Difference Risk of I	3ias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)									-4 -2 0 2 4 Control ARND/Others	
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)

	FAS	SD ai	nd Ba	ackwa	ard D	Digit	Span (	mean/SD) (4 stu	udies)		
	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean D	ifference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Randon	n, 95% Cl	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.67,	df = 3 (P	<sup>9</sup> = 0.6	4); I <sup>2</sup> = (	0%						<u> </u>	<u> </u>
Test for overall effect: Z = 5.60 (P < 0.00	001)								-4 -2 U FASD	Control	4

Risk of bias legend (A) Overall RoB

## pFAS and Backward Digit Span (mean/SD) (1 study)

	, i	FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bia
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)									-4 -2 0 2 4 pFAS Control

Risk of bias legend (A) Overall RoB

Note: Aragon et al 2008b also reports DRST Spatial Measures

	ARNE	)/Othe	ers	Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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 = 0.0	2)								-4 -2 0 2 ARND/Others Control	4
Pick of bias lagond										

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

	F	ASD		C	ontrol			Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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]		+∎	•
Fotal (95% CI)			31			48	100.0%	0.65 [0.18, 1.12]		•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.09, df = 1	(P = 0.7)	6); I <b>2</b> :	= 0%						$\vdash$	<u> </u>	-
Fest for overall effect: Z = 2.73 (P = 0.006)									-4	Control FASD	4

<sup>(</sup>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		C	ontrol			Std. Mean Difference		Std. Mean Diffe	rence	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 9	5% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.74,	df = 1 (P	= 0.39	9); I² = 0	)%					<u> </u>	-2 0	<u>    t     </u>	

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/0	Others	s an	d CA	NTA	B SV	VM T	otal E	rrors (z-scores)	(1 study)	
	ARNI	D/Othe	ers	С	ontrol			Std. Mean Difference	Std. Mean Difference	e Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									ARND/Others Control	4
Risk of bias legend										
(A) Overall RoB										

## Other Spatial Working Memory Measures: DAS Working Memory Percentile

		F	ASD	and D	AS V	VM P	ercenti	le (mean/SD) (1 st	tudy)	
	E	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 3.71	(P = 0.0	002)	36			98	100.0%	-0.74 [-1.14, -0.35]  -  -	4 -2 0 2 FASD Control	

Risk of bias legend (A) Overall RoB

		Academic	
Study Type	Outcome	Data	# of studies
Exposure Studies (light,	Overall academic	Mean and SDs	2 studies: 1 light, 1
moderate, heavy, very	achievement		moderate, 1 heavy, 1 very
heavy, any level, confirmed- unquantifiable)			heavy, 0 any, 0 confirmed unquantifiable
	Literacy/Reading	Mean and SDs; adjusted mean	4 studies: 0 light, 1
		difference and 95% Cls	moderate, 1 heavy, 1 very
			heavy, 0 any, 2 confirmed
			unquantifiable
		OR/aOR and 95% CIs; % or n cases	2 studies:
		with event	
	Numeracy/Maths	Mean and SDs; adjusted mean	3 studies: 0 light, 0
		difference and 95% Cls	moderate, 0 heavy, 1 very
			heavy, 0 any, 2 confirmed
			unquantifiable
		OR/aOR and 95% CIs; % or n cases	1 study:
		with event	
Diagnosed Studies (FASD,	Overall academic	Mean and SDs	8 studies: 4 FASD, 2 FAS, 2
FAS, pFAS, Other FASDs)	achievement		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

## Summary of available outcomes for **academic**

*Note.* No specific age groups all studies included a range of ages from 5 to 19 years.

# GRADE ratings for academic

		Certainty	assessment			Nº of p	oatients		Effect	Certainty
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% Cl)	
EXPOSU	IRE STUDIE	S								
Overall a	academic a	chievement (m	/sd)							
Light pre	enatal alco	hol exposure (1-	20g/w in at le	ast one trimeste	er)					
1	serious <sup>a</sup>	not serious	not serious	not serious	none	2928	3332	-	SMD 0.09 higher (0.04 higher to 0.14 higher)	⊕⊕⊕⊖ Moderate
Modera	te prenatal	alcohol exposu	re (21-100g/w	in at least one	trimest	er)			•	
1	serious <sup>a</sup>	not serious	not serious	not serious	none	947	3332	-	SMD 0.08 higher (0.01 higher to 0.15 higher)	⊕⊕⊕⊖ Moderate
Heavy p	renatal alc	ohol exposure (	101-200g/w in	at least one trin	mester)					
1 Very be:	serious <sup>a</sup>	not serious al alcohol expos	not serious	serious <sup>d</sup>	none	106	3332	-	<b>SMD 0.19 lower</b> (0.38 lower to 0.01 higher)	⊕⊕⊖⊖ Low
1	serious <sup>a</sup>	not serious		very serious <sup>d,e,f</sup>	1	25	21		SMD 0.92 lower	000
T	senous	not serious	not serious	very serious <sup>a,e,</sup>	none	25	21	-	(1.53 lower to 0.30 lower)	⊕OOO Very Low
Any leve	el, Confirme	ed-Unquantifiab	le – no studie:	S						
Literacy,	/Reading (r	m/sd)								
Light pre	enatal alco	hol exposure – r	no studies							
Modera	te prenatal	l alcohol exposu	re (21-100g/w	in at least one	trimest	er)				
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	1561	1536	-	SMD 0.05 higher (0.02 lower to 0.12 higher)	⊕⊕⊖⊖ Low
Heavy p	renatal alc	ohol exposure (	101g-200g/w i	n at least one tr	imeste	r)				
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	39	1536	-	<b>SMD 0.17 lower</b> (0.48 lower to 0.15 higher)	⊕⊕⊖⊖ Low
Very hea	avy prenata	al alcohol expos	· -		T	-		-		
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	25	21	-	<b>SMD 0.70 lower</b> (1.30 lower to 0.10 lower)	⊕⊕⊖⊖ Low
Any leve	el prenatal	alcohol exposur	e – no studies							
Confirm	ed prenata	ll alcohol exposu								
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	112	116	-	<b>SMD 0.44 lower</b> (1.00 lower to 0.12 higher)	⊕○○○ Very Low
Literacy,	/Reading ((	ORs/aOR/Freque	ency)							
Low rea	ding achiev	vement (WRAT-I	R scores < 85)							
Modera	te prenata	l alcohol exposu	re (21-100g/w	in at least one	trimest	er)				
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	1561	1563	<b>OR 0.70</b> (0.30 to 1.63)	-	⊕⊕⊖⊖ Low
Heavy p	renatal alc	ohol exposure (	101-200g/w in	at least one trin	mester)					
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	none	39	1563	<b>OR 1.10</b> (0.50 to 2.42)	-	⊕⊕⊖⊖ Low

0 studie	s for light,	very heavy, any	level, confirm	ed-unquantifiab	le					
				s (based on West			ninimum	standards)		
Nodera	te prenatal	alcohol exposu	re (21-100g/w	in at least one t	trimest	er)		-		
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	none	12	52	<b>OR 0.85</b> (0.44 to 1.64)	-	⊕⊕⊖⊖ Low
leavy p	renatal alco	ohol exposure (	101-200g/w in	at least one trir	nester)					
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	12	52	<b>OR 2.27</b> (1.11 to 4.64)	-	⊕⊕⊖⊖ Low
) studie	s for light,	very heavy, any	level, confirm	ed-unquantifiab	le					
Numera	icy/Maths (	m/sd)								
Very he	avy prenata	al alcohol expos		in at least one tr		r)	-			
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	25	21	-	<b>SMD 0.88 lower</b> (1.49 lower to 0.27 lower)	⊕○○○ Very Low
Confirm	ed prenata	l alcohol exposi	ure-Level Unqu	uantifiable			•			
3	seriousª	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	195	176	-	SMD 0.76 lower (1.36 lower to 0.17 lower)	⊕○○○ Very Low
0 studie	s for light, i	moderate, heav	y, any level					I		
Numera	icy/Maths (	ORs/aOR/Frequ	iency)							
Maths a	chievemen	t below minimu	ım standards (	based on Weste	rn Aust	ralian m	inimum s	standards)		
Modera	te prenatal	alcohol exposu	re (21-100g/w	in at least one	trimest	er)		-		
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	27	135	<b>OR 0.71</b> (0.46 to 1.10)	-	⊕⊕⊕⊖ Moderate
Heavy p	renatal alco	ohol exposure (	101-200g/w in	eat least one tr	imester	r)			•	
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	13	135	<b>OR 0.98</b> (0.52 to 1.85)	-	⊕⊕⊕⊖ Moderate
0 studie	s for light,	very heavy, any	level, confirm	ed-unquantifiab	le			· · · ·		
DIAGNO	DSED STUD	IES								
Academ	ic Achiever	ment								
FASD										
4	serious <sup>a</sup>	not serious	not serious	not serious	none	102	892	-	<b>SMD 0.56 lower</b> (0.79 lower to 0.32 lower)	⊕⊕⊕⊖ Moderate
FAS										
2	serious <sup>a</sup>	serious⁵	not serious	serious <sup>d,e</sup>	none	43	428	-	<b>SMD 0.29 lower</b> (1.07 lower to 0.50 higher)	⊕○○○ Very Low
oFAS (pl	FAS or pFAS	S/FAS or dysmo	rphic)							
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	68	190	-	<b>SMD 0.35 lower</b> (0.88 lower to 0.18 higher)	⊕○○○ Very Low
Other F	ASDs (ARNI	D, ND-AE, SE-AE	, Non-syndron	nal)	<u> </u>		-	-		
2	serious <sup>a</sup>	serious⁵	not serious	very serious <sup>d,e,f</sup>	none	103	190	-	<b>SMD 0.04 higher</b> (0.40 lower to 0.47 higher)	⊕○○○ Very Low
Reading	Ability									

FASD										
5	seriousª	not serious	not serious	not serious	none	282	331	-	<b>SMD 1.05 lower</b> (1.29 lower to 0.82 lower)	⊕⊕⊕⊖ Moderate
FAS										
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	7	186	-	<b>SMD 0.82 lower</b> (1.60 lower to 0.08 lower)	⊕⊕⊖⊖ Low
pFAS (p	oFAS, pFAS/	FAS, dysmorphi	c)							
2	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	39	202	-	<b>SMD 1.59 lower</b> (2.27 lower to 0.91 lower)	⊕⊕⊖⊖ Low
Other I	FASDs (ARNI	D, ND-AE, SE-AE	E, Non-syndror	nal)						
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	21	16	-	<b>SMD 1.05 lower</b> (1.75 lower to 0.35 lower)	⊕⊕⊖⊖ Low
Maths	Ability	•					•		· · · ·	
FASD										
5	seriousª	not serious	not serious	serious <sup>e</sup>	none	298	320	-	<b>SMD 1.49 lower</b> (1.69 lower to 1.29 lower)	⊕⊕⊖⊖ Low
FAS							<b></b>			
2	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	15	209	-	<b>SMD 1.04 lower</b> (1.61 lower to 0.48 lower)	⊕⊕⊖⊖ Low
pFAS (p	oFAS, pFAS/	FAS, dysmorphi	c)							
3	seriousª	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	47	225	-	<b>SMD 1.65 lower</b> (2.71 lower to 0.58 lower)	⊕○○○ Very Low
Other I	ASDs (ARNI	D, ND-AE, SE-AE	, Non-syndror	nal)						
2	seriousª	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	30	39	-	<b>SMD 0.87 lower</b> (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 ( $I^2 > 50\%$  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 academic

**EXPOSURE STUDIES** 

	Ligi	ht PA	E	Co	ontro			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)								-4 -2 U 2 4 Light PAE Control
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)

	Mode	rate P	AE	Co	ontro			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									-4 -2 0 2	<u> </u>
Test for overall effect: Z = 2.11 (P = 0.0	04)								Moderate PAE Control	4
<u>Risk of bias legend</u> ( <b>A</b> ) 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)

	Hea	wy PA	E	Co	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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										<u>├</u>
Test for overall effect: Z = 1.88 (P = 0.0	)6)								Heavy PAE Control	ŧ
<u>Risk of bias legend</u> ( <b>A</b> ) 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)

	Very	Heavy F	PAE	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									-4 -2 0 2 4	
Test for overall effect: Z = 2.93 (P = 0.003)									Very Heavy PAE Control	r
Risk of bias legend										
(A) Overall Risk of Bias										

Literacy/Reading (m/SD)

Moderate PAE and Reading Ability (1 study)

	Мо	derate PA	E	C	ontrol			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 1.34 (P = 0.18)			1561			1536	100.0%	0.05 [-0.02, 0.12]	-4 -2 0 2 Moderate PAE Control	<del> </del> 4
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% Cls.

## Heavy PAE and Reading Ability (1 study)

	H	eavy PAE		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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										10
Test for overall effect: Z = 1.02 (P = 0.31)									-10 -5 0 5 Heavy PAE Control	10
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.

#### Very Heavy PAE and Reading Ability (1 study)

		Heavy F			ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD.	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	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									-4 -2 0 2 4	
Test for overall effect: Z = 2.29 (P = 0.02)									Very Heavy PAE Control	
Risk of bias legend										

(A) Overall Risk of Bias

## Confirmed PAE Level Unquantifiable and Reading Ability (2 studies)

	Confirmed	I-Unquanti	fiable	C	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.13; Chi <sup>2</sup> = 4.70, df = 1 (P = Test for overall effect: Z = 1.53 (P = 0.13)	0.03); I² = 79	%						Confirm	-10 -5 0 5 led-Unquantifiable Control	10

Risk of bias legend (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		Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio Risk of Bias I IV, Random, 95% CI A
O'Callaghan et al. 2007 (WRAT-R reading; 14yrs)	-0.3567	0.4323	1561	1536	100.0%	0.70 [0.30, 1.63]	ıj — <mark>—</mark> — ?
Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.83 (P = 0.41)			1561	1536	100.0%	0.70 [0.30, 1.63]	0.1 0.2 0.5 1 2 5 10 Control Moderate PAE
<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% Cls.

## Heavy PAE and Low Reading Achievement (1 study)

			Heavy PAE	Control		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)							0.1 0.2 0.5 1 2 5 Control Heavy PAE	10
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% Cls.

# READING ACHIEVEMENT BELOW MINIMUM STANDARD (BASED ON WESTERN AUSTRALIAN MINIMUM STANDARDS)

#### Moderate PAE and Reading Achievement below Minimum Standard (1 study)

			Moderate PAE	Control		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 Testfor successity 7 = 0,40 (B = 0,62)								H 0
Test for overall effect: Z = 0.48 (P = 0.63)							Control Moderate PAE	

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)

			Heavy PAE C	ontrol		Odds Ratio	Odds Ratio	<b>Risk of Bias</b>
Study or Subgroup	log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)							0.1 0.2 0.0 1 2 0	10
Testion over all effect. $2 = 2.23$ (1 = 0.02)							Control Heavy PAE	

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)

		Heavy I			Control	<b>.</b>		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD.	Total	Mean	SD.	lotal	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	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]	-88-	•
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)									-4 -2 0 2 4	
									Very Heavy PAE Control	
Risk of bias legend										
(A) Overall Risk of Bias										

## Confirmed PAE Level Unquantifiable and Maths Ability (3 studies)

	Confirmed	I-Unquantif	fiable	0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.24; Chi <sup>2</sup> = 15.53, df = 2 (P = 0.0	)004); I <sup>2</sup> = 87	%								
Test for overall effect: Z = 2.51 (P = 0.01)								Confirm	-4 -2 U 2 4 ed-Unquantifiable Control	ł

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)

		Moderate PAE 0	ontrol		Odds Ratio	Odds Ratio	Risk of Bias
log[Odds Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
-0.3425	0.2215	27	135	100.0%	0.71 [0.46, 1.10]		•
		27	135	100.0%	0.71 [0.46, 1.10]	-	
						0.1 0.2 0.5 1 2 5 10 Control Moderate PAE	
	<u>.</u>		log[Odds Ratio]         SE         Total           -0.3425         0.2215         27	-0.3425 0.2215 27 135	log[Odds Ratio]         SE         Total         Total         Weight           -0.3425         0.2215         27         135         100.0%	log[Odds Ratio]         SE         Total         Total         Weight         IV, Random, 95% CI           -0.3425         0.2215         27         135         100.0%         0.71 [0.46, 1.10]	log[Odds Ratio]         SE         Total         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           -0.3425         0.2215         27         135         100.0%         0.71 [0.46, 1.10]         Image: Constraint of the second seco

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)

.3233				IV, Random, 95% CI	IV, Random, 95% Cl A	
.5255	13	135	100.0%	0.98 [0.52, 1.85]	•	
	13	135	100.0%	0.98 [0.52, 1.85]	0.1 0.2 0.5 1 2 5 10 Control Heavy PAE	
		13	13 135	13 135 100.0%	13 135 100.0% 0.98 [0.52, 1.85]	0.1 0.2 0.5 1 2 5 10

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)

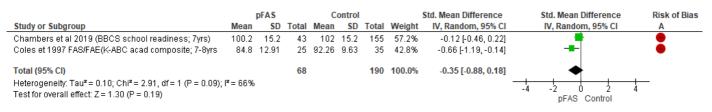
	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
1.1.1 Low-Moderate Risk of Bias										
Aragon et al 2008a (IPDA; 6-7yrs)	16.42	5.69	23	20.96	6.03	57	20.1%	-0.76 [-1.26, -0.26]		?
Kodituwakku et al 2006b (IPDA; 6-7yrs) Subtotal (95% CI)	16.9	3.41	22 <b>45</b>	21.25	5.6	60 117	19.6% <b>39.8%</b>	-0.84 [-1.35, -0.34] - <b>0.80 [-1.15, -0.44]</b>	•	?
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.05, df = 1 (P = 0 Test for overall effect: Z = 4.41 (P < 0.0001)	.82); I² =	:0%								
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) Subtotal (95% CI)	107	13.3	8 57	112.3	10.4	331 <b>775</b>	10.6% 60.2%	-0.51 [-1.21, 0.20] -0.39 [-0.67, -0.12]	•	•
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.11, df = 1 (P = 0 Test for overall effect: Z = 2.83 (P = 0.005)	.74); I²=	:0%								
Total (95% CI)			102			892	100.0%	-0.56 [-0.79, -0.32]	•	
Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 3.31, df = 3 (P = 0 Test for overall effect: Z = 4.67 (P < 0.00001) Test for subgroup differences: Chi <sup>2</sup> = 3.14, df = 1 (P			20%					-	-4 -2 0 2 FASD Control	<u>↓</u> 4

#### FAS and Academic Achievement (2 studies)

		FAS		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.22; Chi <sup>2</sup> = 2.89, df = 1 (P = 0.09)	); l² = 65	%								-
Test for overall effect: Z = 0.71 (P = 0.47)									FAS Control	

Risk of bias legend (A) Risk of Bias

### pFAS and Academic Achievement (2 study)



## Risk of bias legend

(A) Risk of Bias

#### Other FASDs and Academic Achievement (2 studies)

	AR	ND/Othe	er	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Tau² = 0.06; Chi² = 2.58, df = 1 (P = 0.11); Test for overall effect: Z = 0.17 (P = 0.86)	I² = 61%		103			190	100.0%	0.04 [-0.40, 0.47]	-4 -2 0 2 ARND/Other Control	<u> </u>

Risk of bias legend (A) Risk of Bias

## Reading Ability (m/SD)

## FASD and Reading Ability (4 studies/5 samples)

	F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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. Test for overall effect: Z = 8.79 (P < 0.00001)	.16); I <sup>z</sup> = 1	39%							-4 -2 0 2 4 FASD Control	1

Risk of bias legend

(A) Risk of Bias

### FAS and Reading Ability (1 study)

	F	AS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 2.17 (P = 0.03)			7			186	100.0%	-0.84 [-1.60, -0.08]	-4 -2 0 2 4 FAS Control	_

Risk of bias legend (A) Risk of Bias

#### pFAS and Reading Ability (2 studies)

		pFAS		C	Control			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.14; Chi <sup>2</sup> = 2.14, df = 1 (P = Test for overall effect: Z = 4.57 (P < 0.00001)	0.14); I <sup>z</sup>	= 53%							-4 -2 0 2 pFAS Control	4

Risk of bias legend (A) Risk of Bias

## Other FASDs and Reading Ability (1 study)

	ARN	D/Oth	er	C	ontrol	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	<b>◆</b>	
Heterogeneity: Not applicable Test for overall effect: Z = 2.95 (P = 0.003)									-4 -2 0 2 4 ARND/Other Control	

## Math Ability (m/SD)

## FASD and Maths Ability (4 studies/5 samples)

	1	FASD		C	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 4.43, df = 4 (P = $0.3$ Test for overall effect: Z = 14.90 (P < $0.00001$ )	5); I <b>²</b> = 10	%							-4 -2 0 2 FASD Control	<u>↓</u> 4

#### Risk of bias legend

(A) Risk of Bias

## FAS and Maths Ability (2 studies)

		FAS		(	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
Ben-Shachar 2020 (WIATnum operations, 16yrs)	57.5	16.5	8	74.1	18.4	23	45.3%	-0.90 [-1.74, -0.06]	-8-	•
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.21, df = 1 (P = 0	0.65); I <sup>2</sup> :	= 0%								
Test for overall effect: Z = 3.62 (P = 0.0003)									FAS Control	

Risk of bias legend (A) Risk of Bias

## pFAS and Maths Ability (3 studies)

		pFAS			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD.	Total	Mean	SD.	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	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]	_ <b>-</b>	•
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: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 12.17, df = 2 (P =	0.002);	l <sup>2</sup> = 849	6							
Test for overall effect: Z = 3.02 (P = 0.003)	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,								-4 -2 U 2 4 pFAS Control	

<u>Risk of bias legend</u> (A) Risk of Bias

## Other FASDs and Maths Ability (2 studies)

	ARM	D/Oth	er	С	ontrol			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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: Tau <sup>2</sup> = 1.76; Chi <sup>2</sup> = 12.10, df = 1 (P = 0.000 Test for overall effect: Z = 0.89 (P = 0.37)	5); I² = 9;	2%							-4 -2 0 2 4 ARND/Other Control	4

<u>Risk of bias legend</u> (A) Risk of Bias

	Adaptive beha	viour	
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	<del>N/A</del>	
Diagnosed Studies	Adaptive Composite – Caregiver: SIB-R, VABS, ABAS	mean/SD	<b>4 studies:</b> 4 FASD, 2 pFAS, 2 ARND/Others
	Adaptive Composite – Teacher: VABS, ABAS	mean/SD	<b>6 studies:</b> 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	<b>14 studies:</b> 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	<b>8 studies:</b> 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	<b>9 studies:</b> 8 FASD, 1 FAS, 2 pFAS, 2 ARND/Others

## Summary of available outcomes for **adaptive behaviour**

# GRADE ratings for adaptive behaviour

		Certainty	assessment			Nº of p	patients		Effect	Certainty
Nº of	Risk of	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative	Absolute	
studies	bias							(95% CI)	(95% CI)	
	RE STUDIE									
-	-	te – Caregiver: \	VABS, BSID							
Confirm	ed unquar		1							
4	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	336	485	-	SMD 0.84 lower (1.47 lower to 0.20 lower)	⊕○○○ Very low
Adaptiv	e: Socialisa	ation – Caregive	r: VABS				<u> </u>		· · ·	
Confirm	ed unquar	ntifiable								
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	218	327	-	<b>SMD 0.73 lower</b> (1.22 lower to 0.25 lower)	⊕○○○ Very low
Adaptiv	e: Daily Liv	ving Skills – Care	giver: VABS							
Confirm	ed unquar	ntifiable								
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	218	327	-	<b>SMD 0.88 lower</b> (1.50 lower to 0.26 lower)	⊕○○○ Very low
Adaptiv	e: Commu	nication – Careg	<b>siver</b> : VABS, BS	SID						
Confirm	ed unquar	ntifiable								
4	seriousª	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	360	487	-	<b>SMD 1.06 lower</b> (1.78 lower to 0.35 lower)	⊕○○○ Very low
DIAGNO	SED STUD	IES								
Adaptiv	e Composi	te – Caregiver: S	SIB-R, VABS, A	BAS						
FASD										
4	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	156	114	-	<b>SMD 2.12 lower</b> (2.70 lower to 1.55 lower)	⊕○○○ Very low
pFAS										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	66	73	-	<b>SMD 1.09 lower</b> (3.39 lower to 1.21 higher)	⊕○○○ Very low
ARND/C	Other									
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	58	73	-	SMD 2.43 lower (3.21 lower to 1.65 lower)	⊕⊕⊖⊖ Low
Adaptiv	e Composi	te – Teacher: V/	ABS, SIB-R, ABA	AS						
FAS										
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	7	186	-	<b>SMD 0.59 lower</b> (1.35 lower to 0.17 higher)	⊕○○○ Very low
pFAS										
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	19	186	-	<b>SMD 1.18 lower</b> (1.66 lower to 0.69 lower)	⊕⊕⊖⊖ Low
Adaptiv	e: Socialisa	ation – Caregive	r: VABS							
FASD										

11	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	502	880	-	SMD 1.25 lower (1.70 lower to 0.81 lower)	⊕○○○ Very low
FAS									lowery	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	SMD 0.18 higher (0.70 lower to 1.06 higher)	⊕⊕⊖⊖ Low
pFAS									• • • •	
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>d,e</sup>	none	109	830	-	SMD 0.64 lower (1.44 lower to 0.17 higher)	⊕○○○ Very low
ARND/0	Others									
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>d,e</sup>	none	144	831	-	<b>SMD 0.87 lower</b> (1.77 lower to 0.03 higher)	⊕○○○ Very low
Adaptiv	e: Socialisa	tion – Teacher:	VABS							
FASD										
3	serious <sup>a</sup>	not serious	not serious	not serious	none	116	1052	-	<b>SMD 0.58 lower</b> (0.78 lower to 0.39 lower)	⊕⊕⊕⊖ Moderate
FAS			-				-	-		
1	seriousª	not serious	not serious	very serious <sup>d,e,f</sup>	none	7	186	-	SMD 0.35 lower (1.11 lower to 0.40 higher)	⊕○○○ Very low
pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	19	186	-	<b>SMD 0.79 lower</b> (1.27 lower to 0.32 lower)	⊕⊕⊖⊖ Low
Adaptiv	e: Daily Liv	ing Skills – Care	giver: VABS						· · ·	
FASD										
8	serious <sup>a</sup>	serious <sup>b</sup>	not serious	not serious	none	323	811	-	<b>SMD 1.16 lower</b> (1.71 lower to 0.62 lower)	⊕⊕⊖⊖ Low
FAS				•						
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	SMD 0.59 higher (0.29 lower to 1.47 higher)	⊕⊕⊖⊖ Low
pFAS										
2	seriousª	not serious	not serious	not serious	none	85	815	-	<b>SMD 0.36 lower</b> (0.60 lower to 0.11 lower)	⊕⊕⊕〇 Moderate
ARND/0	Others									
2	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	120	815	-	SMD 0.22 lower (0.45 lower to 0.01 higher)	⊕⊕⊖⊖ Low
-	e: Daily Liv	ing Skills – Teac	cher: VABS							
FASD										
3	serious <sup>a</sup>	not serious	not serious	not serious	none	116	1052	-	SMD 0.43 lower (0.64 lower to 0.21 lower)	⊕⊕⊕⊖ Moderate
FAS	1		1	1	1	l		1	,	
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	7	186	-	SMD 0.50 lower (1.26 lower to 0.25 higher)	⊕○○○ Very low
			1	1				1	ייטייטייי/	

pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	19	186	-	<b>SMD 1.01 lower</b> (1.49 lower to 0.53 lower)	⊕⊕⊖⊖ Low
-	ve: Commu	nication – Care	<b>giver</b> : VABS							
FASD										
9	serious <sup>a</sup>	serious⁵	not serious	not serious	none	372	815	-	<b>SMD 1.58 lower</b> (2.15 lower to 1.02 lower)	⊕⊕⊖⊖ Low
FAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	SMD 0.35 higher (0.53 lower to 1.23 higher)	⊕⊕⊖⊖ Low
pFAS										
2	serious <sup>a</sup>	not serious	not serious	not serious	none	89	815	-	<b>SMD 4.69 lower</b> (7.98 lower to 1.40 lower)	⊕⊕⊕⊖ Moderate
ARND/	Other			-			-			
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	120	815	-	SMD 6.16 lower (10.84 lower to 1.48 lower)	⊕⊕⊖⊖ Low
Adapti	ve: Commu	nication – Teacl	ner: VABS							
FASD										
3	serious <sup>a</sup>	not serious	not serious	not serious	none	116	1052	-	<b>SMD 0.49 lower</b> (0.69 lower to 0.30 lower)	⊕⊕⊕⊖ Moderate
FAS	•			•				•	·	
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	7	186	-	<b>SMD 0.70 lower</b> (1.46 lower to 0.06 higher)	⊕○○○ Very low
pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	19	186	-	<b>SMD 1.28 lower</b> (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<sup>2</sup> >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 Le	vel Un	quant	ifiab	le an	d Ac	lapt	ive Co	omposite - Ca	<b>aregiver</b> (4 studies)	
	Confirme	d Unquanti	fiable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.38; Chi <sup>2</sup> = 44.98, df = 3 (F Test for overall effect: $Z = 2.58$ (P = 0.010)	P < 0.00001);	; I² = 93%							-4 -2 0 2	4
reactor overall enect. 2 = 2.36 (F = 0.010)								Confirm	ed Unquantifiable Control	
								Confirm	ied Unquantifiable Control	

Risk of bias legend (A) Overall risk of bias

### Adaptive Socialisation – Caregiver: VABS

#### Confirmed PAE Level Unquantifiable and Adaptive Socialisation – Caregiver (3 studies) Confirmed Unquantifiable Control Std. Mean Difference Std. Mean Difference **Risk of Bias** Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI 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: Tau<sup>2</sup> = 0.13; Chi<sup>2</sup> = 7.55, df = 2 (P = 0.02); l<sup>2</sup> = 74% -5 4 Ó Test for overall effect: Z = 2.96 (P = 0.003) Confirmed Unquantifiable Control

Risk of bias legend (A) Overall risk of bias

(A) Overall risk of bia

## Adaptive Daily Living - Caregiver: VABS

## Confirmed PAE Level Unquantifiable and Adaptive Daily Living – Caregiver (3 studies)

	Confirmed	l Unquantif	fiable	0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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: Tau <sup>2</sup> = 0.24; Chi <sup>2</sup> = 11.57, df = 2 (F Test for overall effect: $Z = 2.79$ (P = 0.005)	? = 0.003); I <sup>2</sup> :	= 83%							4 -2 0 2	4

Risk of bias legend (A) Overall risk of bias

#### Adaptive: Communication – Caregiver: VABS

#### Confirmed PAE Level Unquantifiable and Adaptive Communication – Caregiver (4 studies) Confirmed Unquantifiable Std. Mean Difference Std. Mean Difference Control Risk of Bias Mean Study or Subgroup SD Mean IV, Random, 95% CI IV, Random, 95% CI Total SD Total Weight Crocker et al 2009 (6-13yrs; VABS) 77.23 22.89 103.25 11.73 22 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 10.69 102.4 16.39 160 26.5% -1.84 [-2.11, -1.57] 142 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] 487 100.0% -1.06 [-1.78, -0.35] 360

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Confirmed Unquantifiable

Total (95% Cl) Heterogeneity: Tau<sup>2</sup> = 0.48; Chi<sup>2</sup> = 51.28, df = 3 (P < 0.00001); I<sup>2</sup> = 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

	FA	SD ar	nd Ac	laptiv	e Cor	npos	site – (	<b>Caregiver</b> (4 stud	dies)		
		FASD		C	ontrol			Std. Mean Difference	Std. Me	an Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Ran	dom, 95% Cl	Α
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: Tau <sup>2</sup> = 0.24; Chi <sup>2</sup> = 9.93,	df = 3 (P	= 0.02)	; I² = 70	)%					-4 -2		
Test for overall effect: Z = 7.21 (P ≤ 0.00	001)								FAS	DControl	4

Risk of bias legend (A) Overall ROB Rating



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] 73 100.0% -1.09 [-3.39, 1.21] Total (95% CI) 66 Heterogeneity: Tau<sup>2</sup> = 2.64; Chi<sup>2</sup> = 23.52, df = 1 (P < 0.00001); l<sup>2</sup> = 96% -4 . b ń Ż 4 Test for overall effect: Z = 0.93 (P = 0.35) Control pFAS

#### Risk of bias legend (A) Overall ROB Rating

Study or Subgroup

## ARND/Others and Adaptive Composite – Caregiver (2 studies)

	ARN	D/Othe	rs	C	ontrol	•		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	<b></b>	•
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: Tau <sup>2</sup> = 0.19; Chi <sup>2</sup> = 2.26, df = 1 (P = 0.	13); I² =	56%							-4 -2 0 2	4
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 a	and	Adaj	otive	Com	posi	te – Te	eacher (1 study	)		
		FAS		0	Control			Std. Mean Difference	S	td. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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]	L	-	
Heterogeneity: Not applicable Test for overall effect: Z = 1.53 (P = 0.13)									-4 -	2 0 2 FAS Control	4

Risk of bias legend (A) Overall ROB Rating

## pFAS and Adaptive Composite - Teacher (1 study)

	P								,,		
		pFAS		0	Control			Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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									-4	-2 0 2	4
Test for overall effect: Z = 4.75 (P < 0.00001)										pFAS Control	

Risk of bias legend (A) Overall ROB Rating

## Adaptive Socialisation - Caregiver: VABS

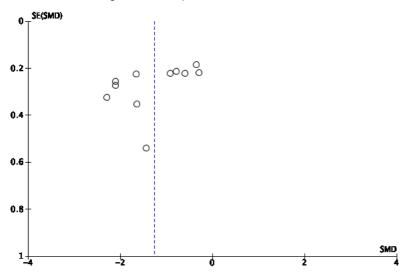
### FASD and Adaptive Socialisation - Caregiver (11 studies)

		FASD		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	- <b>-</b> -	?
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]	- <b>-</b>	•
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]	- <b>-</b> -	•
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]	<b>_</b>	•
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]	- <b>-</b> -	•
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: Tau <sup>2</sup> = 0.49; Chi <sup>2</sup> = 88.60,		° < 0.00	001); I²	= 89%					-4 -2 0 2	4
Test for overall effect: Z = 5.53 (P < 0.000)	01)								FASD Control	•

Risk of bias legend (A) Overall ROB Rating Risk of Bias

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Funnel Plot: FASD diagnosis and Adaptive Socialisation



## FAS and Adaptive Socialisation – Caregiver (1 study)

	F	AS		Co	ntro	1		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
Chambers et al 2019 (6-7yrs; VABS)	102.4	17	5	100.4	11	761	100.0%	0.18 [-0.70, 1.06]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.40 (P = 0.6§	3)		5			761	100.0%	0.18 [-0.70, 1.06]	-4 -2 0 2 FAS Control	4

Risk of bias legend (A) Overall ROB Rating

## pFAS and Adaptive Socialisation - Caregiver (3 studies)

		pFAS		С	ontrol			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.44; Chi <sup>2</sup> = 19.09, df = 2 (F	° < 0.000	01); I <b>2</b> =	90%							-
Test for overall effect: Z = 1.54 (P = 0.12)									pFAS Control	4

Risk of bias legend (A) Overall ROB Rating

## ARND/Others and Adaptive Socialisation - Caregiver (3 studies)

Study or Subgroup	ARND Mean	)/Other SD	s Total	Co Mean	ontrol SD	Total	Weight	Std. Mean Difference IV, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl	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: Tau <sup>2</sup> = 0.56; Chi <sup>2</sup> = 26.78, df = : Test for overall effect: Z = 1.89 (P = 0.06)	2 (P < 0.00	)001); P	²= 93%						-4 -2 0 2 ARND/Others Control	4

Risk of bias legend (A) Overall ROB Rating

### Adaptive: Socialisation – Teacher: VABS, ABAS **FASD and Adaptive Socialisation – Teacher (3** studies)

	F	ASD	and	Adap	tive	Socia	lisatio	<b>n – Teacher</b> (3 stu	dies)	
	F	ASD		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> =	0.31, df:	= 2 (P	= 0.86)	; I² = 0%	,			H		
Test for overall effect: Z = 5.90 (P <	0.00001	1)							FASD Control	4

Risk of bias legend (A) Overall ROB Rating

		FAC			Control			Ctd. Maan Difference	Ctd Maan Difference	Dials of Diag
Study or Subgroup	Mean	FAS	Total	Mear	Control	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% Cl	Risk of Bias A
May et al 2015 (6-7yrs; VABS - Classroom Ed.)	99.1		7		5 15.4		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)									-4 -2 0 2	4
									FAS Control	
Risk of bias legend										
(A) Overall ROB Rating										
p	FAS a	nd /	Adar	otive	Socia	alisat	tion –	Teacher (1 stu	dy)	
•		pFAS	•		Control			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean			I Mea			Weight			A
May et al 2015 (6-7yrs; VABS - Classroom Ed.)	92.3	14.43	19	3 104.	5 15.4	186	100.0%	-0.79 [-1.27, -0.32]		•
Total (95% CI)			19	9		186	100.0%	-0.79 [-1.27, -0.32]	•	
Heterogeneity: Not applicable									-4 -2 0 2	4
Test for overall effect: Z = 3.25 (P = 0.001)									pFAS Control	-
Risk of bias legend										
(A) Overall ROB Rating										
	Ada	otiv	e: D	ailv I	living	z Skil	lls – C	aregiver: VAB	5	
EA						-		-		
F <i>P</i>	FASD an		dap		Dally ntrol	LIVII	•	aregiver (8 stuc itd. Mean Difference	•	Dick of Dice
Study or Subgroup Mea		D Tot	al N	/lean		Total N	a Weight	IV, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl	Risk of Bias A
Kerns et al 2016 (8-14yrs; VABS-II) 81				06.3	15.4		11.7%	-1.67 [-2.37, -0.98]		?
Crawford et al 2020 (8-12yrs; VABS-II) 77.3	83 8.	3 3		2.66		29	11.8%	-2.68 [-3.36, -2.00]		•
Fagerlund et al 2012 (8-20yrs; VABS) 73.1				99.9			13.3%	-1.49 [-1.93, -1.06]		
May et al 2020a (6-7yrs; VABS-II) 104 May et al 2020b (6-7yrs; VABS-II) 99			351 24	08.5 106	14.4 16.9		13.6% 13.3%	-0.28 [-0.65, 0.08] -0.38 [-0.81, 0.05]		
May et al 2020c (6-7yrs; VABS) 99				03.5	11.5		13.6%	-0.32 [-0.69, 0.04]		ĕ
May et al 2021 (6-7yrs; VABS-II) 83	.5 15	5	4 1	06.3	14.8	50	9.4%	-1.51 [-2.57, -0.45]		•
Quattlebaum et al 2013 (6-12yrs; VABS) 62.	47 16.5	1 !	97 8	4.54	16.43	28	13.2%	-1.33 [-1.78, -0.88]		•
Total (95% CI)		3	23			811	100.0%	-1.16 [-1.71, -0.62]	•	
Heterogeneity: Tau <sup>2</sup> = 0.54; Chi <sup>2</sup> = 69.09, df = 7	(P < 0.0			9%					-4 -2 0 2	
Test for overall effect: Z = 4.17 (P < 0.0001)									FASD Control	4
Dick of bice legend										
Risk of bias legend (A) Overall ROB Rating										
	AS a	nd A	dap	tive	Dailv	Livir	ng – Ca	aregiver (1 stud	lv)	
-	FAS			Contr	-		-	Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup Mean	n SD	Total	Mea	n S	D Tota	I Wei	ight I\	/, Random, 95% Cl	IV, Random, 95% Cl	Α
Chambers et al 2019 (6-7yrs; VABS) 107	7 13.6	5	100.	.7 10.	6 761	100	.0%	0.59 [-0.29, 1.47]		•
Total (95% CI)		5			761	I 100	0%	0.59 [-0.29, 1.47]		
Heterogeneity: Not applicable		5			701	1 100	.070	0.59 [-0.29, 1.47]		_
Test for overall effect: Z = 1.32 (P = 0.19)								-4		4
									FAS Control	
Risk of bias legend										
(A) Overall ROB Rating										
pF			dap		•	Livir	ng – Ca	aregiver (2 stud		
Study or Subgroup		AS	Tot-I		Control	Tetel	Maint	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup Chambers et al 2019 (6-7yrs; VABS)	Mean 95.9	50 10.5	Total 44	Mear 100.7			Weight 62.6%			A
	103.2 1				12.94			• • •		ĕ
T / 1/05/ 01									•	
Total (95% CI) Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.02, df = 1 (P	- 0.241	<b>12</b> – 200	89			815	100.0%	-0.36 [-0.60, -0.11]	▼	
Test for overall effect: $Z = 2.85$ (P = 0.004)	= 0.31),	17 = 2%	)						-4 -2 0 2	4
,									pFAS Control	
Risk of bias legend										
(A) Overall ROB Rating										
ARND	/Othe	rs a	nd A	dap	tive D	Daily	Living	<b>– Caregiver</b> (2	studies)	
-	ARND/			•	Control	-		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean		, Total	Mear		Total	Weight			A
Chambers et al 2019 (6-7yrs; VABS; ARND)	97.8	11.3	44	100.3	7 10.6	i 761	56.9%	-0.27 [-0.58, 0.03]		
Howell et al 2006 (15yrs; VABS; HE) 1	03.62 1	6.19	76	105.74	4 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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.31, df = 1 (P	= 0.58);	I <b>²</b> = 0%								i
Test for overall effect: Z = 1.84 (P = 0.07)									ARND/Others Control	7
Risk of bias legend										

FAS and Adaptive Socialisation – Teacher (1 study)

<u>Risk of bias legend</u> (A) Overall ROB Rating

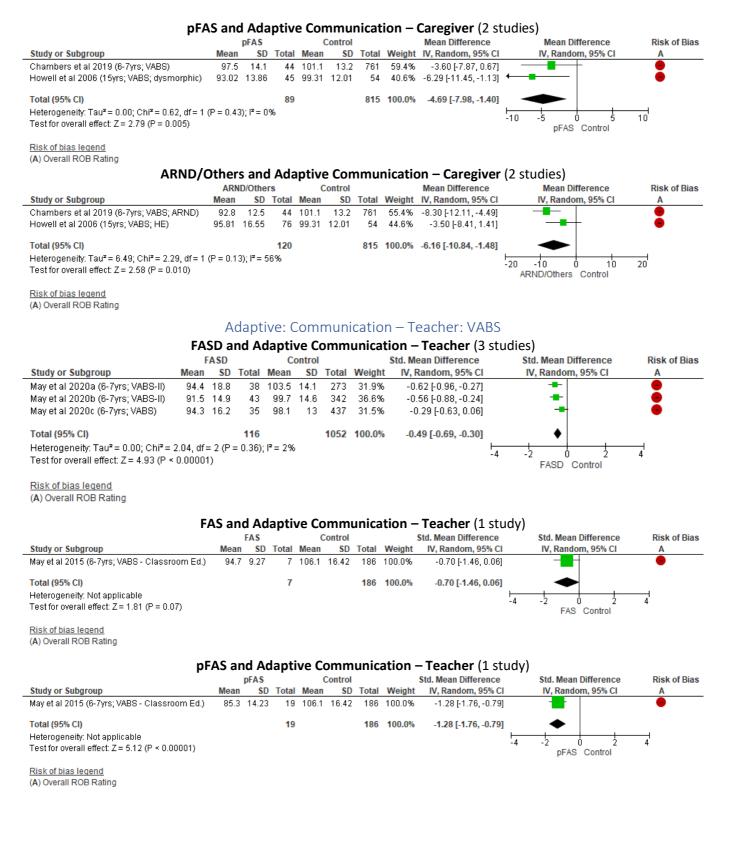
	-						-					
			and		ptive Control		Y LIVI	•	eacher (3 stue ean Difference		Maan Difference	Diak of Dia
Study or Subgroup	Mean		Total	Mean			Weigh		Random, 95% Cl		Mean Difference Random, 95% Cl	Risk of Bia A
May et al 2020a (6-7yrs; VABS-II)	95.2			104.9		273	32.29		.56 [-0.91, -0.22]	,	- <b>-</b> -	-
May et al 2020b (6-7yrs; VABS-II)		14.8		100.3		342	36.09		.51 [-0.83, -0.19]		-	ĕ
May et al 2020c (6-7yrs; VABS)	96.6		35		13.2	437	31.89		).20 [-0.55, 0.14]			ĕ
T-4-1/054/ CD			440			4050	400.00		421004 0241			
Total (95% CI)	40 df-	- 2 /D -	116	17 - 20	07	1052	100.09	∕o -U.	43 [-0.64, -0.21]		•	
Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2. Test for overall effect: Z = 3.90 (P ≤ 0		: 2 (P =	0.29),	F= 20	170				-	4 -2	0 2 FASD Control	4
Risk of bias legend												
(A) Overall ROB Rating			_									
		FAS		Ada	ptive		-	ng – T	eacher (1 stu			
Study of Subgroup		Meen	FAS		Maa	Contro		Moight	Std. Mean Difference		Std. Mean Difference	Risk of Bia
Study or Subgroup May et al 2015 (6-7yrs; VABS - Classroo	m Ed \	Mean	11.7	D Tota		n <u>st</u> 6 16.39		Weight 100.0%	IV, Random, 95% -0.50 [-1.26, 0.2		IV, Random, 95% CI	A
imay et al 2015 (6-7 yrs, VABS - Classrou	m Eu.)	99.4	• • • • •	9	/ 10/.	0 10.3	9 180	100.0%	-0.50 [-1.26, 0.2	20]		•
Total (95% CI)				1	7		186	100.0%	-0.50 [-1.26, 0.2	25]	. 🔶	
Heterogeneity: Not applicable Test for overall effect: Z = 1.30 (P = 0.19)										-4	-2 0 2	4
Testion overall ellect. Z = 1.50 (F = 0.13)											FAS Control	
Risk of bias legend												
(A) Overall ROB Rating												
		pFAS	6 and	d Ada	ptiv	e Dai	ly Liv	ing – 1	T <b>eacher</b> (1 stu			
			pFAS			Contro			Std. Mean Difference		Std. Mean Difference	Risk of Bia
Study or Subgroup		Mean	1 S 3 18.2		Mea	n <u>SL</u> 6 16.39		Weight 100.0%	IV, Random, 95%		IV, Random, 95% Cl	A
May et al 2015 (6-7yrs; VABS - Classroo	III Eu.)	90.c	) 10.2	5 13	9 107.	0 10.3	9 100	100.0%	-1.01 [-1.49, -0.5	101	-	•
Total (95% CI)				19	9		186	100.0%	-1.01 [-1.49, -0.5	[3]	•	
Heterogeneity: Not applicable Test for successful affects Z = 4.44 (B = 9.00)	043									-4	-2 0 2	4
Test for overall effect: Z = 4.11 (P < 0.000	)))										pFAS Control	
Risk of bias legend												
(A) Overall ROB Rating												
		Ad	apti	ve: C	Comr	nuni	catio	n – Ca	regiver: VAE	3S		
	FAS								Caregiver (9			
		FAS				ntrol			d. Mean Difference		td. Mean Difference	Risk of Bia
Study or Subgroup	Me	ean	SD T	otal I	Mean	SD	Total V	Veight	IV, Random, 95% C	I I	V, Random, 95% Cl	Α
Kerns et al 2016 (8-14yrs; VABS-II)			6.8		108.9	13.7	22	9.7%	-2.94 [-3.82, -2.07	-		2
Crawford et al 2020 (8-12yrs; VABS-II)			5.2		98.76			10.7%	-2.70 [-3.39, -2.02	-		
Fagerlund et al 2012 (8-20yrs; VABS)		.89 21			107.1			11.8%	-1.73 [-2.18, -1.28			
May et al 2020a (6-7yrs; VABS-II)	-		17		113.8	25.6		12.1%	-0.57 [-0.93, -0.21	-		
May et al 2020b (6-7yrs; VABS-II) May at al 2020a (6 7yrs; VABS-II)			16 4.1		105.1 106.2	17.5		11.8%	-0.82 [-1.26, -0.38	-		
May et al 2020c (6-7yrs; VABS) May et al 2021 (6-7yrs; VABS-II)			4.1 7.7		106.2	12.7 16.1	292 50	12.0% 8.9%	-0.64 [-1.01, -0.27 -1.14 [-2.18, -0.10	-		<b>X</b>
Quattlebaum et al 2013 (6-12yrs; VABS-II)		5.5 4.8 15		4 97		14.82		6.9% 11.7%	-1.36 [-1.81, -0.91	-	_ <b>_</b>	, i i i i i i i i i i i i i i i i i i i
Rockhold et al 2021 (11-12yrs; VABS)		4.8 10 .41 11			95.5 05.91	9.68		11.3%	-2.68 [-3.24, -2.12	-		ĕ
				373			054 4	00.0*/	4 60 5 3 46 4 03	1 .		
Total (95% CI) Hotorogeneity: TouZ = 0.66: ChiZ = 90.1	1 df - 1	) /D - 0		372 \\ Z0	10/		851 1	00.0%	-1.58 [-2.15, -1.02	·		
Heterogeneity: Tau <sup>2</sup> = 0.66; Chi <sup>2</sup> = 89.1 Test for overall effect: $Z = 5.48$ (P < 0.00		s (⊢ < U.	00001	), in = 91	170					-4 -	2 0 2	4
FOR THE OVERALL ENERGY Z = 3.40 (P ≤ 0.0)	,501)										FASD Control	

Risk of bias legend (A) Overall ROB Rating

FAS and Adaptive Communication – Caregiver (1 study)

		4114	/	P			neatio		Judy			
		FAS		C	ontrol			Std. Mean Difference	Std. Mean Dif	ference	Risk of Bias	
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random,	95% CI	Α	
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]		<u> </u>	•	
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)	)								-4 -2 0 FAS C	2 ontrol	4	

Risk of bias legend (A) Overall ROB Rating



## Summary of available outcomes for **behaviour** (i.e., externalising, internalising)

	Behav	iour	
Study type	Outcomes	Data	# studies
Exposure Studies	Total Behaviour – Caregiver Report: CBCL	T-score	<b>5 studies:</b> 4 confirmed unquantifiable, 1 Any PAE
	Total Behaviour – Caregiver Report: CBCL	Frequency/OR	<b>4 studies:</b> 1 light, 3 moderate and 1 heavy
	Total Behaviour – Caregiver Report: SDQ	mean difference	<b>1 study:</b> 1 light
	Total Behaviour – Teacher Report: SDQ	Frequency/OR	1 study: 1 moderate
	Total Behaviour – Self Report: SDQ	Frequency/OR	<b>1 study:</b> 1 confirmed unquantifiable
	Total Externalising Behaviour – Caregiver	T-score	4 studies: 1 very heavy, 1 Any PAE and
	Report: CBCL		2 confirmed unquantifiable
	Total Externalising Behaviour – Caregiver Report: CBCL	Frequency/OR	<b>2 studies:</b> 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	<b>4 studies:</b> 1 very heavy, 1 Any PAE and 2 confirmed unquantifiable
	Total Internalising Behaviour – Caregiver Report: CBCL	Frequency/OR	<b>2 studies:</b> 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	<b>2 studies:</b> 1 light, 1 confirmed unquantifiable
	Ext: Conduct Problems – Caregiver Report: CBCL, SDQ	Frequency/OR	<b>1 studies:</b> 1 light
	Ext: Conduct Problems – Self Report: SDQ	Frequency/OR	<b>1 studies:</b> 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	<b>4 studies:</b> 1 very heavy, 1 Any PAE and 2 confirmed unquantifiable
	Ext: Aggression – Caregiver Report: CBCL	Frequency/OR	<b>2 studies:</b> 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	<b>3 studies:</b> 2 confirmed unquantifiable, 1 any PAE
	Ext: Rule-Breaking Behaviour – Caregiver Report: CBCL	Frequency/OR	<b>2 studies:</b> 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:	T-score	<b>1 study:</b> 1 very heavy
	CBCL		
	Ext: Hyperactivity – Caregiver Report: SDQ	mean/SD (MD)	1 study: 1 light
	Ext: Hyperactivity – Caregiver Report: SDQ	OR/Frequency	<b>3 studies:</b> 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	<b>1 study:</b> 1 light
	Ext: Attention/	N/A	
	Hyperactivity – Caregiver Report	-	
	Int: Anxious/ Depressed – Caregiver Report: CBCL	T-score	<b>3 studies:</b> 1 Any PAE, 2 confirmed unquantifiable
	Int: Anxious/ Depressed – Caregiver	OR/Frequency	<b>1 study:</b> 1 moderate
	Report: CBCL		
	Int: Anxious/ Depressed – Teacher Report	N/A	
	Int: Anxious/Depressed – Self-report: SDQ	OR/Frequency	<b>1 study:</b> 1 confirmed unquantifiable
	Int: Anxious/ Depressed – Self Report: CBCL	T-score	<b>1 study:</b> 1 light, 1 moderate
	Int: Anxiety – Caregiver Report: CBCL	T-score	1 study: 1 very heavy
	Int: Anxiety – Caregiver Report: CBCL	OR/Frequency	<b>1 study:</b> 1 light, 1 heavy
	Int: Anxiety – Teacher Report	N/A	
	Int: Withdrawn/ Depressed – Caregiver Report: CBCL	T-score	<b>3 studies:</b> 1 Any PAE and 2 confirmed/unquantifiable
	Int: Withdrawn/ Depressed – Caregiver Report: CBCL	OR/Frequency	<b>2 studies:</b> 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	<b>3 studies:</b> 1 Any PAE and 2 confirmed/unquantifiable
	Int: Somatic Complaints – Caregiver Report: CBCL	OR/Frequency	<b>2 studies:</b> 1 light, 1 moderate, 1 heavy
	Int: Somatic Complaints – Self Report	N/A	
	Int: Thought Problems – Caregiver Report: CBCL	T-score	<b>3 studies:</b> 1 Any PAE and 2 confirmed unquantifiable
	Int: Thought Problems – Caregiver Report: CBCL	OR/Frequency	<b>1 study:</b> 1 light, 1 heavy
	Int: Thought Problems – Self Report	N/A	
	Int: Affective Problems – Caregiver	N/A	
	Report 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	Total Behaviour – Caregiver Report: CBCL	Frequency/OR	1 study: 1 FASD
Studies	<b>Total Behaviour – Caregiver Report</b> : CBCL, PBCL-36	T-score	12 studies: 9 FASD, 3 FAS, 2 pFAS
	<b>Total Behaviour – Teacher Report</b> : TRF, PBCL-36	T-score	<b>4 studies:</b> 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	<b>1 study</b> : 1 pFAS, 1 ARND/Others

Total Externalising Behaviour – Caregiver Report: CBCL	T-score	<b>12 studies:</b> 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	<b>6 studies:</b> 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	<b>1 study:</b> 1 pFAS, 1 ARND/Others
Total Internalising Behaviour – Caregiver Report: CBCL	T-score	<b>13 studies:</b> 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	<b>6 studies:</b> 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	<b>1 study:</b> 1 pFAS, 1 ARND/Others
Ext: Conduct Problems – Caregiver Report: CBCL	T-score	<b>5 studies:</b> 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others
Ext: Conduct Problems – Teacher Report: TRF	T-score	<b>5 studies:</b> 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others
Ext: Oppositional Defiant – Caregiver Report: CBCL	T-score	<b>5 studies:</b> 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	<b>5 studies:</b> 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others
Ext: Aggression – Caregiver Report: CBCL	T-score	<b>6 studies:</b> 5 FASD, 1 FAS, 1 pFAS, 1 ARND/Others
Ext: Aggression – Teacher Report: TRF/CBCL	T-score	<b>5 studies:</b> 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others
Ext: Aggression – Self Report: ASR	T-score	<b>1 study:</b> 1 pFAS, 1 ARND/Others
Ext: Rule-Breaking Behaviour – Caregiver Report: CBCL	T-score	<b>7 studies:</b> 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	<b>4 studies:</b> 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
<b>Ext: Hyperactivity – Caregiver Report</b> : 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	<b>5 studies:</b> 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others

Ext: Attention/ Hyperactivity – Teacher	T-score	<b>4 study:</b> 3 FASD, 1 FAS, 1 pFAS, 1
Report: CBCL/TRF		ARND/Others
Int: Anxious/ Depressed – Caregiver Report: CBCL, CBRS	T-score	<b>8 studies:</b> 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	<b>4 studies:</b> 3 FASD, 1 FAS, 1 pFAS, 1 ARND/Others
Int: Anxious/ Depressed – Self Report: CBCL	T-score	<b>1 study:</b> 1 pFAS, 1 ARND/Others
Int: Anxiety – Caregiver Report: CBCL	T-score	<b>6 studies</b> : 5 FASD, 1 FAS, 1 pFAS, 1 ARND/Others
Int: Anxiety – Teacher Report: TRF	T-score	<b>4 studies:</b> 3 FASD, 1 FAS, 1 pFAS, 1 ARND/Others
Int: Withdrawn/ Depressed – Caregiver Report: CBCL	T-score	<b>7 studies:</b> 6 FASD, 1 FAS, 1 pFAS, 1 ARND/Others
Int: Withdrawn/ Depressed – Teacher Report: TRF	T-score	<b>4 studies:</b> 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	<b>5 studies:</b> 4 FASD, 1 FAS, 1 pFAS, 1 ARND/Others
 Int: Affective Problems – Teacher Report: TRF	T-score	<b>4 studies:</b> 3 FASD, 1 FAS, 1 pFAS, 1 ARND/Others

# GRADE ratings for behaviour

		Certainty	assessment			Nº of	patients		Effect	Certainty
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% CI)	Absolute (95% Cl)	
	IRE STUDIES							(55/6 CI)		
CBCL To	tal Behaviou	ur Caregiver Rep	oort (T-score)							
Any PAE	E									
1	seriousª	not serious	not serious	not serious	none	2518	7201	-	SMD 0.20 higher (0.15 higher to 0.24 higher)	⊕⊕⊕⊖ Moderate
Confirm	ied unquant	ifiable								
4	seriousª	serious⁵	not serious	serious <sup>e,f</sup>	none	348	393	-	SMD 2.29 higher (1.40 higher to 3.18 higher)	⊕○○○ Very Low
0 studie	s for light, m	noderate, heavy	or very heavy	/						
CBCL/SE	DQ Total Beh	aviour Caregive	er Report (Fre	quency/OR) ((	Odds of sco	oring in 'o	linical rar	ige'/'abnorr	nal' scores/score >6	50 of CBCL)
Light										
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	208	690	<b>OR 1.17</b> (0.74 to 1.85)	-	⊕⊕⊕⊖ Moderate
Modera	ite									
3	not serious	not serious	not serious	serious <sup>f</sup>	none	688	1,060	<b>OR 1.69</b> (1.17 to 2.43)	-	⊕⊕⊕⊖ Moderate
Heavy										
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	57	690	<b>OR 1.62</b> (0.85 to 3.11)	-	⊕⊕⊕⊖ Moderate
0 studie	s for any, co	nfirmed unqua	ntifiable or ve	ry heavy						
SDQ Tot	tal Behaviou	r Caregiver Rep	ort (adjusted	Mean Differer	nce)					
Light										
1	not serious	not serious	not serious	serious <sup>d</sup>	none	1963	5547		aMD 0.04 higher (0.33 lower to 0.42 higher)	⊕⊕⊕⊖ Moderate
SDQ Tot	tal Behaviou	r Teacher Repo	rt (Frequency,	/OR) (Odds of	'Abnormal	/Borderl	ine' score	)		
Modera	ite									
1	not serious		not serious	very serious <sup>d,e,f</sup>	none	195	758	<b>aOR 1.1</b> (0.6 to 2.1)		⊕⊕⊖⊖ Low
		r Self Report (a	djusted Frequ	ency/OR) (Cut	-offs unclea	ar)				
	ed unquant			· _ 1	<b></b>				,	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	57	690	<b>aOR 1.25</b> (0.99 to 1.58		⊕⊕⊖⊖ Low
0 studie	s for any, lig	ht, moderate, h	eavy or very l	neavy						
CBCL Ex	ternalising B	ehaviour Careg	iver Report (T	-score)						
Very he	avy									
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	20	19	-	SMD 1.35 higher (0.65 higher to 2.05 higher)	⊕⊕⊖⊖ Low
Any PAE	E					<u>.</u>				
1	serious <sup>a</sup>	not serious	not serious	not serious	none	2518	7201	-	SMD 0.16 higher	⊕⊕⊕⊖ Moderate

									(0.11 higher to	
									0.20 higher)	
Confirn	ned unquant	ifiable	•							
2	seriousª	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	160	168	-	SMD 1.78 higher (0.52 higher to 3.03 higher)	⊕○○○ Very low
0 studie	es for light, m	oderate or hea	ivy	11					0.000	
CBCL To	otal Externalis	sing Behaviour	Caregiver Rep	ort (Frequenc	y/OR) (Od	ds of scor	ring in 'cli	inical range	'/'abnormal' scores)	
Light										
1	not	not serious	not serious	serious <sup>d</sup>	none	208	690	OR 1.10		$\oplus \oplus \oplus \bigcirc$
	serious							(0.73 to 1.66)		Moderate
Modera	ate			11		1 1		2.007	11	
1	seriousª	not serious	not serious	serious <sup>d</sup>	none	389	117	OR 1.79 (1.00 to 3.20)		⊕⊕⊖⊖ Low
Heavy										
1	not serious	not serious	not serious	serious <sup>d</sup>	none	57	690	OR 1.00 (0.53 to 1.89)		⊕⊕⊕⊖ Moderate
0 studie	es for any cor	nfirmed unquar	ntifiable or ver	y heavy						
CBCL To	otal Externalis	sing Behaviour	Caregiver Rep	ort – IBQ (me	an/SD)					
Modera	ate									
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	39	54	-	SMD 0.37 higher (0.04 lower to 0.79 higher)	⊕○○C Very low
0 studie	es for light, he	eavy, very heav	'Y							
CBCL To	otal Internalis	ing Behaviour	Caregiver Rep	ort (T-score)						
Very he	eavy									
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	20	19	-	SMD 0.71 higher (0.06 higher to 1.36 higher)	⊕⊕⊖⊖ Low
Any PA	E									
1	seriousª	not serious	not serious	not serious	none	2518	7201	-	SMD 0.14 higher (0.10 higher to 0.19 higher)	⊕⊕⊕⊖ Moderate
Confirn	ned unquant	ifiable								
2	seriousª	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	160	168	-	SMD 1.01 (0.08 lower to 2.11 higher)	⊕○○C Very low
0 studie	es for light, m	oderate & hea	vy	1		<u> </u>		-	,	
CBCL To	otal Internalis	ing Behaviour	Caregiver Rep	ort (Frequenc	y/OR) (Odd	ls of scor	ing in 'cli	nical range'	/'abnormal' scores)	
Light										
1	not serious	not serious	not serious	serious <sup>d</sup>	none	208	690	<b>OR 1.14</b> (0.67 to 1.94)	1 fewer per 1,000 (from 2 fewer to 1 fewer)	⊕⊕⊕⊖ Moderate
Modera	ate					<u> </u>		<u> </u>	· ·	
1	serious <sup>a</sup>	not serious	not serious	Serious <sup>d,e</sup>	none	389	117	<b>OR 1.67</b> (0.90 to	2 fewer per 1,000 (from 3 fewer to 1	⊕⊕⊖⊖ Low
						1 1		3.10)	fewer)	

1				0		<b>F7</b>	600	00 2 64	2 6	-
	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	57	690	<b>OR 2.64</b> (1.36 to	<b>3 fewer per 1,000</b> (from 5 fewer to 1	⊕⊕⊖⊖ Low
								5.14)	fewer)	2011
CBCL/SE	DQ Conduct F	Problems Careg	giver Report (n	nean diff/T-sc	ore)			- /	,	
ight										
1	not serious	not serious	not serious	serious <sup>d</sup>	none	1967	5547	-	aMD 0.04 higher	$\oplus \oplus \oplus \bigcirc$
									(0.07 lower to	Moderate
									0.15 higher)	
Confirm	ned unquant	ifiable								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e, f</sup>	none	61	55	-	SMD 0.88 higher	$\oplus \oplus \bigcirc \bigcirc$
									(0.50 higher to	Low
0 studio	for any mo	oderate, heavy							1.27 higher)	
	-	-								
		ems Caregiver I	Report (Freque	ency/OR) (Cut		ear)				
Light	. I	_	<u> </u>			1 1			1	
1	not serious	not serious	not serious	serious <sup>d</sup>	none	150	348	<b>OR 1.20</b> (0.95 to		⊕⊕⊕⊖ Moderate
								1.52)		Wouerate
SDQ Co	nduct Proble	ms Self Report	(adjusted Free	quency/OR) ((	Cut-offs no	t clear)		1.52)		
	ned unguant	•		,						
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	850	5299	aOR 1.24		$\oplus \oplus \bigcirc \bigcirc$
-	serious	not serious	not serious	serious	none	050	5255	(0.99 to		Low
								1.56)		
بالدينية د	s for any, mo	oderate, heavy	or very heavy							
U studie										
	-	ms Teacher Re	port (Frequen	cy/OR) (Odds	of 'Abnorn	nal/Borde	erline' sco	ore)		
SDQ Co	-	ms Teacher Re	port (Frequen	cy/OR) (Odds	of 'Abnorn	nal/Borde	erline' sco	ore)		
SDQ Co	-	ms Teacher Re not serious	port (Frequen not serious	cy/OR) (Odds very	of 'Abnorn none	nal/Borde	erline' sco 126	ore) OR 1.37	1	⊕⊕○○
SDQ Co Light	nduct Proble					-		<b>OR 1.37</b> (0.9 to		⊕⊕⊖⊖ Low
SDQ Co Light 1	nduct Proble	not serious	not serious	very		-		OR 1.37		
SDQ Co Light 1 CBCL Ag	nduct Proble not serious gression Car		not serious	very		-		<b>OR 1.37</b> (0.9 to		
SDQ Co Light 1	nduct Proble not serious gression Car	not serious	not serious	very serious <sup>d,e,f</sup>		70	126	<b>OR 1.37</b> (0.9 to		Low
SDQ Co Light 1 CBCL Ag	nduct Proble not serious gression Car	not serious	not serious	very		-		<b>OR 1.37</b> (0.9 to	SMD 0.92 higher	Low DOC
SDQ Co Light 1 CBCL Ag Very He	nduct Proble not serious gression Car	not serious egiver Report (	not serious (T-score)	very serious <sup>d,e,f</sup>	none	70	126	<b>OR 1.37</b> (0.9 to	(0.26 higher to	Low
SDQ Co Light 1 CBCL Ag Very He 1	nduct Proble not serious gression Car eavy serious <sup>a</sup>	not serious egiver Report (	not serious (T-score)	very serious <sup>d,e,f</sup>	none	70	126	<b>OR 1.37</b> (0.9 to		Low DOC
SDQ Co Light 1 CBCL Ag Very He 1 Any PA	nduct Proble not serious gression Car eavy serious <sup>a</sup> E	not serious regiver Report ( not serious	not serious (T-score) not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup>	none	20	126	<b>OR 1.37</b> (0.9 to	(0.26 higher to 1.59 higher)	Low O Low
SDQ Co Light 1 CBCL Ag Very He 1	nduct Proble not serious gression Car eavy serious <sup>a</sup>	not serious egiver Report (	not serious (T-score)	very serious <sup>d,e,f</sup>	none	70	126	<b>OR 1.37</b> (0.9 to	(0.26 higher to 1.59 higher) SMD 0.11 higher	
SDQ Co Light 1 CBCL Ag Very He 1 Any PA	nduct Proble not serious gression Car eavy serious <sup>a</sup> E	not serious regiver Report ( not serious	not serious (T-score) not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup>	none	20	126	<b>OR 1.37</b> (0.9 to	(0.26 higher to 1.59 higher)	Low O Low
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI	nduct Proble not serious gression Car eavy serious <sup>a</sup> E	not serious egiver Report ( not serious not serious	not serious (T-score) not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup>	none	20	126	<b>OR 1.37</b> (0.9 to	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to	
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI	nduct Proble not serious gression Car eavy serious <sup>a</sup> serious <sup>a</sup>	not serious egiver Report ( not serious not serious	not serious (T-score) not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup>	none	20	126	<b>OR 1.37</b> (0.9 to	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to	
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI 1 Confirm	nduct Proble not serious gression Car eavy serious <sup>a</sup> serious <sup>a</sup> eed unquant	not serious regiver Report ( not serious not serious <b>ifiable</b>	not serious (T-score) not serious not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious	none	70       20       2518	126 19 7201	<b>OR 1.37</b> (0.9 to	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher (0.72 higher to	Low $\oplus \oplus \bigcirc \bigcirc$ Low $\oplus \oplus \oplus \bigcirc$ Moderate
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI 1 Confirm 2	nduct Proble not serious gression Car eavy serious <sup>a</sup> serious <sup>a</sup> eed unquant serious <sup>a</sup>	not serious egiver Report ( not serious not serious ifiable serious <sup>b</sup>	not serious (T-score) not serious not serious not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious	none	70       20       2518	126 19 7201	<b>OR 1.37</b> (0.9 to	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher	Low $\oplus \oplus \bigcirc \bigcirc$ Low $\oplus \oplus \oplus \bigcirc$ Moderate $\oplus \bigcirc \bigcirc \bigcirc$
SDQ Co Light 1 CBCL Ag Very He 1 Any PA 1 1 Confirm 2	nduct Proble not serious gression Car eavy serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup>	not serious regiver Report ( not serious not serious ifiable serious <sup>b</sup>	not serious (T-score) not serious not serious not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious serious <sup>e,f</sup>	none none none	70         20         2518         140	126 19 7201 188	<b>OR 1.37</b> (0.9 to	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher (0.72 higher to	Low $\oplus \oplus \bigcirc \bigcirc$ Low $\oplus \oplus \oplus \bigcirc$ Moderate $\oplus \bigcirc \bigcirc \bigcirc$
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI 1 Confirm 2 O studie CBCL Ag	nduct Proble not serious gression Car eavy serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup>	not serious egiver Report ( not serious not serious ifiable serious <sup>b</sup>	not serious (T-score) not serious not serious not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious serious <sup>e,f</sup>	none none none	70         20         2518         140	126 19 7201 188	<b>OR 1.37</b> (0.9 to	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher (0.72 higher to	Low $\oplus \oplus \bigcirc \bigcirc$ Low $\oplus \oplus \oplus \bigcirc$ Moderate $\oplus \bigcirc \bigcirc \bigcirc$
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI 1 Confirm 2 O studie CBCL Ag	nduct Proble not serious gression Car eavy serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup>	not serious regiver Report ( not serious not serious ifiable serious <sup>b</sup>	not serious (T-score) not serious not serious not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious serious <sup>e,f</sup>	none none none	70         20         2518         140	126 19 7201 188	<b>OR 1.37</b> (0.9 to	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher (0.72 higher to	Low $\oplus \oplus \bigcirc \bigcirc$ Low $\oplus \oplus \oplus \bigcirc$ Moderate $\oplus \bigcirc \bigcirc \bigcirc$
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI 1 2 Confirm 2 0 studie CBCL Ag	nduct Proble not serious gression Car eavy serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup>	not serious regiver Report ( not serious not serious ifiable serious <sup>b</sup>	not serious (T-score) not serious not serious not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious serious <sup>e,f</sup>	none none none	70         20         2518         140	126 19 7201 188	OR 1.37 (0.9 to 2.07) - - - - - - OR 1.06	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher (0.72 higher to	Low $\oplus \oplus \bigcirc \bigcirc$ Low $\oplus \oplus \oplus \bigcirc$ Moderate $\oplus \bigcirc \bigcirc \bigcirc$ Very low $\oplus \oplus \oplus \bigcirc \bigcirc$
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI 1 Confirm 2 O studie CBCL Ag Light	nduct Proble not serious gression Car eavy serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup>	not serious regiver Report ( not serious not serious ifiable serious <sup>b</sup> oderate or hea	not serious (T-score) not serious not serious not serious Ny (Frequency/Of	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious serious <sup>e,f</sup>	none none none	70 20 2518 140	126 19 7201 188	OR 1.37 (0.9 to 2.07) - - - - - - - - - - - - - - - - - - -	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher (0.72 higher to	Low $\oplus \oplus \bigcirc \bigcirc$ Low $\oplus \oplus \oplus \bigcirc$ Moderate $\oplus \bigcirc \bigcirc \bigcirc$ Very low
SDQ Co Light 1 CBCL Ag Very He 1 1 Any PAI 1 2 O studie CBCL Ag Light 1	nduct Proble not serious gression Car savy serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> not serious	not serious regiver Report ( not serious not serious ifiable serious <sup>b</sup> oderate or hea	not serious (T-score) not serious not serious not serious Ny (Frequency/Of	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious serious <sup>e,f</sup>	none none none	70 20 2518 140	126 19 7201 188	OR 1.37 (0.9 to 2.07) - - - - - - OR 1.06	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher (0.72 higher to	Low $\oplus \oplus \bigcirc \bigcirc$ Low $\oplus \oplus \oplus \bigcirc$ Moderate $\oplus \bigcirc \bigcirc \bigcirc$ Very low $\oplus \oplus \oplus \bigcirc \bigcirc$
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI 1 Confirm 2 0 studie CBCL Ag Light 1 Modera	nduct Proble not serious gression Car eavy serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> not serious not serious	not serious egiver Report ( not serious not serious ifiable serious oderate or hea regiver Report ( not serious	not serious (T-score) not serious not serious not serious Vy (Frequency/OF not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious serious <sup>e,f</sup> (Odds of sco serious <sup>d</sup>	none none none none none	70         20         2518         140         al range'         208	126 19 7201 188 ) 690	OR 1.37 (0.9 to 2.07) - - - - - - - - - - - - - - - - - - -	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher (0.72 higher to	Low $\oplus \oplus \bigcirc \bigcirc$ Moderate $\oplus \bigcirc \bigcirc \bigcirc$ Very low $\oplus \oplus \oplus \bigcirc$ Moderate
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI 1 Confirm 2 O studie CBCL Ag Light 1	nduct Proble not serious gression Car savy serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> not serious	not serious regiver Report ( not serious not serious ifiable serious <sup>b</sup> oderate or hea	not serious (T-score) not serious not serious not serious Ny (Frequency/Of	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious serious <sup>e,f</sup>	none none none	70 20 2518 140	126 19 7201 188	OR 1.37 (0.9 to 2.07) - - - - - - - - - - - - - - - - - - -	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher (0.72 higher to	Low $\oplus \oplus \bigcirc \bigcirc$ Moderate $\oplus \oplus \oplus \bigcirc \bigcirc$ Very low Moderate $\oplus \oplus \oplus \bigcirc \bigcirc$
SDQ Co Light 1 CBCL Ag Very He 1 Any PAI 1 Confirm 2 0 studie CBCL Ag Light 1 Modera	nduct Proble not serious gression Car eavy serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> not serious not serious	not serious egiver Report ( not serious not serious ifiable serious oderate or hea regiver Report ( not serious	not serious (T-score) not serious not serious not serious Vy (Frequency/OF not serious	very serious <sup>d,e,f</sup> serious <sup>e,f</sup> not serious serious <sup>e,f</sup> (Odds of sco serious <sup>d</sup>	none none none none none	70         20         2518         140         al range'         208	126 19 7201 188 ) 690	OR 1.37 (0.9 to 2.07) - - - - - - - - - - - - - - - - - - -	(0.26 higher to 1.59 higher) SMD 0.11 higher (0.07 higher to 0.16 higher) SMD 1.64 higher (0.72 higher to	Low $\oplus \oplus \bigcirc \bigcirc$ Moderate $\oplus \bigcirc \bigcirc \bigcirc$ Very low $\oplus \oplus \oplus \bigcirc$ Moderate

studies for any, confirmed unquantifiable or very heavy         BCR Rule-Breaking Behaviour Caregiver Report (T-score)         ny PAE         1       serious*         confirmed unquantifiable         2       serious*         and serious       not serious         not serious       not serious         studies for light, moderate or heavy         BCR Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range')         ght         1       not serious         not serious       not serious         studies for light, moderate or heavy         BCR Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range')         ght       not serious         1       not serious         not serious       not serious         Serious**       none         208       690       OR 1.60 (0.78 to 3.28)         1       not serious       not serious         1       serious**       none       389       117       OR 3.20 (0.04 to       Moderat         1       serious*       not serious       serious**       none       57       690       OR 0.28 (0.04 to       Uow         1       serious*       not seriou									_		
studies for any, confirmed unquantifiable or very heavy         Studies for any, confirmed unquantifiable or very heavy         1       serious*       not serious       not serious       not serious       not serious*       not serious*       fdtttt         1       serious*       not serious       not serious       not serious*       not serious       fdttttt       fdtttttttttt         2       serious*       not serious       not serious       serious**       none       107       188       -       SMD 1.6 higher (0.04 higher)       fdtttttttttttttttttttttttttttttttttt	1	not serious	not serious	not serious	Serious <sup>d,e</sup>	none	57	690			$\oplus \oplus \oplus \bigcirc$
studies for any, confirmed unquantifiable or very heavy       Image: serious and serious in the serious is serious in the serious is in the serious is serious in the serious is in the serious i											Moderate
BCL Rule-Breaking Behaviour Caregiver Report (T-score) my PAE 1 serious <sup>4</sup> not serious not serious not serious none 2518 7201 · SMD 0.09 higher (0.04 higher to 0.03 higher to 0.04 h		- f	- <b>f</b> :						5.01)		
ny PAE       not serious       not serious       not serious       none       2518       7201       ·       SMD 0.09 higher (0.04 higher to 0.13 higher)       Moderat         1       serious*       not serious       not serious       serious*       none       107       188       -       SMD 1.16 higher (0.89 higher to 1.14 higher)       Uow         2       serious*       not serious       serious*       none       107       188       -       SMD 1.16 higher (0.89 higher to 1.42 higher)         5tudies for light, moderate or heavy       BCL Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range')       ght       -       SMD 1.16 higher (0.89 higher to 1.42 higher)         1       not serious       not serious       Serious*       none       208       690       OR 1.60       0		-	-								
1       serious*       not serious       not serious       none       2518       7201       -       SMD 0.09 higher (0.04 higher to 0.03 higher)       000 derate         2       serious*       not serious       not serious       serious**       none       107       188       -       SMD 0.09 higher to 0.03 higher)       Moderat         2       serious*       not serious       not serious       serious**       none       107       188       -       SMD 1.16 higher (0.89 higher to 1.42 higher)       0.00         studies for light, moderate or heavy       RCL Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range')       #			Benaviour Care	giver Report (	I-score)						
and immed unquantifiable       (0.04 higher to 0.13 higher to 0.13 higher to 0.13 higher to 0.13 higher to 0.142 higher)       Moderati 0.125 higher (0.89 higher to 1.42 higher)       Moderati 0.89 higher to 1.42 higher)         studies for light, moderate or heavy         BCL Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range') ght       mone       208       690       OR 1.60       ⊕ ⊕⊕⊕C (0.78 to 3.28)         1       not serious       not serious       Serious**       none       389       117       OR 3.20 (0.078 to 3.28)       ⊕ ⊕⊕⊕C (0.04 to 1.35 to         1       serious*       not serious       serious*       none       57       690       OR 0.28 (0.04 to 1.95)       ⊕ ⊕⊕⊖C Uow         1       serious*       not serious       serious*       none       57       690       OR 0.28 (0.04 to 1.95)       ⊕ ⊕⊖C Uow         1       serious*       not serious       serious*       none       18       21       -       SMD 0.26 higher (0.38 lower to 0.38 lower to 0.38 lower to 0.38 lower to 0.38 lower to 0.38 lower to 0.38 lower to 0.08 higher)       ⊕ ⊕⊖C Uow         1       serious*       not serious       serious*       none       18       21       -       SMD 0.26 higher (0.38 lower to 0.38 lower to 0.38 lower to 0.08 higher)       ⊕ ⊕ ⊖C Uow         1       serious*       not se		т т					,				
	1	serious <sup>a</sup>	not serious	not serious	not serious	none	2518	7201	-	-	
onfirmed unquantifiable       interious       serious**       none       107       188       -       SMD 1.16 higher (0.89 higher to Low         2       serious*       not serious       not serious       serious**       none       107       188       -       SMD 1.16 higher (0.89 higher to Low         studies for light, moderate or heavy       ECR Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range')       ght       mot serious       not serious*       not serious**       none       208       690       OR 1.60       0.08 to C.078 to											woderate
2       serious <sup>a</sup> not serious       not serious       serious <sup>a</sup> none       107       188       -       SMD 1.16 higher (0.89 higher to 1.42 higher)         3tudies for light, moderate or heavy       BCL Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range')       ##         1       not serious       not serious       Serious <sup>4,e</sup> none       208       690       OR 1.60 (0.78 to 3.28)       ####################################	onfirm	ed unquanti	fiable							0.15 fligher)	
studies for light, moderate or heavy         BCL Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range')         ght         1       not serious       not serious       not serious       Serious <sup>4,e</sup> none       208       690       OR 1.60       0.078 to 3.281         1       not serious       not serious       Serious <sup>4,e</sup> none       389       117       OR 3.20       Moderate         1       serious <sup>5</sup> not serious       not serious       serious <sup>4</sup> none       389       117       OR 3.20       0.000 (1.35 to (1.35 to 7.60)       Moderate         1       serious <sup>5</sup> not serious       not serious       serious <sup>4</sup> none       57       690       OR 0.28 (0.04 to 1.95)       0.000 (25 higher (0.38 lower to 0.89 higher)       0.000 (25 higher (0.38 lower to 0.89 higher)       0.000 (25 higher (0.38 lower to 0.89 higher)       0.000 (25 higher (0.020 (Very Low 0.89 higher)       0.000 (Very Low 0.89 higher)       0.000 (Very Low 0.89 higher)         1       serious <sup>4</sup> not serious       not serious       very serious <sup>4,d</sup> none       18       21       -       SMD 0.25 higher (0.38 lower to 0.89 higher)       0.000 (Very Low 0.89 higher)         1       serious <sup>4</sup> not serious       serious <sup>4,d</sup> none		· · ·		not serious	serious <sup>e,f</sup>	none	107	188	-	SMD 1 16 higher	
studies for light, moderate or heavy         Studies for light, moderate or heavy         BCL Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'Clinical range')         ght         1       not serious       not serious       Serious <sup>4,a</sup> none       208       690       OR 1.60       (0.73 to 3.28)         1       serious <sup>a</sup> not serious       not serious       serious <sup>a</sup> none       389       117       OR 3.20       (0.04 to (0.73 to 3.28)         1       serious <sup>a</sup> not serious       not serious       serious <sup>a</sup> none       57       690       OR 0.28       (0.04 to 1.95)       0.04 cot         1       serious <sup>a</sup> not serious       not serious       serious <sup>d</sup> none       57       690       OR 0.28       0.04 cot       0.04 cot         1       serious <sup>a</sup> not serious       serious <sup>a</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.28 higher)       0.00 CO       0.02 higher (0.38 lower to 0.28 higher)       0.00 CO       0.02 higher (0.38 lower to 0.28 higher)       0.00 CO       0.00 CO<	2	Schous	not serious	not serious	Schous	none	107	100		-	
BCL Rule-Breaking Behaviour Caregiver Report (Frequency/OR) (Odds of scoring 'clinical range')         ght         1       not serious       not serious       not serious       Serious <sup>6,n</sup> none       208       690       OR 1.60 (0.78 to 3.28)       Moderate         1       serious <sup>n</sup> not serious       not serious       serious <sup>n</sup> none       389       117       OR 3.20 (1.35 to 7.60)       Ø⊕⊕⊕C Moderate         1       serious <sup>n</sup> not serious       not serious       serious <sup>n</sup> none       57       690       OR 0.28 (0.04 to 1.95)       Ø⊕⊕CC (0.38 lower to 0.04 to 1.95)         studies for any, confirmed unquantifiable or very heavy       serious <sup>4,c/1</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.38 higher)       Ø⊕OCC Very Low 0.038 lower to 0.28 higher)         1       serious <sup>3</sup> not serious       not serious       very serious <sup>4,c/1</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.38 higher)       Ø⊕OCC Very Low 0.028 higher)         1       serious <sup>3</sup> not serious       not serious       serious <sup>4,c/1</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.28 higher)       0.20 CC Very Low 0.28 higher)         1       serious <sup>3</sup> not serious       <										. –	
ght       not serious       not serious       Serious <sup>4,e</sup> none       208       690       OR 1.60       ●●●●○         1       not serious       not serious       not serious       serious <sup>4</sup> none       389       117       OR 3.20       ●●●●○         1       serious <sup>4</sup> not serious       not serious       serious <sup>4</sup> none       389       117       OR 3.20       ●●●●○         1       serious <sup>4</sup> not serious       not serious       serious <sup>6</sup> none       57       690       OR 0.28       ●●●○○       Low         1       serious <sup>4</sup> not serious       not serious       serious <sup>6</sup> none       57       690       OR 0.28       ●●●○○       Low         studies for any, confirmed unquantifiable or very heavy       serious <sup>4,e,f</sup> none       18       21       -       SMD 0.26 higher       ●○○○       ○○○       Very Low         studies for any PAE, confirmed unquantifiable, light, moderate or heavy PAE       DO       0.39 higher)       0.39 higher)       0.39 higher)       0.28 higher)       0.00       0.28 higher       0.28 higher)       0.28 higher)       0.00       0.00       0.28 higher)       0.28 higher)       0.28 higher)       0.00       0.00       0.28	) studie	s for light, m	oderate or hea	vy							
1not seriousnot seriousSeriousSeriousnone208690OR 1.60 (0.78 to 3.20 $\oplus \oplus \oplus \bigcirc$ Moderate1serious*not seriousnot seriousserious*none389117OR 3.20 (1.35 to 7.60) $\oplus \oplus \oplus \bigcirc$ Moderate1serious*not seriousnot seriousserious*none57690OR 0.28 (0.04 to 1.95) $\oplus \oplus \oplus \bigcirc$ Low1serious*not seriousnot seriousserious*none57690OR 0.28 (0.04 to 1.95) $\oplus \oplus \bigcirc \bigcirc$ Low1serious*not seriousnot seriousserious*none1821-(0.38 lower to 0.39 higher) $\oplus \oplus \bigcirc \bigcirc$ Low1serious*not seriousnot seriousvery serious*.none1821-(0.38 lower to 0.39 higher) $\oplus \bigcirc \bigcirc \bigcirc$ Low1serious*not seriousnot seriousvery serious*.none1821-(0.38 lower to 0.39 higher) $\oplus \bigcirc \bigcirc \bigcirc$ Low1serious*not seriousnot seriousserious*.none19635547-aMD 0.11 higher (0.06 lower to 0.28 higher) $\oplus \bigcirc \bigcirc \bigcirc$ Low1serious*not seriousnot seriousserious*.none19635547-aMD 0.11 higher (0.61 lower to 0.28 higher)1serious*not seriousnot seriousserious*.none158355OR 1.25 (0.99 to) 1.59)Moderate DOC <b< td=""><td>BCL Ru</td><td>Ile-Breaking I</td><td>Behaviour Care</td><td>giver Report (</td><td>Frequency/OF</td><td>R) (Odds of</td><td>scoring '</td><td>clinical ra</td><td>inge')</td><td></td><td></td></b<>	BCL Ru	Ile-Breaking I	Behaviour Care	giver Report (	Frequency/OF	R) (Odds of	scoring '	clinical ra	inge')		
Inderate       Image: model of the serious of the serio	ight										
Inderate       Image: model of the serious of the serio		not serious	not serious	not serious	Serious <sup>d,e</sup>	none	208	690	OR 1.60		$\oplus \oplus \oplus \bigcirc$
ioderate       Image: Serious*       not serious       none       389       117       OR 3.20 (1.35 to 7.60)       Image: Moderate         1       serious*       not serious       not serious       serious*       none       57       690       OR 0.28 (0.04 to 1.95)       Image: Moderate         1       serious*       not serious       not serious       serious*       none       57       690       OR 0.28 (0.04 to 1.95)       Image: Moderate         2       serious*       not serious       not serious       serious*       none       18       21       -       SMD 0.26 higher       0.00 (0.38 lower to 0.89 higher)         1       serious*       not serious       not serious       very serious*       none       18       21       -       SMD 0.26 higher       0.00 (0.38 lower to 0.89 higher)         1       serious*       not serious       not serious       very serious*       none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       0.00 (0.00       0.00 (0.00       0.28 higher)       0.00 (0.00									(0.78 to		Moderate
1       serious <sup>a</sup> not serious       serious <sup>a</sup> none       389       117       OR 3.20       (1.35 to 7.60)       Moderate         eavy       1       serious <sup>a</sup> not serious       serious <sup>a</sup> none       57       690       OR 0.28       (0.04 to 1.95)       0.004 to 1.95)         studies for any, confirmed unquantifiable or very heavy       serious <sup>4</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.89 higher)       0.00 (Very Low 0.89 higher)         1       serious <sup>a</sup> not serious       not serious <sup>4,e,f</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.89 higher)       0.00 (Very Low 0.89 higher)         1       serious <sup>4</sup> not serious       not serious <sup>4,e,f</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.89 higher)       0.00 (Very Low 0.89 higher)         20Q Hyperactivity Caregiver Report (adjusted mean difference)       ght       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       0.00 (Low 0.28 higher)       0.28 higher)       -       Low 0.28 higher)       0.28 higher)       -       Low 0.28 higher)       -       .       .       .       .       .       .       .       .       .       .       .       .       .									3.28)		
eavy       (1.35 to       Moderati         1       serious <sup>a</sup> not serious       serious <sup>d</sup> none       57       690       OR 0.28       0.04 to       0.004 to		<u>г г</u>		1			· · ·		1	· · · · · ·	
7.607.607.607.607.607.607.60Reavy1Serious <sup>d</sup> not serious serious <sup>d</sup> none57690OR 0.28(0.04 to 1.95) $0.004$ to 1.95)Studies for any, confirmed unquantifiable or very heavyBCL Hyperactivity Caregiver Report (T-score)ery heavy1serious <sup>a</sup> not seriousvery serious <sup>d,e,f</sup> none1821-SMD 0.26 higher (0.38 lower to 0.89 higher) $0.00$ 20 Hyperactivity Caregiver Report (adjusted mean difference)ght $0.00$ $0.02$ higher (0.06 lower to 0.028 higher) $0.00$ $0.00$ studies for any, confirmed unquantifiable moderate, heavy or very heavy PAE DQ Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')aMD 0.11 higher (0.06 lower to 0.28 higher) $0.02$ totaw1not seriousnot seriousserious <sup>d</sup> none158355OR 1.25 (0.99 to (0.62 to (0.82 to to $0.02$ 1ser	1	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	389	117			$\Theta \Theta \Theta O$
eavy       1       serious <sup>a</sup> not serious       not serious       serious <sup>d</sup> none       57       690       OR 0.28       (0.04 to       1.95)         studies for any, confirmed unquantifiable or very heavy       BCL Hyperactivity Caregiver Report (T-score)       ery heavy       1       Serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.389 higher)       ♥○○○         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.389 higher)       ♥○○○○         20       Hyperactivity Caregiver Report (adjusted mean difference)       ght       1       serious <sup>a</sup> not serious       serious <sup>d,e,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       Low         20       Hyperactivity Caregiver Report (adjusted mean difference)       ght       1       serious <sup>a</sup> not serious       serious <sup>d</sup> .e       none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       Low         20       Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')       ght       0.89 higher)       1       not serio											Moderate
1       serious <sup>a</sup> not serious       not serious       serious <sup>d</sup> none       57       690       OR 0.28 (0.04 to 1.95)       0.04 to 1.95)         studies for any, confirmed unquantifiable or very heavy       BCL Hyperactivity Caregiver Report (T-score)       ery heavy         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.89 higher)       0 CO Very Low         204 Hyperactivity Caregiver Report (adjusted mean difference)       get       -       SMD 0.11 higher (0.06 lower to 0.28 higher)       0 CO Low         1       serious <sup>a</sup> not serious       not serious       serious <sup>d,e,f</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       0 CO Low         204 Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')       get       -       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       0 CO Low         1       not serious       not serious       serious <sup>d</sup> none       158       355       OR 1.25 (0.99 to 1.59)       -       -       Moderate         1       serious <sup>a</sup> not serious       not serious       serious <sup>d</sup> none       657       9088       OR 1.05 (0.82 to1.34) <td>leavy</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>7.00)</td> <td></td> <td></td>	leavy								7.00)		
studies for any, confirmed unquantifiable or very heavy       Low         BCL Hyperactivity Caregiver Report (T-score)       ery heavy         1       serious <sup>a</sup> not serious       very serious <sup>d,e,f</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.38 higher)       OCO Very Low 0.39 higher)         studies for any PAE, confirmed unquantifiable, light, moderate or heavy PAE       none       18       21       -       SMD 0.26 higher (0.38 lower to 0.38 higher)       OCO Very Low 0.39 higher)         OL Hyperactivity Caregiver Report (adjusted mean difference)       ght       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       0.00 Cover to 0.28 higher)         1       serious <sup>a</sup> not serious       not serious       serious <sup>d,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       Low         1       serious <sup>a</sup> not serious       not serious       serious <sup>d,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       Low         0.04 Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')       ght       -       -       aMD 0.11 higher (0.09 higher)       0.99 higher)       Moderate         1       serious <sup>a</sup> not serious       not serious       serious <sup>d</sup>	=	seriousa	not serious	not serious	serious <sup>d</sup>	none	57	690	OR 0 28	<u>г</u>	
studies for any, confirmed unquantifiable or very heavy         BCL Hyperactivity Caregiver Report (T-score)         ery heavy         1       serious <sup>a</sup> not serious       not serious         very serious <sup>d,e,f</sup> none         18       21         21       -         SMD 0.26 higher $\oplus \bigcirc \bigcirc$	Ŧ	Serious	not senous	not senous	serious	none	57	090			
BEL Hyperactivity Caregiver Report (T-score)         ery heavy       1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.89 higher)       Very Low 0.89 higher)         studies for any PAE, confirmed unquantifiable, light, moderate or heavy PAE       DQ Hyperactivity Caregiver Report (adjusted mean difference)       ght       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       0.28 higher)       0.28 higher)       Uover to 0.28 higher)       0.00 lower to 0.28 higher)       0.00											
ery heavy         1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.89 higher)         very Low       serious <sup>d</sup> or any PAE, confirmed unquantifiable, light, moderate or heavy PAE       DQ Hyperactivity Caregiver Report (adjusted mean difference)         ght       1       serious <sup>a</sup> not serious       not serious       serious <sup>d,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       Uow         1       serious <sup>a</sup> not serious       not serious       serious <sup>d,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       Uow         studies for any, confirmed unquantifiable moderate, heavy or very heavy PAE       DQ Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')       ght       -       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       Uow         1       not serious       not serious       serious <sup>d</sup> none       158       355       OR 1.25 (0.99 to 1.59)       Moderate         1       serious <sup>a</sup> not serious       serious <sup>d</sup> none       657       9088       OR 1.05 (0.82 to 1.34)       Uow         1       serious <sup>a</sup> <td>) studie</td> <td>s for any, co</td> <td>nfirmed unqua</td> <td>ntifiable or ve</td> <td>ry heavy</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>	) studie	s for any, co	nfirmed unqua	ntifiable or ve	ry heavy						
1       serious <sup>a</sup> not serious       not serious       very serious <sup>d,e,f</sup> none       18       21       -       SMD 0.26 higher (0.38 lower to 0.89 higher)       Very Low Very Low Very Low 0.89 higher)         studies for any PAE, confirmed unquantifiable, light, moderate or heavy PAE       DQ Hyperactivity Caregiver Report (adjusted mean difference)       mone       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       0.28 higher)       0.00         1       serious <sup>a</sup> not serious       not serious       serious <sup>d,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       0.00       0.28 higher)       0.00       <	CBCL Hy	peractivity C	aregiver Repor	t (T-score)							
serious <sup>d.e.f</sup> (0.38 lower to 0.89 higher)       Very Low 0.89 higher)         studies for any PAE, confirmed unquantifiable, light, moderate or heavy PAE         DQ Hyperactivity Caregiver Report (adjusted mean difference)         ght         1       serious <sup>a</sup> not serious       serious <sup>d.e.</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       DQ Hyperactivity Caregiver Report (adjusted mean difference)         ght	/ery he	avy									
studies for any PAE, confirmed unquantifiable, light, moderate or heavy PAE         DQ Hyperactivity Caregiver Report (adjusted mean difference)         ght         1       serious <sup>a</sup> not serious       serious <sup>d,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       ⊕⊕⊖○○ Low         studies for any, confirmed unquantifiable moderate, heavy or very heavy PAE       DQ Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')       ght         1       not serious       not serious       serious <sup>d</sup> none       158       355       OR 1.25 (0.99 to 1.59)       ⊕⊕⊕○○ Moderate         1       not serious       not serious       serious <sup>d</sup> none       657       9088       OR 1.05 (0.82 to1.34)       ⊕⊕○○○ Low         eavy       1       serious <sup>a</sup> not serious       serious <sup>d</sup> none       258       9088       OR 0.90 (0.61 to       ⊕⊕○○○ Low	1	serious <sup>a</sup>	not serious	not serious	very	none	18	21	-	SMD 0.26 higher	000
studies for any PAE, confirmed unquantifiable, light, moderate or heavy PAE         DQ Hyperactivity Caregiver Report (adjusted mean difference)         ght         1       serious <sup>a</sup> not serious       not serious       serious <sup>d,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       DQ 0.13 higher         studies for any, confirmed unquantifiable moderate, heavy or very heavy PAE       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       DQ Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')         ght       -       1       not serious       not serious       serious <sup>d</sup> none       158       355       OR 1.25 (0.99 to 1.59)       OR 1.25 (0.99 to 1.59)         1       serious <sup>a</sup> not serious       serious <sup>d</sup> none       657       9088       OR 1.05 (0.82 to 1.34)       DQ -C Low         1       serious <sup>a</sup> not serious       serious <sup>d</sup> none       258       9088       OR 0.90 (0.61 to       DOC Low					serious <sup>d,e,f</sup>					(0.38 lower to	Very Low
DQ Hyperactivity Caregiver Report (adjusted mean difference)         ght       1       serious <sup>a</sup> not serious       not serious       serious <sup>d,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       DC Low         studies for any, confirmed unquantifiable moderate, heavy or very heavy PAE       -       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       - </td <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>0.89 higher)</td> <td></td>										0.89 higher)	
ght       1       serious <sup>a</sup> not serious       not serious       serious <sup>d,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       ####################################				•	<b>U</b>		PAE				
1       serious <sup>a</sup> not serious       not serious       serious <sup>d,e</sup> none       1963       5547       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       0.06 lower to 0.28 higher)       0.08 higher)       0.00         studies for any, confirmed unquantifiable moderate, heavy or very heavy PAE       DQ Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')       ght       -       aMD 0.11 higher (0.06 lower to 0.28 higher)       0.00         1       not serious       not serious       serious <sup>d</sup> none       158       355       OR 1.25 (0.99 to 1.59)       0.09 to 1.59)       0.00         1       serious <sup>a</sup> not serious       serious <sup>d</sup> none       657       9088       OR 1.05 (0.82 to 1.34)       0       0         1       serious <sup>a</sup> not serious       serious <sup>d</sup> none       657       9088       OR 0.90 (0.61 to       0       0	DQ Hy	peractivity Ca	aregiver Report	: (adjusted me	an difference	)					
Image: serious and serious are and serious and serious and serious are	.ight										
studies for any, confirmed unquantifiable moderate, heavy or very heavy PAE       0.28 higher)         DQ Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')         ght         1       not serious       not serious       serious <sup>d</sup> none       158       355       OR 1.25 (0.99 to 1.59)	1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	1963	5547	-		$\oplus \oplus \bigcirc \bigcirc$
studies for any, confirmed unquantifiable moderate, heavy or very heavy PAE         DQ Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')         ght         1       not serious       not serious       not serious       serious <sup>d</sup> none       158       355       OR 1.25 (0.99 to 1.59)											Low
DQ Hyperactivity Caregiver Report (Frequency/OR) (Cut-offs unclear/Odds of 'Abnormal Score')         ght         1       not serious       not serious       serious <sup>d</sup> none       158       355       OR 1.25       (0.99 to 1.59)       Moderate         1       serious <sup>a</sup> not serious       not serious       serious <sup>d</sup> none       657       9088       OR 1.05       0.82       Low         1       serious <sup>a</sup> not serious       serious <sup>d</sup> none       657       9088       OR 0.90       Low         1       serious <sup>a</sup> not serious       serious <sup>d</sup> none       258       9088       OR 0.90       0.61 to	م : اما : م	- for only - only		atific la un o de	wata kaavuva					0.28 higher)	
ght         1       not serious       not serious       serious <sup>d</sup> none       158       355       OR 1.25 $(0.99 \text{ to})$ Moderate         1       serious <sup>a</sup> not serious       not serious       serious <sup>d</sup> none       657       9088       OR 1.05 $(0.82)$ Low         1       serious <sup>a</sup> not serious       not serious       serious <sup>d</sup> none       657       9088       OR 1.05 $(0.82)$ Low         eavy       1       serious <sup>a</sup> not serious       not serious       serious <sup>d</sup> none       258       9088       OR 0.90 $\oplus \oplus \bigcirc \bigcirc$			•			•					
1not seriousnot seriousnot seriousseriousnone158355OR 1.25 (0.99 to 1.59) $\bigoplus \bigoplus $		peractivity Ca	aregiver Report	. (Frequency/C	JR) (CUT-Offs L	inclear/Od	as ot 'Ab	normal So	Lore)		
InderateImage: NoderateModerate1serious <sup>a</sup> not seriousnot seriousserious <sup>d</sup> none6579088OR 1.05 (0.82 to1.34) $\bigoplus \bigoplus \bigcirc \bigcirc$		I									
Inderate       Image: Serious and serious are serious and serious and serious and serious are serious and serious and serious and serious are serious and serious and serious are serious and serious are serious and serious are ser	1	not serious	not serious	not serious	serious <sup>d</sup>	none	158	355			
Indefate       1       serious <sup>a</sup> not serious       not serious       serious <sup>d</sup> none       657       9088       OR 1.05 (0.82 to1.34) $\bigoplus \bigoplus \bigcirc \bigcirc$ eavy       1       serious <sup>a</sup> not serious       serious <sup>d</sup> none       258       9088       OR 0.90 (0.61 to $\bigoplus \bigoplus \bigcirc \bigcirc$											wouerate
1seriousanot seriousnot seriousseriousdnone6579088OR 1.05 (0.82 to1.34) $\bigoplus \bigoplus \bigcirc \bigcirc$	Modera	ite		1					1.55	1	
eavyImage: 1Serious a constraint of serious and serious are serious and serious and serious and serious are serious and serious and serious are serious and serious are serious			not serious	not serious	serious <sup>d</sup>	none	657	9088	OR 1.05		$\oplus \oplus \bigcirc \bigcirc$
eavy     to1.34)       1     serious <sup>a</sup> not serious     not serious <sup>d</sup> none     258     9088     OR 0.90 (0.61 to          ⊕⊕○○ Low	-	5011003	not serious		5011003	none	557	2000			
1serious <sup>a</sup> not seriousnot seriousserious <sup>d</sup> none2589088 <b>OR 0.90</b> (0.61 to $\bigoplus \bigoplus \bigcirc \bigcirc$ Low									•		
(0.61 to Low	leavy										
	1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	258	9088	OR 0.90		$\oplus \oplus \bigcirc \bigcirc$
											Low
									1.32)		

SDQ Hy	peractivity Se	elf-report (adju	sted OR) (Cut-	offs unclear)						
Confirm	ed unquant	ifiable								
1	serious <sup>a</sup>	not serious	not serious	not serious	none	850	5229	<b>aOR 1.39</b> (1.15 to 1.69)		⊕⊕⊕⊖ Moderate
0 studie	s for any or	very heavy	•					• •		
SDQ Hy	peractivity To	eacher Report (	Frequency/OI	R) (Cut-offs ur	iclear)					
Light										
1	not serious	not serious	not serious	serious <sup>d,e,f</sup>	none	107	272	OR 0.93 (0.67 to 1.29)	-	⊕⊕⊖⊖ Low
CBCL An	nxious/Depre	essed Caregiver	Report (T-sco	ore)						
Any PAE	E									
1	seriousª	not serious	not serious	not serious	none	2518	7201	-	SMD 0.08 higher (0.04 higher to 0.13 higher)	⊕⊕⊕⊖ Moderate
Confirm	ed unquant	ifiable								
2	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	107	188	-	SMD 0.73 higher (0.48 higher to 0.98 higher)	⊕⊕⊖⊖ Low
	-	oderate, heavy	-							
CBCL An	nxious/Depre	essed Caregiver	Reports (Freq	juency/OR) (O	dds of scor	ing in 'cl	inical ran	ige')		
Modera	ite							-		
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	389	117	OR 2.42 (0.70 to 8.40)		⊕⊕⊖⊖ Low
0 studie	s for light, he	eavy or very he	avy							
		ssed Self-Repor	t (mean/SD) (	Cut-offs not cl	ear)					
Confirm	ed Unquant	ifiable								
1	seriousª	not serious	not serious	serious <sup>d</sup>	none	850	5299	<b>aOR 1.16</b> (0.93 to 1.45)	-	⊕⊕⊖⊖ Low
CBCL An	ixious/Depre	essed Self-Repo	rt (T-score)					,		
Light										
1	serious <sup>a</sup>	not serious	not serious	not serious	none	2536	2530	-	SMD 0.07 higher (0.01 higher to 0.12 higher)	⊕⊕⊕⊖ Moderate
Modera	ite									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	66	2530	-	<b>SMD 0.05 lower</b> (0.29 lower to 0.20 higher)	⊕⊕⊖⊖ Low
0 studie	s for any, co	nfirmed unqua	ntifiable, heav	y or very heav	vy			•		
CBCL An	xiety Caregi	ver Report (T-s	core)							
Very He	avy									
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	20	19	-	SMD 0.20 higher (0.43 lower to 0.83 higher)	⊕○○○ Very Low
		nfirmed unqua			-					
	ixiety Caregi	ver Report (Fre	quency/OR) (	Odds of scorin	g in 'clinica	l range')				
Light										
1	not serious	not serious	not serious	serious <sup>e</sup>	none	208	690	OR 2.24		⊕⊕⊕⊖ Moderate

0 studies fo CBCL Withd Any PAE 1 Se Confirmed 2 Se 0 studies fo CBCL Withd Light 1 not Moderate 1 Se Heavy 1 not 0 studies fo CBCL Somat Any PAE 1 Se Confirmed	ndrawn/De serious <sup>a</sup> d unquant serious <sup>a</sup> for light, m ndrawn/De ot serious	not serious nfirmed unqua pressed Caregi not serious ifiable not serious oderate, heavy pressed Caregi not serious	iver Report (T- not serious not serious y or very heav iver Report (O not serious	not serious serious <sup>f</sup>	none	57 57 2518 107 inical ran	690 7201 188 ge') 690	(1.16 to 4.34) OR 2.82 (1.07 to 7.43) - - - OR 0.56	SMD 0.07 higher (0.03 higher to 0.12 higher) SMD 0.80 higher (0.55 higher to 1.05 higher)	<ul> <li>⊕⊕⊕○ Moderate</li> <li>⊕⊕⊕○ Moderate</li> <li>⊕⊕⊖○ Low</li> </ul>
1     not       0 studies fo       CBCL Withd       Any PAE       1     Se       0 studies fo       Confirmed       2     Se       0 studies fo       CBCL Withd       1     not       1     not       Moderate       1     se       Heavy     not       1     not       0 studies fo       CBCL Somat       Any PAE       1     se       CBCL Somat       Any PAE       1     se       Se	for any, co ndrawn/De serious <sup>a</sup> d unquant serious <sup>a</sup> for light, m ndrawn/De ot serious	nfirmed unqua epressed Caregi not serious ifiable not serious epressed Caregi not serious	ntifiable, mod iver Report (T- not serious not serious y or very heav- iver Report (O not serious	erate or very l -score) not serious serious <sup>f</sup> y R) (Odds of sco	none none	2518 107 inical ran	7201 188 ge')	OR 2.82 (1.07 to 7.43)	(0.03 higher to 0.12 higher) SMD 0.80 higher (0.55 higher to	Moderate
1     not       0 studies fo       CBCL Withd       Any PAE       1     Se       Confirmed       2     Se       0 studies fo       CBCL Withd       Light       1     not       Moderate       1     se       Heavy     1       1     not       O studies fo       CBCL Somat       Any PAE       1     se       CBCL Somat       Any PAE       1     se       Confirmed	for any, co ndrawn/De serious <sup>a</sup> d unquant serious <sup>a</sup> for light, m ndrawn/De ot serious	nfirmed unqua epressed Caregi not serious ifiable not serious epressed Caregi not serious	ntifiable, mod iver Report (T- not serious not serious y or very heav- iver Report (O not serious	erate or very l -score) not serious serious <sup>f</sup> y R) (Odds of sco	none none	2518 107 inical ran	7201 188 ge')	(1.07 to 7.43) - - - OR 0.56	(0.03 higher to 0.12 higher) SMD 0.80 higher (0.55 higher to	Moderate
O studies fo CBCL Withd Any PAE 1 Se Confirmed 2 Se 0 studies fo CBCL Withd Light 1 not Moderate 1 Se Heavy 1 not 0 studies fo CBCL Somat Any PAE 1 Se Confirmed	for any, co ndrawn/De serious <sup>a</sup> d unquant serious <sup>a</sup> for light, m ndrawn/De ot serious	nfirmed unqua epressed Caregi not serious ifiable not serious epressed Caregi not serious	ntifiable, mod iver Report (T- not serious not serious y or very heav- iver Report (O not serious	erate or very l -score) not serious serious <sup>f</sup> y R) (Odds of sco	none none	2518 107 inical ran	7201 188 ge')	(1.07 to 7.43) - - - OR 0.56	(0.03 higher to 0.12 higher) SMD 0.80 higher (0.55 higher to	Moderate
CBCL Withd Any PAE 1 Se Confirmed 2 Se 0 studies fo CBCL Withd Light 1 not Moderate 1 Se Heavy 1 not 0 studies fo CBCL Somat Any PAE 1 Se Confirmed	drawn/De serious <sup>a</sup> d unquant serious <sup>a</sup> for light, m ndrawn/De ot serious	pressed Caregi not serious ifiable not serious oderate, heavy pressed Caregi not serious	iver Report (T- not serious not serious y or very heav iver Report (O not serious	-score) not serious serious <sup>f</sup> y R) (Odds of sco	none none oring in 'cl	107 inical ran	188 ge')	- - OR 0.56	(0.03 higher to 0.12 higher) SMD 0.80 higher (0.55 higher to	Moderate ⊕⊕⊖⊖ Low
CBCL Withd Any PAE 1 Se Confirmed 2 Se 0 studies fo CBCL Withd Light 1 not Moderate 1 Se Heavy 1 not 0 studies fo CBCL Somat Any PAE 1 Se Confirmed	drawn/De serious <sup>a</sup> d unquant serious <sup>a</sup> for light, m ndrawn/De ot serious	pressed Caregi not serious ifiable not serious oderate, heavy pressed Caregi not serious	iver Report (T- not serious not serious y or very heav iver Report (O not serious	-score) not serious serious <sup>f</sup> y R) (Odds of sco	none none oring in 'cl	107 inical ran	188 ge')		(0.03 higher to 0.12 higher) SMD 0.80 higher (0.55 higher to	Moderate ⊕⊕⊖⊖ Low
Any PAE       1     Set       1     Set       2     Set       0 studies fo     CBCL Withd       1     not       Moderate     1       1     set       0 studies fo     CBCL Somate       1     not       0 studies fo     CBCL Somate       1     set       1     set       1     set       0 studies fo     CBCL Somate       1     set       1     set	serious <sup>a</sup> d unquant serious <sup>a</sup> for light, m ndrawn/De ot serious	not serious ifiable not serious oderate, heavy pressed Caregi not serious	not serious not serious y or very heavy iver Report (O not serious	not serious serious <sup>f</sup> Y R) (Odds of sc	none oring in 'cl	107 inical ran	188 ge')		(0.03 higher to 0.12 higher) SMD 0.80 higher (0.55 higher to	Moderate ⊕⊕⊖⊖ Low
1     set       2     set       2     set       0 studies fo     costudies fo       CBCL Withd     not       1     not       Moderate     1       1     not       O studies fo     costudies fo       CBCL Somat     Any PAE       1     set       1     set       Confirmed     set	d unquant serious <sup>a</sup> for light, m ndrawn/De ot serious	ifiable not serious oderate, heavy pressed Caregi not serious	not serious y or very heavy iver Report (O not serious	serious <sup>f</sup> y R) (Odds of sc	none oring in 'cl	107 inical ran	188 ge')		(0.03 higher to 0.12 higher) SMD 0.80 higher (0.55 higher to	Moderate ⊕⊕⊖⊖ Low
Confirmed 2 Se 0 studies fo CBCL Withd Light 1 not Moderate 1 Se Heavy 1 not 0 studies fo CBCL Somat Any PAE 1 Se Confirmed	d unquant serious <sup>a</sup> for light, m ndrawn/De ot serious	ifiable not serious oderate, heavy pressed Caregi not serious	not serious y or very heavy iver Report (O not serious	serious <sup>f</sup> y R) (Odds of sc	none oring in 'cl	107 inical ran	188 ge')		(0.03 higher to 0.12 higher) SMD 0.80 higher (0.55 higher to	Moderate ⊕⊕⊖⊖ Low
2     set       0 studies fo       CBCL Withd       Light       1     not       Moderate       1     set       Heavy       1     not       0 studies fo       CBCL Somat       Any PAE       1     set       1     set       Confirmed	serious <sup>a</sup> for light, m ndrawn/De ot serious	not serious oderate, heavy pressed Caregi not serious	y or very heave iver Report (O not serious	y R) (Odds of sco	oring in 'cl	inical ran	ge')		(0.55 higher to	Low
0 studies fo CBCL Withd 1 not Moderate 1 so Heavy 1 not 0 studies fo CBCL Somat Any PAE 1 so Confirmed	for light, m ndrawn/De ot serious	oderate, heavy pressed Caregi not serious	y or very heave iver Report (O not serious	y R) (Odds of sco	oring in 'cl	inical ran	ge')		(0.55 higher to	Low
CBCL Withd Light 1 not Moderate 1 se Heavy 1 not 0 studies fo CBCL Somat Any PAE 1 se Confirmed	ot serious	pressed Careg	not serious	R) (Odds of sc	-				1 1	
Light 1 not Moderate 1 se Heavy 1 not 0 studies fo CBCL Somat Any PAE 1 se Confirmed	ot serious	not serious	not serious		-				1	
1     not       Moderate     1       1     se       Heavy     1       1     not       0 studies fo     CBCL Somate       Any PAE     1       1     se       Confirmed	2			serious <sup>d</sup>	none	208	600		, , , , , , , , , , , , , , , , , , ,	
1     not       Moderate     1       1     se       Heavy     1       1     not       0 studies fo     CBCL Somate       Any PAE     1       1     se       Confirmed	2			serious <sup>d</sup>	none	208	600		1	
1     set       Heavy     1       1     not       0 studies fo       CBCL Somat       Any PAE       1     set       1     set       Confirmed		not serious	- -				030	(0.27 to 1.15)		⊕⊕⊕⊖ Moderate
Heavy 1 not 0 studies fo CBCL Somat Any PAE 1 se Confirmed	serious <sup>a</sup>	not serious	1						• • • •	
1     not       0 studies fo       CBCL Somat       Any PAE       1     se       Confirmed			not serious	Serious <sup>d,e</sup>	none	389	117	<b>OR 1.30</b> (0.50 to 3.40)		⊕⊕⊖⊖ Low
0 studies fo CBCL Somat Any PAE 1 Se Confirmed								, , , , , , , , , , , , , , , , , , ,	1 1	
CBCL Somat Any PAE 1 se Confirmed	ot serious	not serious	not serious	Serious <sup>d,e</sup>	none	57	690	<b>OR 1.26</b> (0.48 to 3.30)		⊕⊕⊕⊖ Moderate
Any PAE 1 se Confirmed	for any, co	nfirmed unqua	ntifiable or ve	ry heavy						
1 se Confirmed	atic Comp	laints Caregive	r Report (T-sco	ore)						
Confirmed										
	serious <sup>a</sup>	not serious	not serious	not serious	none	2518	7201	-	SMD 0.12 higher (0.07 higher to 0.16 higher)	⊕⊕⊕⊖ Moderate
2 se	d unquant	ified	-						• • • •	
	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	107	188	-	SMD 0.63 higher (0.08 higher to 1.19 higher)	⊕⊕⊖⊖ Low
0 studies fo	for light, m	oderate, heavy	y or very heav	y						
CBCL Somat	atic Comp	laints Caregive	r Report (Freq	uency/OR) (Oo	dds of scor	ing in 'cli	nical rang	ge')		
Light										
		not serious	not serious	serious <sup>d</sup>	none	208	690	<b>OR 1.07</b> (0.61 to 1.88)	<b>1 fewer per 1,000</b> (from 2 fewer to 1 fewer)	⊕⊕⊕⊖ Moderate
Moderate	ot serious									
1 se			not serious	Serious <sup>d,e</sup>	none	389	117	<b>OR 1.41</b> (0.60 to 3.30)	1 fewer per 1,000 (from 3 fewer to 1 fewer)	⊕⊕⊖⊖ Low
Heavy		not serious	not schous					5.557		

1	not serious	not serious	not serious	serious <sup>e</sup>	none	57	690	<b>OR 2.74</b> (1.47 to 5.12)	<b>3 fewer per 1,000</b> (from 5 fewer to 1 fewer)	⊕⊕⊕⊖ Moderate
0 studie	s for any, co	nfirmed unqua	ntifiable or ve	ry heavy		1 1		0.122)	,	
CBCL Th	ought Prob	lems Caregiver I	Report (T-scor	e)						
Any PAI	-	0	1 1	,						
1	serious <sup>a</sup>	not serious	not serious	not serious	none	2518	7201	-	SMD 0.14 higher (0.09 higher to 0.18 higher)	⊕⊕⊕⊖ Moderate
Confirm	ed unquant	tified								
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	107	188	-	<b>SMD 0.92 higher</b> (0.66 higher to 1.17 higher)	⊕⊕⊖⊖ Low
0 studie	s for light, n	noderate, heavy	or very heav	Y						
CBCL Th	ought Prob	lems Caregiver I	Report (Frequ	ency/OR) (Odd	ds of scorin	g in 'clini	cal range	e')		
Light										
1	not serious	not serious	not serious	serious <sup>d</sup>	none	208	690	<b>OR 1.12</b> (0.51 to 2.47)		⊕⊕⊕⊖ Moderate
Heavy										
1	not serious	not serious	not serious	serious <sup>d,e</sup>	none	57	690	<b>OR 0.84</b> (0.15 to 4.69)		⊕⊕⊕⊖ Moderate
0 studie	s for any, co	onfirmed unqua	ntifiable, mod	erate or very	heavy PAE					
BITSEA -	– Maternal I	Report (adjusted	d odds of scor	ing <1SD belov	w the mear	n): Possik	le Proble	em		
Modera	te PAE									
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	74	126	<b>aOR 0.59</b> (0.23 to 1.53)	-	⊕⊕⊕⊖ Moderate
BITSEA -	– Maternal I	Report (adjusted	d odds of scor	ing <1SD belov	w the mear	n): Possib	le Comp	,	cit	
Modera	te PAE					-				
1	not serious	not serious	not serious	serious <sup>d,f</sup>	none	74	126	<b>aOR 1.17</b> (0.47 to 2.90)	-	⊕⊕⊕⊖ Moderate
Infant B	ehaviour Qu	uestionnaire Car	egiver Report	: Negative Eff	ect			•		
Modera	te PAE									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	74	126	-	SMD 0.55 higher (0.13 higher to 0.97 higher)	⊕⊕⊖⊖ Low
Infant B	ehaviour Qu	uestionnaire Car	egiver Report	: Effortful Con	trol					
Modera	te PAE									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	74	126	-	SMD 0.08 higher (0.33 lower to 0.50 higher)	⊕⊕⊖⊖ Low
DIAGNO	SED STUDI	ES					I	l	mgner)	
		ur Caregiver Rep	port (Frequen	cv/OR) (Odds)	of scoring i	n 'clinica	range' >	63 T-score)		
FASD			Jon (in equelit					55 1 30010)		
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	73	40	OR 25.09 (1.47 to 429.38)	-	⊕⊕⊖⊖ Low
CBCL To	tal Behavio	ur Caregiver Rep	port (T-score)							

FASD										
9	serious <sup>a</sup>	serious <sup>b</sup>	not serious	not serious	none	390	322	-	SMD 1.52 higher (1.14 higher to 1.91 higher)	⊕⊕⊖⊖ Low
FAS										
3	serious <sup>a</sup>	not serious	not serious	not serious	none	73	386	-	SMD 0.62 higher (0.35 higher to 0.89 higher)	⊕⊕⊕⊖ Moderate
pFAS										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	37	319	-	<b>SMD 1.10 higher</b> (0.39 higher to 1.81 higher)	⊕○○○ Very low
0 studie	s for ARND/	Others								
TRF Tota	al Behaviour	Teacher Repor	t (T-score)							
FASD										
2	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	155	75	-	SMD 0.88 higher (0.58 higher to 1.17 higher)	⊕⊕⊖⊖ Low
FAS									· · · ·	
2	serious <sup>a</sup>	not serious	serious <sup>c</sup>	not serious	none	135	293	-	SMD 0.53 higher (0.31 higher to 0.74 higher)	⊕⊕⊖⊖ Low
pFAS										
2	seriousª	not serious	serious <sup>c</sup>	not serious	none	139	293	-	SMD 0.54 higher (0.33 higher to 0.74 higher)	⊕⊕⊖⊖ Low
ARND/C	Others		•							
2	serious <sup>a</sup>	not serious	serious <sup>c</sup>	serious <sup>f</sup>	none	74	293	-	SMD 0.91 higher (0.65 higher to 1.18 higher)	⊕○○○ Very low
SSRS To	tal Behaviou	r Caregiver Rep	oort (m/SD)							
FASD										
1	seriousª	not serious	not serious	serious <sup>f</sup>	none	30	30	-	SMD 1.63 higher (1.04 higher to 2.22 higher)	⊕⊕⊖⊖ Low
SSRS To	tal Behaviou	r Teacher Repo	ort (m/SD)							
FASD										
2	seriousª	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	42	42	-	<b>SMD 2.22 higher</b> (0.22 lower to 4.66 higher)	⊕○○○ Very low
ASR Tota	al Behaviour	Self Report (T-	score)							
pFAS										
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	47	58	-	SMD 2.61 higher (2.08 higher to 3.14 higher)	⊕⊕⊖⊖ Low
ARND/C	Others									
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	34	58	-	SMD 4.59 higher (3.79 higher to 5.39 higher)	⊕⊕⊖⊖ Low
0 studie	s for FASD o	r FAS								
CBCL To	tal Externali	sing Behaviour	Caregiver Rep	ort (T-score)						
FASD										

9	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	318	990	-	SMD 0.93 higher	000
									(0.59 higher to 1.26 higher)	Very Low
AS										
2	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	30	80	-	<b>SMD 0.29 higher</b> (0.22 lower to 0.81 higher)	⊕○○○ Very Low
oFAS										
2	seriousª	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	64	787	-	<b>SMD 0.97 higher</b> (0.34 lower to 2.27 higher)	⊕○○○ Very low
ARND/C	Others									
3	seriousª	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	95	822	-	SMD 0.95 higher (0.29 higher to 1.62 higher)	⊕○○○ Very low
CBCL/SI	B-R Total Ext	ernalising Beha	aviour Caregiv	er Report (Od	ds of 'marg	inally se	rious' and	d 'moderate	to serious' score, o	dds of
scoring	in 'clinical ra	nge' >63 CBCL <sup>·</sup>	T-score)							
FASD										
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	96	63	<b>OR 15.54</b> (2.76 to 87.50)		⊕⊕⊖⊖ Low
0 studie	s for FAS, pF	AS or ARND/Ot	hers:							
SSRS To	tal Externalis	sing Behaviour	Caregiver Rep	ort (m/sd)						
FASD										
1	seriousª	not serious	not serious	very serious <sup>d,e,f</sup>	none	23	37	-	SMD 0.02 lower (0.54 lower to 0.51 higher)	⊕○○○ Very Low
0 studie	s for FAS, pF	AS or ARND/Ot	hers							
TRF Tot	al Externalisi	ng Behaviour T	eacher Report	t (T-score)						
FASD		-	•							
5	serious <sup>a</sup>	not serious	not serious	not serious	none	254	1132	1	SMD 0.78 higher	
_	serious	not serious	not serious	not senous	none	234	1152	-	(0.52 higher to 1.05 higher)	⊕⊕⊕⊖ Moderate
FAS										
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	5	771	-	<b>SMD 0.64 higher</b> (0.24 lower to 1.52 higher)	⊕⊕⊖⊖ Low
pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	771	-	<b>SMD 0.07 lower</b> (0.37 lower to 0.24 higher)	⊕⊕⊖⊖ Low
ARND/O	Others									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	44	71	-	SMD 0.82 higher (0.51 higher to 1.12 higher)	⊕⊕⊖⊖ Low
SSRS To	tal Externalis	sing Behaviour	Teacher Repo	rt (m/sd)						
FASD										
1	seriousª	not serious	not serious	very serious <sup>d,e,f</sup>	none	23	37	-	SMD 0.24 lower (0.77 lower to 0.28 higher)	⊕○○○ Very Low
0 studie	s for FAS, pF	AS or ARND/Ot	hers							
ASR Tot	al Externalis	ing Behaviour S	elf Report (T-s	score)						
oFAS		-								

1										
-	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	47	58	-	SMD 2.00 higher (1.53 higher to 2.47 higher)	⊕⊕⊖⊖ Low
ARND/	) Others								2.47 mgner/	
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	34	58	-	SMD 4.08 higher (3.34 higher to 4.82 higher)	⊕⊕⊖⊖ Low
0 studie	s for FASD o	r FAS								
CBCL To	otal Internali	sing Behaviour	Caregiver Rep	ort (T-score)						
FASD										
10	seriousª	serious <sup>b</sup>	not serious	not serious	none	440	1278	-	SMD 0.64 higher (0.41 higher to 0.87 higher)	⊕⊕⊖⊖ Low
FAS										
2	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	30	806	-	<b>SMD 0.15 lower</b> (0.59 lower to 0.30 higher)	⊕⊕⊖⊖ Low
pFAS										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>d,e</sup>	none	68	787	-	SMD 1.19 higher (0.53 lower to 2.90 higher)	⊕○○○ Very low
ARND/	Others		•							
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>d,e</sup>	none	95	822	-	SMD 0.69 higher (0.06 lower to	<b>⊕</b> 000
				er Report (Odd	ls of 'marg	inally ser	rious' and	'moderate	1.44 higher) to serious' score, or	Very low
CBCL/SI in 'clinic		ernalising Beha 3 CBCL T-score) not serious		er Report (Odd serious <sup>e,f</sup>	ls of 'marg none	inally ser	rious' and	'moderate OR 15.47 (2.86 to	1.44 higher)	
CBCL/SI in 'clinic FASD 2	cal range' >6	3 CBCL T-score) not serious	not serious					OR 15.47	1.44 higher)	dds of scorin ⊕⊕○○
CBCL/SI in 'clinic FASD 2 0 studie	serious <sup>a</sup> serious <sup>a</sup>	3 CBCL T-score) not serious AS and ARND/0	not serious Others	serious <sup>e,f</sup>				<b>OR 15.47</b> (2.86 to	1.44 higher)	dds of scorin ⊕⊕○○
CBCL/SI in 'clinic <b>FASD</b> 2 0 studie SSRS To	serious <sup>a</sup> serious <sup>a</sup>	3 CBCL T-score) not serious	not serious Others	serious <sup>e,f</sup>				<b>OR 15.47</b> (2.86 to	1.44 higher)	dds of scorin ⊕⊕○○
CBCL/SI in 'clinic FASD 2 0 studie SSRS To FASD	serious <sup>a</sup> serious <sup>a</sup> s for FAS, pF tal Internalis	3 CBCL T-score) not serious AS and ARND/0 ing Behaviour 0	not serious Dthers Caregiver Repo	serious <sup>e,f</sup> ort (m/sd)	none	96	63	<b>OR 15.47</b> (2.86 to	1.44 higher) to serious' score, or -	dds of scorin ⊕⊕○○ Low
CBCL/SI in 'clinic <b>FASD</b> 2 0 studie SSRS To	serious <sup>a</sup> serious <sup>a</sup>	3 CBCL T-score) not serious AS and ARND/0	not serious Others	serious <sup>e,f</sup>				<b>OR 15.47</b> (2.86 to	1.44 higher)	dds of scorin ⊕⊕○○
CBCL/SI in 'clinic FASD 2 0 studie SSRS To FASD 1 0 studie	serious <sup>a</sup> serious <sup>a</sup> s for FAS, pF tal Internalis serious <sup>a</sup>	3 CBCL T-score) not serious AS and ARND/0 ing Behaviour ( not serious	not serious Others Caregiver Repo not serious Others	serious <sup>e,f</sup> ort (m/sd) very serious <sup>d,e,f</sup>	none	96	63	<b>OR 15.47</b> (2.86 to	1.44 higher) to serious' score, ou - - SMD 0.37 higher (0.16 lower to	dds of scorin ⊕⊕○○ Low
CBCL/SI in 'clinic FASD 2 0 studie SSRS To FASD 1 0 studie TRF/CB	serious <sup>a</sup> serious <sup>a</sup> s for FAS, pF tal Internalis serious <sup>a</sup>	3 CBCL T-score) not serious AS and ARND/( sing Behaviour ( not serious	not serious Others Caregiver Repo not serious Others	serious <sup>e,f</sup> ort (m/sd) very serious <sup>d,e,f</sup>	none	96	63	<b>OR 15.47</b> (2.86 to	1.44 higher) to serious' score, ou - - SMD 0.37 higher (0.16 lower to	dds of scorin ⊕⊕○○ Low
CBCL/SI in 'clinic FASD 2 0 studie SSRS To FASD 1 0 studie	serious <sup>a</sup> serious <sup>a</sup> s for FAS, pF tal Internalis serious <sup>a</sup>	3 CBCL T-score) not serious AS and ARND/0 ing Behaviour ( not serious	not serious Others Caregiver Repo not serious Others	serious <sup>e,f</sup> ort (m/sd) very serious <sup>d,e,f</sup>	none	96	63	<b>OR 15.47</b> (2.86 to	1.44 higher) to serious' score, ou - - SMD 0.37 higher (0.16 lower to	dds of scorin ⊕⊕○○ Low
CBCL/SI in 'clinic FASD 2 0 studie SSRS To FASD 1 0 studie TRF/CB	serious <sup>a</sup> serious <sup>a</sup> s for FAS, pF tal Internalis serious <sup>a</sup>	3 CBCL T-score) not serious AS and ARND/0 ing Behaviour ( not serious	not serious Others Caregiver Repo not serious Others	serious <sup>e,f</sup> ort (m/sd) very serious <sup>d,e,f</sup>	none	96	63	<b>OR 15.47</b> (2.86 to	1.44 higher) to serious' score, ou - - SMD 0.37 higher (0.16 lower to	dds of scorin ⊕⊕○○ Low
CBCL/SI in 'clinic FASD 2 0 studie SSRS To FASD 1 0 studie TRF/CBU FASD 5	serious <sup>a</sup> serious <sup>a</sup> s for FAS, pF tal Internalis serious <sup>a</sup> s for FAS, pF CL Total Inte	3 CBCL T-score) not serious AS and ARND/0 ing Behaviour ( not serious AS and ARND/0 rnalising Behav	not serious Others Caregiver Repo not serious Others iour Teacher F	serious <sup>e,f</sup> ort (m/sd) very serious <sup>d,e,f</sup> Report (T-score	none none	96	63	<b>OR 15.47</b> (2.86 to	1.44 higher) to serious' score, ou - SMD 0.37 higher (0.16 lower to 0.89 higher) SMD 0.68 higher (0.51 higher to	dds of scorin ⊕⊕⊖⊖ Low ⊕⊖⊖⊖ Very Low
CBCL/SI in 'clinic FASD 2 0 studie SSRS To FASD 1 0 studie TRF/CBU FASD 5	serious <sup>a</sup> serious <sup>a</sup> s for FAS, pF tal Internalis serious <sup>a</sup> s for FAS, pF CL Total Inte	3 CBCL T-score) not serious AS and ARND/0 ing Behaviour ( not serious AS and ARND/0 rnalising Behav	not serious Others Caregiver Repo not serious Others iour Teacher F	serious <sup>e,f</sup> ort (m/sd) very serious <sup>d,e,f</sup> Report (T-score	none none	96	63	<b>OR 15.47</b> (2.86 to	1.44 higher) to serious' score, ou - SMD 0.37 higher (0.16 lower to 0.89 higher) SMD 0.68 higher (0.51 higher to	dds of scorin ⊕⊕⊖⊖ Low ⊕⊖⊖⊖ Very Low
CBCL/SI in 'clinic FASD 2 0 studie SSRS To FASD 1 0 studie TRF/CB0 FASD 5 FAS	serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup>	3 CBCL T-score) not serious AS and ARND/( ing Behaviour ( not serious AS and ARND/( rnalising Behav not serious	not serious Others Caregiver Repo not serious Others iour Teacher F not serious	serious <sup>e,f</sup> ort (m/sd) very serious <sup>d,e,f</sup> Report (T-score not serious	none none	96 37 251	63	<b>OR 15.47</b> (2.86 to	1.44 higher) to serious' score, ou - - SMD 0.37 higher (0.16 lower to 0.89 higher) SMD 0.68 higher (0.51 higher to 0.85 higher) SMD 0.30 higher (0.58 lower to	dds of scorin $\oplus \oplus \bigcirc \bigcirc$ Low $\oplus \bigcirc \bigcirc \bigcirc$ Very Low $\oplus \oplus \oplus \bigcirc$ Moderate $\oplus \oplus \bigcirc \bigcirc$

ARND/0	Others									
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	44	771	-	SMD 0.48 higher (0.18 higher to 0.79 higher)	⊕⊕⊖⊖ Low
	tal Internalis	sing Behaviour	Teacher Repo	rt (T-score)						
FASD 1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	37	23	-	SMD 0.22 higher (0.30 lower to	⊕○○○ Very Low
									0.74 higher)	,
	-	AS or ARND/O								
	al Internalisi	ng Behaviour A	dult Report (T	-score)						
pFAS			1							
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	47	58	-	SMD 3.56 higher (2.94 higher to 4.19 higher)	⊕⊕⊖⊖ Low
ARND/0	Others							-		
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	34	58	-	<b>SMD 3.91 higher</b> (3.20 higher to 4.63 higher)	⊕⊕⊖⊖ Low
0 studie	es for FASD o	r FAS								
CBCL Co	onduct Probl	ems Caregiver I	Report (T-scor	e)						
FASD										
4	serious <sup>a</sup>	not serious	not serious	not serious	none	143	1087	-	SMD 0.52 higher (0.35 higher to 0.70 higher)	⊕⊕⊕⊖ Moderate
FAS										
1	serious <sup>a</sup>	not serious	not serious	not serious	none	5	761	-	<b>SMD 0.19 higher</b> (0.69 lower to 1.07 higher)	⊕⊕⊕⊖ Moderate
pFAS			•							
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	<b>SMD 0.13 higher</b> (0.17 lower to 0.44 higher)	⊕⊕⊖⊖ Low
ARND/0	Others	•								
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	44	761	-	<b>SMD 1.06 higher</b> (0.75 higher to 1.37 higher)	⊕⊕⊖⊖ Low
TRF Cor	nduct Proble	ms Teacher Rep	oort (T-score)							
FASD										
4	seriousª	not serious	not serious	not serious	none	128	1098	-	SMD 0.59 higher (0.32 higher to 0.86 higher)	⊕⊕⊕⊖ Moderate
FAS									· · · · ·	
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	<b>SMD 0.03 higher</b> (0.85 lower to 0.91 higher)	⊕⊕⊖⊖ Low
pFAS	-		-	·		<u> </u>	-		· · · I	
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	<b>SMD 0.02 higher</b> (0.29 lower to 0.32 higher)	⊕⊕⊖⊖ Low
ARND/0	Others									
1	serious⁵	not serious	not serious	serious <sup>e</sup>	none	44	761	-	SMD 0.82 higher (0.52 higher to 1.13 higher)	⊕⊕⊖⊖ Low
			•							

FASD 4 FAS 1 PFAS 1 ARND/Ot 1 Vanderbil FASD 1	serious <sup>a</sup> serious <sup>a</sup> serious <sup>a</sup> :hers serious <sup>a</sup>	not serious not serious not serious not serious not serious	not serious not serious not serious	not serious serious <sup>d</sup> serious <sup>e</sup>	none	143       5       44	1087 761 761	-	SMD 0.46 higher (0.20 higher to 0.72 higher) SMD 0.25 higher (0.63 lower to 1.13 higher) SMD 0.37 higher	$ \begin{array}{c}                                     $
FAS 1 pFAS 1 ARND/Ot 1 Vanderbil FASD 1	serious <sup>a</sup> serious <sup>a</sup> :hers serious <sup>a</sup> It-C Opposi	not serious not serious not serious	not serious not serious not serious	serious <sup>d</sup> serious <sup>e</sup>	none	5	761	-	(0.20 higher to 0.72 higher) SMD 0.25 higher (0.63 lower to 1.13 higher) SMD 0.37 higher	Moderate ⊕⊕⊖⊖ Low
1 pFAS 1 ARND/Ot 1 Vanderbil FASD 1	serious <sup>a</sup> : <b>hers</b> serious <sup>a</sup> It-C Opposi	not serious not serious	not serious not serious	serious <sup>e</sup>	none			-	(0.63 lower to 1.13 higher) SMD 0.37 higher	Low
pFAS 1 ARND/Ot 1 Vanderbil FASD 1	serious <sup>a</sup> : <b>hers</b> serious <sup>a</sup> It-C Opposi	not serious not serious	not serious not serious	serious <sup>e</sup>	none			-	(0.63 lower to 1.13 higher) SMD 0.37 higher	Low
1 ARND/Ot 1 Vanderbil FASD 1	thers serious <sup>a</sup> lt-C Opposi	not serious	not serious			44	761	-	-	⊕⊕⊖⊖
ARND/Ot 1 Vanderbil FASD 1	thers serious <sup>a</sup> lt-C Opposi	not serious	not serious			44	761	-	-	$\oplus \oplus \bigcirc \bigcirc$
1 Vanderbil FASD	serious <sup>a</sup> lt-C Opposi			serious <sup>e</sup>	none				(0.06 higher to 0.67 higher)	Low
Vanderbil FASD	lt-C Opposi			serious <sup>e</sup>	none					
FASD 1		tional Defiant [	Disorder Careg			44	761	-	SMD 1.29 higher (0.98 higher to 1.60 higher)	⊕⊕⊖⊖ Low
1	seriousª			giver Report (n	n/sd)					
	serious <sup>a</sup>									
0 studies		not serious	not serious	serious <sup>e,f</sup>	none	16	21	-	<b>SMD 1.67 higher</b> (0.91 higher to 2.44 higher)	⊕⊕⊖⊖ Low
	for FAS, pF	AS and ARND/(	Others							
TRF Oppo	sitional De	fiant Disorder 1	Teacher Repor	rt (T-score)						
FASD										
4	seriousª	not serious	not serious	not serious	none	128	1098	-	SMD 0.42 higher (0.17 higher to 0.66 higher)	⊕⊕⊕⊖ Moderate
FAS										
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	5	761	-	<b>SMD 0.92 higher</b> (0.04 higher to 1.81 higher)	⊕⊕⊖⊖ Low
pFAS										
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	<b>SMD 0.11 higher</b> (0.19 lower to 0.41 higher)	⊕⊕⊖⊖ Low
ARND/Ot	thers									
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	44	761	-	SMD 0.76 higher (0.46 higher to 1.07 higher)	⊕⊕⊖⊖ Low
			<del>بر</del> ۱							
CBCL Aggr FASD	ression Car	egiver Report (	I-score)							
	coriousa	serious <sup>b</sup>	not corious	coriouse	2000	176	1120		SMD 0 60 bishes	
	serious <sup>a</sup>	senous	not serious	serious <sup>e</sup>	none	1/0	1120	-	<b>SMD 0.69 higher</b> (0.36 higher to 1.03 higher)	⊕○○○ Very low
FAS			1							
1	seriousª	not serious	not serious	serious <sup>d</sup>	none	5	761	-	<b>SMD 0.18 higher</b> (0.70 lower to 1.06 higher)	⊕⊕⊖⊖ Low
pFAS			1	<u> </u>		<u> </u>				
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	44	761	-	SMD 0.35 higher (0.05 higher to 0.66 higher)	⊕⊕⊖⊖ Low

ARND/	Others									
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	44	761	-	SMD 1.26 higher (0.95 higher to 1.57 higher)	⊕⊕⊖⊖ Low
TRF Agg FASD	ression lead	cher Report (T-s	score)							
4	seriousª	not serious	not serious	not serious	none	128	1098	-	SMD 0.52 higher (0.25 higher to 0.79 higher)	⊕⊕⊕⊖ Moderate
FAS			•					•		
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	SMD 0.64 higher (0.24 lower to 1.52 higher)	⊕⊕⊖⊖ Low
pFAS	•					<u> </u>				
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	<b>SMD 0.12 higher</b> (0.18 lower to 0.43 higher)	⊕⊕⊖⊖ Low
ARND/	Others		•							
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	44	761	-	SMD 0.79 higher (0.48 higher to 1.09 higher)	⊕⊕⊖⊖ Low
ASR Agg	gression Self	Report (T-score	2)							
pFAS										
1	seriousª	not serious	not serious	serious <sup>e, f</sup>	none	47	58	-	SMD 2.48 higher (1.96 higher to 2.99 higher)	⊕⊕⊖⊖ Low
ARND/	Others									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	34	58	-	SMD 4.39 higher (3.62 higher to 5.17 higher)	⊕⊕⊖⊖ Low
0 studie	s for FASD a	nd FAS							- 0-,	
CBCL Rι	ule-Breaking	Behaviour Care	giver Report (	T-score)						
FASD										
5	seriousª	serious⁵	not serious	serious <sup>e</sup>	none	176	1120	-	SMD 0.48 higher (0.19 higher to 0.77 higher)	⊕○○○ Very Low
FAS	•		•			•	-	•		
2	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	30	796	-	<b>SMD 0.45 higher</b> (0.06 lower to 0.96 higher)	⊕⊕⊖⊖ Low
pFAS	1		ī			1	1	T		
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	44	761	-	SMD 0.19 higher (0.02 lower to 0.49 higher)	⊕⊕⊖⊖ Low
ARND/	Others									
2	seriousª	serious <sup>b</sup>	not serious	serious <sup>e</sup>	none	106	796	-	SMD 0.76 higher (0.20 higher to 1.31 higher)	⊕○○○ Very low
unclear		eaking Behaviou	ır Caregiver Re	eport (Freque	ncy of 'mar	ginally se	erious' an	d 'moderate	e to serious' score/o	cut-off
FASD		a state h		east-ru of		27	40	00.5.34	1 1	
2	serious <sup>a</sup>	serious⁵	not serious	serious <sup>e,f</sup>	none	37	49	<b>OR 5.31</b> (1.93 to 14.60	-	⊕○○○ Very low

0 studie	s for FAS, pF	AS and ARND/	Others							
rrf/cb	CL Rule-Brea	king Behaviour	Teacher Repo	ort (T-score)						
ASD										
3	seriousª	not serious	not serious	not serious	none	124	1048	-	SMD 0.60 higher (0.41 higher to 0.79 higher)	⊕⊕⊕⊖ Moderate
AS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	<b>SMD 0.00</b> (0.88 lower to 0.88 higher)	⊕⊕⊖⊖ Low
oFAS			-							
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	SMD 0.02 higher (0.29 lower to 0.32 higher)	⊕⊕⊖⊖ Low
ARND/0	Others									
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	44	761	-	SMD 0.80 higher (0.49 higher to 1.10 higher)	⊕⊕⊖⊖ Low
	e-Breaking B	ehaviour Self R	eport (T-score	e)						
pFAS			T			•				
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	47	58	-	SMD 1.25 higher (0.82 higher to 1.67 higher)	⊕⊕⊖⊖ Low
ARND/0	Others									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	34	58	-	SMD 1.26 higher (0.79 higher to 1.72 higher)	⊕⊕⊖⊖ Low
0 studie	s for FASD o	r FAS								
CBRS Hy	peractivity (	Caregiver Repo	rt (T-score)							
FASD										
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	25	13	-	SMD 2.10 higher (1.26 higher to 2.94 higher)	⊕⊕⊖⊖ Low
) studie	s for FAS, pF	AS and ARND/	Others							
CBCL Ηγ	/peractivity (	Caregiver Repo	rt (Frequency/	'OR) (Cut-off u	nclear)					
ASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	16/17 (94.1%	10/26 (38.5%)	<b>OR 25.60</b> (2.93 to 224.05)	<b>557 more per</b> <b>1000</b> (from 262 more to 608 more)	⊕⊕⊖⊖ Low
) studie	s for FAS, pF	AS and ARND/	Others							
DBD/SS	RS Hyperacti	vity Caregiver I	Report (m/SD)							
ASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	37	23	-	SMD 0.76 higher (0.22 higher to 1.30 higher)	⊕⊕⊖⊖ Low
oFAS										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	45	117	-	SMD 0.41 higher (0.30 lower to 1.13 higher)	⊕○○○ Very low
· · · · · · · · · · · · · · · · · · ·										
) studie	s for FAS and	d ARND/Others	;							

FASD										
1	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	37	23	-	<b>SMD 0.28 lower</b> (0.81 lower to 0.24 higher)	⊕○○○ Very low
pFAS	-	•	1	-			<b></b>			
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	45	117	-	SMD 0.39 higher (0.19 lower to 0.97 higher)	⊕○○○ Very low
0 studie	es for FAS, pl	AS and ARND	Others	1			<u> </u>			
CBCL At	ttention/Hyp	eractivity Care	giver Report (1	Г-score)						
FASD										
4	seriousª	not serious	not serious	not serious	none	143	1087	-	SMD 0.48 higher (0.30 higher to 0.66 higher)	⊕⊕⊕⊖ Moderate
FAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	761	-	<b>SMD 0.57 higher</b> (0.31 lower to 1.45 higher)	⊕⊕⊖⊖ Low
pFAS		T	1	<u>г</u>		1				
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	SMD 0.29 higher (0.01 lower to 0.60 higher)	⊕⊕⊖⊖ Low
ARND/	Others									
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	44	761	-	<b>SMD 1.08 higher</b> (0.77 higher to 1.39 higher)	⊕⊕⊖⊖ Low
CBCL/T	RF Attention	/Hyperactivity	Teacher Repoi	rt (T-score)			• • •			
FASD										
3	serious <sup>a</sup>	not serious	not serious	not serious	none	124	1048	-	SMD 0.65 higher (0.46 higher to 0.83 higher)	⊕⊕⊕⊖ Moderate
FAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	5	761	-	SMD 0.98 higher (0.10 higher to 1.86 higher)	⊕⊕⊖⊖ Low
pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	761	-	SMD 0.23 higher (0.08 lower to 0.53 higher)	⊕⊕⊖⊖ Low
ARND/	Others									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	44	761	-	SMD 0.85 higher (0.55 higher to 1.16 higher)	⊕⊕⊖⊖ LOw
CBCL/C	BRS Anxious	/Depressed Car	egiver Report	(T-score)			· .			
FASD										
7	serious <sup>a</sup>	not serious	not serious	not serious	none	239	1171	-	SMD 0.60 higher (0.40 higher to 0.80 higher)	⊕⊕⊕⊖ Moderate
FAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	771	-	<b>SMD 0.01 lower</b> (0.89 lower to 0.87 higher)	⊕⊕⊖⊖ Low
pFAS									(0.89 lower to	

1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	771	-	SMD 0.18 higher	$\oplus \oplus \bigcirc \bigcirc$
									(0.12 lower to	Low
									0.49 higher)	
ARND/C		-					<u> </u>			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	44	771	-	SMD 0.59 higher	$\oplus \oplus \bigcirc \bigcirc$
									(0.29 higher to 0.90 higher)	Low
Vander	hilt-C Anxiou	s/Depressed Ca	aregiver Renor	rt (m/sd)					0.90 fligher)	
ASD		3/ Depressed ea								
				· of		1.6				0 0
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	16	21	-	SMD 1.09 higher	$\oplus \oplus \bigcirc \bigcirc$
									(0.38 higher to 1.79 higher)	Low
) studie	s for FAS, pF	AS and ARND/	) Dthers						1.75 mgner/	
	-	sed Teacher Re								
FASD	lious/Depies	seu reacher ne	poit (1-30012)							
	• •					424	1010			
3	serious <sup>a</sup>	not serious	not serious	not serious	none	124	1048	-	SMD 0.67 higher (0.43 higher to	$\Theta \oplus \Theta \bigcirc$
									0.91 higher)	Moderate
FAS									0.51 mgner/	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	5	771		SMD 0.46 higher	$\oplus \oplus \bigcirc \bigcirc$
-	5011003	not serious	not serious	Schous	none	5	<i>,,,</i>		(0.42 lower to	Low
									1.34 higher)	2011
pFAS			•	-			-			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	771	-	SMD 0.19 higher	$\oplus \oplus \bigcirc \bigcirc$
									(0.11 lower to	Low
									0.50 higher)	
ARND/0	Others									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	44	771	-	SMD 0.36 higher	$\oplus \oplus \bigcirc \bigcirc$
									(0.05 higher to	Low
									0.66 higher)	
	nxious/Depre	essed Self-Repo	rt (T-score)							
pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	47	58	-	SMD 3.62 higher	$\oplus \oplus \bigcirc \bigcirc$
									(2.99 higher to	Low
									4.25 higher)	
ARND/0	-					1	<u>т т</u>			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>f</sup>	none	34	58	-	SMD 3.83 higher	$\Theta \Theta O O$
									(3.37 higher to	Low
CBCL Ar	viety Caregi	ver Report (T-so	Core)						4.29 higher)	
FASD	incer caregi									
						407	1000			
5	serious <sup>a</sup>	not serious	not serious	not serious	none	187	1099	-	SMD 0.60 higher (0.37 higher to	⊕⊕⊕⊖ Moderate
									0.82 higher)	mouchate
FAS	1		1	<u> </u>		1	<u>ı                                     </u>			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	5	771	-	SMD 0.07 higher	$\oplus \oplus \bigcirc \bigcirc$
-	501005	100 501005	not serious	501005	none				(0.81 lower to	Low
									0.95 higher)	
pFAS			•			•	- 1			
PI 73						1	т т			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	771	-	SMD 0.31 higher	$\oplus \oplus ()()$
	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	771	-	SMD 0.31 higher (0.00 to 0.61	⊕⊕⊖⊖ Low

ARND/	Others									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	44	771	-	SMD 0.54 higher (0.24 higher to 0.85 higher)	⊕⊕⊖⊖ Low
TRF An:	kiety Teacher	r Report (T-scor	e)							
FASD										
3	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	124	1048	-	SMD 0.76 higher (0.46 higher to 1.06 higher)	⊕⊕⊖⊖ Low
FAS										
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	5	771	-	<b>SMD 0.70 higher</b> (0.18 lower to 1.58 higher)	⊕⊕⊖⊖ Low
pFAS										
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	44	771	-	SMD 0.14 higher (0.17 lower to 0.44 higher)	⊕⊕⊖⊖ Low
ARND/	Others									
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	44	771	-	SMD 0.42 higher (0.12 higher to 0.73 higher)	⊕⊕⊖⊖ Low
CBCL W	'ithdrawn/De	epressed Careg	iver Report (T-	-score)						
FASD										
6	seriousª	not serious	not serious	not serious	none	215	1154	-	SMD 0.66 higher (0.41 higher to 0.90 higher)	⊕⊕⊕⊖ Moderate
FAS										
1	serious⁵	not serious	not serious	serious <sup>d</sup>	none	5	771	-	<b>SMD 0.11 lower</b> (0.99 lower to 0.77 higher)	⊕⊕⊖⊖ Low
pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	none	44	771	-	SMD 0.32 higher (0.01 higher to 0.62 higher)	⊕⊕⊖⊖ Low
ARND/	Others									
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	44	771	-	SMD 0.48 higher (0.18 higher to 0.78 higher)	⊕⊕⊖⊖ Low
TRF Wi	:hdrawn/Dep	pressed Teache	r Report (T-sco	ore)						
FASD										
3	serious <sup>a</sup>	not serious	not serious	not serious	none	124	1048	-	SMD 0.71 higher (0.50 higher to 0.92 higher)	⊕⊕⊕⊖ Moderate
FAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	5	771	-	<b>SMD 0.22 lower</b> (1.10 lower to 0.66 higher)	⊕⊕⊖⊖ Low
pFAS										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,e</sup>	none	44	771	-	SMD 0.03 lower (0.34 lower to 0.27 higher)	⊕⊕⊖⊖ Low

ARND/0	Others									
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	44	771	-	<b>SMD 0.39 higher</b> (0.09 higher to 0.70 higher)	⊕⊕⊖⊖ Low
	thdrawn/Dep	pressed Self Rep	port (T-score)							
pFAS 1	seriousª	not serious	not serious	Serious <sup>e,f</sup>	none	47	58	-	SMD 2.42 higher (1.91 higher to 2.93 higher)	⊕⊕⊖⊖ Low
ARND/0	Others	l						1	2.00 mgner/	
1	seriousª	not serious	not serious	Serious <sup>e, f</sup>	none	34	58	-	SMD 3.44 higher (2.78 higher to 4.10 higher)	⊕⊕⊖⊖ Low
	es for FASD o									
	BRS Somatic	Complaints Car	egiver Report	(T-score)						
FASD	<u> </u>							1		
3	seriousª	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	76	89	-	SMD 0.68 higher (0.05 lower to 1.42 higher)	⊕○○○ Very low
0 studie	es for FAS, pF	AS or ARND/Ot	hers				-	-		
CBCL So	omatic Self C	omplaints Self F	Report (T-scor	e)						
pFAS										
1	serious <sup>a</sup>	not serious	not serious	Serious <sup>e,f</sup>	none	47	58	-	<b>SMD 1.77 higher</b> (1.31 higher to 2.22 higher)	⊕⊕⊖⊖ Low
ARND/0	Others						-	-		
1	seriousª	not serious	not serious	Serious <sup>e,f</sup>	none	34	58	-	SMD 1.78 higher (1.28 higher to 2.28 higher)	⊕⊕⊖⊖ Low
0 studie	es for FASD o	r FAS						•		
CBCL/CI	BRS Thought	Complaints Ca	regiver Report	: (T-score)						
FASD										
2	seriousª	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	43	58	-	SMD 1.14 higher (0.52 lower to 2.81 higher)	⊕○○○ Very low
	-	AS or ARND/Ot								
	nought Comp	plaints Self Repo	ort (T-score)							
pFAS		1	1					1		
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	47	58	-	SMD 0.82 higher (0.42 higher to 1.22 higher)	⊕⊕⊖⊖ Low
ARND/0	Others									
1	seriousª	not serious	not serious	Serious <sup>e,f</sup>	none	34	58	-	SMD 3.58 higher (2.90 higher to 4.26 higher)	⊕⊕⊖⊖ Low
	es for FASD o									
	fective Prob	lems Caregiver	Report (T-sco	re)						
FASD										
4	serious <sup>a</sup>	not serious	not serious	not serious	none	143	1087	-	SMD 0.78 higher (0.52 higher to 1.04 higher)	⊕⊕⊕⊖ Moderate

FAS										
1	seriousª	not serious	not serious	serious <sup>d</sup>	none	5	771	-	<b>SMD 0.10 higher</b> (0.78 lower to 0.98 higher)	⊕⊕⊖⊖ Low
pFAS									• • • •	
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	44	771	-	<b>SMD 0.26 higher</b> (0.04 lower to 0.57 higher)	⊕⊕⊖⊖ Low
ARND/	Others									
1	seriousª	not serious	not serious	serious <sup>e</sup>	none	44	771	-	SMD 0.48 higher (0.17 higher to 0.78 higher)	⊕⊕⊖⊖ Low
TRF Affe	ective Proble	ems Teacher Re	port (T-score)							
FASD										
3	seriousª	not serious	not serious	not serious	none	124	1048	-	SMD 0.83 higher (0.64 higher to 1.02 higher)	⊕⊕⊕⊖ Moderate
FAS		•	•							
1	seriousª	not serious	not serious	Serious <sup>d,e</sup>	none	5	771	-	SMD 0.02 lower (0.90 lower to 0.86 higher)	⊕⊕⊖⊖ Low
pFAS		-								
1	seriousª	not serious	not serious	serious <sup>d,e</sup>	none	44	771	-	<b>SMD 0.17 higher</b> (0.13 lower to 0.48 higher)	⊕⊕⊖⊖ Low
ARND/	Others									
1	seriousª	not serious	not serious	serious <sup>e</sup>	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 (l<sup>2</sup> >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)

•	An	y PAE			ontrol			Std. Mean Difference	score) (1 study) Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	•	•
Fotal (95% CI)			2518			7201	100.0%	0.20 [0.15, 0.24]		
Heterogeneity: Not applicable								I		
Test for overall effect: Z = 8.49 (P < 0.00001)	)								Control Any PAE	4

(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)

										/
	Unquant	ifiable/Any	PAE	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
6.1.1 Any PAE										
Lees et al 2020 (9-11yrs; CBCL-Total-C) Subtotal (95% CI)	47.2	10.8	2518 <b>2518</b>		11.3	7201 <b>7201</b>	20.6% <b>20.6%</b>	0.20 [0.15, 0.24] 0.20 [0.15, 0.24]	7	•
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]	_ <b>−</b> •−	•
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) Subtotal (95% CI)	68.01	8.03	85 <b>348</b>	41.72	8.03	133 <b>393</b>	20.2% <b>79.4%</b>	3.26 [2.85, 3.67] <b>2.29 [1.40, 3.18]</b>	•	- 😐
Heterogeneity: Tau <sup>2</sup> = 0.75; Chi <sup>2</sup> = 59.46, df = 3 (P < 0.0	10001); I <sup>z</sup> = !	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: Tau <sup>2</sup> = 2.02; Chi <sup>2</sup> = 441.64, df = 4 (P < 0	.00001); I <b>?</b> =	99%						F		-
Test for overall effect: Z = 2.88 (P = 0.004)									4 -2 U 2 Control Unguantifiable	4 or Any PAE
Test for subgroup differences: Chi <sup>2</sup> = 21.11, df = 1 (P <	0.00001), P	°= 95.3%							Control Oriquantinable	or Any I AL
Risk of bias legend										

(A) Overal RoB

-

## CBCL Total Behaviour – Caregiver Report (Frequency/OR)

Light PAE a	and CBCL Tota	al Beha	aviour -	- Caregiver Repo	o <b>rt (OR)</b> (1 study)
				Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
O'Leary et al 2010 (8yrs; CBCL-Total-C)	0.157	0.2337	100.0%	1.17 [0.74, 1.85]	•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.67 (P = 0.50)			100.0%	1.17 [0.74, 1.85]	0.01 0.1 1 10 100 Control Light PAE

Risk of bias legend (A) Overal RoB

## Moderate PAE and CBCL Total Behaviour – Caregiver Report (Frequency/OR) (3 studies)

				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	<b>_</b>	•
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.50, df: Test for overall effect: $Z = 2.80$ (P = 0.005)	= 2 (P = 0.47); I <sup>2</sup> = 0	1%			0.01 0.1 1 10 10 Control Moderate PAE	

## Heavy PAE and CBCL Total Behaviour - Caregiver Report (OR) (1 study)

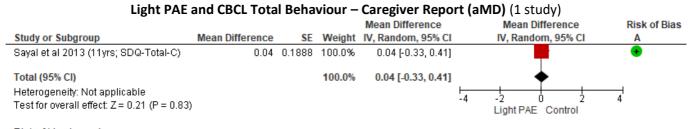
Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI	Odds Ratio Risk of Bias
O'Leary et al 2010 (8yrs; CBCL-Total-C)	0.4849	0.3309	100.0%	1.62 [0.85, 3.11]	
Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 1.47 (P = 0.14)			100.0%	1.62 [0.85, 3.11]	0.01 0.1 1 10 100 Control Heavy PAE

## Risk of bias legend

(A) Overal RoB

Note: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, as well as CBCL results from 2yrs, 5yrs, and 8yrs. Data from participants at 8yrs and exposed in the 1<sup>st</sup> 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)



Risk of bias legend (A) Overal RoB

## SDQ Total Behaviour Teacher Report (Frequency/aOR)

## Moderate PAE and SDQ Total Behaviour - Teacher (aOR) (1 study)

				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
Skogerbo et al 2013 (5yrs; SDQ-Total-T)	0.1156	0.3196	100.0%	1.12 [0.60, 2.10]		•
Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.36 (P = 0.72)			100.0%	1.12 [0.60, 2.10]	0.1 0.2 0.5 1 2 5 10 Control Moderate PAE	ī

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-Leve	l Unquantifia	ble and	d CBCL	<b>Total Behaviour</b>	- Self-report (aOR) (1 stud	y)
				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
Pfinder et al 2020 (0-17yrs; SDQ-SR)	0.2237	0.1193	100.0%	1.25 [0.99, 1.58]		?
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.88 (P = 0.06)			100.0%	1.25 [0.99, 1.58]	0.1 0.2 0.5 1 2 5 Control Confirmed Ung	
Disk of bios logand						

Risk of bias legend (A) Overal RoB

## CBCL Externalising Behaviour Caregiver Report (T-score)

	Very Heavy PAE			Control				Std. Mean Difference	Std. Mean Difference			е	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% C	I	Α
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]					•
Fotal (95% CI)			20			19	100.0%	1.35 [0.65, 2.05]			•		
Heterogeneity: Not applicable									-4	-2 1		2	4 \$
Fest for overall effect: Z = 3.77 (P = 0.000	2)								-	Control	Very Hea	avy PAE	,

Risk of bias legend (A) Overall RoB

Note: Brown et al 1991 also reports a 'destructive' subdomain.

	Ar	ıy PAE		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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										4
Test for overall effect: Z = 6.80 (P < 0.00	001)								Control Any PAE	4
Risk of bias legend										

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) Confirmed-Unquantifiable Control Std. Mean Difference Std. Mean Difference **Risk of Bias** Total Mean SD Total Weight Study or Subgroup Mean SD IV, Random, 95% CI IV, Random, 95% CI Δ 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: Tau<sup>2</sup> = 0.78; Chi<sup>2</sup> = 20.21, df = 1 (P < 0.00001); l<sup>2</sup> = 95% -4 -2 ό Test for overall effect: Z = 2.78 (P = 0.005) Control Confirmed-Unquantifiable

Risk of bias legend (A) Overall RoB

## CBCL Externalising Behaviour Caregiver Report (Frequency/OR)

Light PAE ar	nd CBCL Exteri	nalising	g Behav	viour – Caregive	er (OR)	) (1 study)	
				Odds Ratio		Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
O'Leary et al 2009 (2, 5, 8yrs; CBCL-Ext-C)	0.0953	0.2092	100.0%	1.10 [0.73, 1.66]		-	•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.46 (P = 0.65)			100.0%	1.10 [0.73, 1.66]	⊢ 0.01	0.1 1 10 Control Light PAE	100

Risk of bias legend (A) Overall RoB

## Moderate PAE and CBCL Externalising Behaviour - Caregiver (OR) (1 study)

				Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
Sood et al 2001 (6-7yrs; CBCL-Ext-C)	0.5816	0.2967	100.0%	1.79 [1.00, 3.20]	
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.96 (P = 0.05)	1		100.0%	1.79 [1.00, 3.20]	0.01 0.1 1 10 100 Control Moderate PAE

Risk of bias legend (A) Overall RoB

## Heavy PAE and CBCL Externalising Behaviour - Caregiver (OR) (1 study)

				Odds Ratio		Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
O'Leary et al 2009 (2, 5, 8yrs; CBCL-Ext-C)	0	0.3239	100.0%	1.00 [0.53, 1.89]			•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.00 (P = 1.00)			100.0%	1.00 [0.53, 1.89]	L 0.01	0.1 1 10 Control Heavy PAE	100

Risk of bias legend (A) Overall RoB

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> 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) Moderate PAE Control Std. Mean Difference Std. Mean Difference **Risk of Bias** Mean SD Total Mean SD Weight IV, Random, 95% CI IV, Random, 95% CI Study or Subgroup Total 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 -4 -2 ά 4 Test for overall effect: Z = 1.76 (P = 0.08) Control Moderate PAE

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) Very Heavy PAE Control Std. Mean Difference Std. Mean Difference Risk of Bias Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Α 0.71 [0.06, 1.36] 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% Heterogeneity: Not applicable -4 ż . '? 4 Test for overall effect: Z = 2.14 (P = 0.03) Control Very Heavy PAE

Risk of bias legend (A) Overall RoB

## Any PAE and CBCL Internalising Behaviour – Caregiver (T-score) (1 study)

	Ar	iy PAE		C	ontrol			Std. Mean Difference	Std. Mean	Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rand	om, 95% Cl	Α
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 < 0.00(	001)								-4 -2 Control	0 2 Any PAE	4

## 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)

	Confirmed	l-Unquantif	iable	C	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD.	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.59; Chi <sup>2</sup> = 18.43, df	= 1 (P ≺ 0.00	i01); i² = 95	%					H	4 -2 0 2	4
Test for overall effect: Z = 1.81 (P = 0.07)									Control Confirmed-Ur	quantifiable

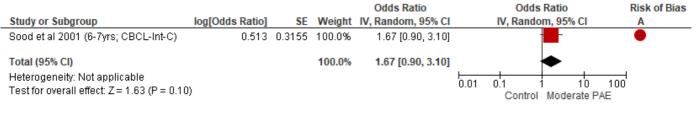
Risk of bias legend

## CBCL Total Internalising Behaviour Caregiver Report (Frequency/OR)

Light PAE and CBCL Internalising Behaviour – Caregiver (OR) (1 study)											
				Odds Ratio		Odds Ratio	Risk of Bias				
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α				
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					0.01		100				
Test for overall effect: Z = 0.48 (P = 0.63)					0.01	Control Light PAE					
Disk of bias lagond											

Risk of bias legend (A) Overall RoB

## Moderate PAE and CBCL Internalising Behaviour - Caregiver (OR) (1 study)



				Odds Ratio		Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
O'Leary et al 2010 (2, 5, 8yrs; CBCL-Int-C)	0.9723	0.3392	100.0%	2.64 [1.36, 5.14]			•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 2.87 (P = 0.004)			100.0%	2.64 [1.36, 5.14]	<b>—</b>	0.1 1 10 Control Heavy PAE	100

Risk of bias legend (A) Overall RoB

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> 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)											
				Mean Difference	Mean Difference	Risk of Bias					
Study or Subgroup	Mean Difference	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α					
Sayal et al 2013 (11yrs; SDQ-C)	0.04	0.0561	100.0%	0.04 [-0.07, 0.15]		٠					
Total (95% CI)			100.0%	0.04 [-0.07, 0.15]							
Heterogeneity: Not applicable	- 0.40				-0.2 -0.1 0 0.1 0.2	_					
Test for overall effect: Z = 0.71 (P =	= 0.48)				Control Light PAE						

Risk of bias legend (A) Overall RoB

## **Confirmed PAE-Level Unquantifiable and CBCL Conduct Problems – Caregiver (T-score)** (1 study)

	Confirmed-	Unquantif	fiable	Co	ntro	I		Std. Mean Difference	Std. Mean Difference F	isk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 < 0.000	01)								-4 -2 0 2 4 Control Confirmed-Unguan	tifiable

Risk of bias legend (A) Overall RoB

## CBCL/SDQ Conduct Problems Caregiver Report (Frequency/OR)

				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)				0.7 0.85 1 1.2 1.5 Control Light PAE	

(A) Overall RoB

Note: Sayal et al 2007 also reports data from 3 and 6yrs.

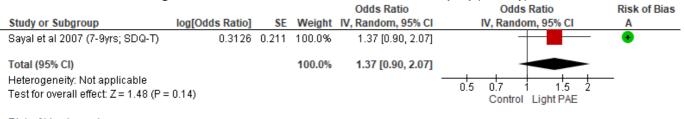
## CBCL/SDQ Conduct Problems Self Report (Frequency/OR)

				Odds Ratio	Odds Ratio	Risk of Bia
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 = 0.0	16)				Control Confirmed-Un	quantifiable

(A) Overall RoB

## SDQ Conduct Problems Teacher Report (Frequency/OR)

## Light PAE and SDQ Conduct Problems - Teacher (OR) (1 study)



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)

Vei	y heav	vy PA	AE an	d CBC	CL Ag	ggres	sion -	Caregiver (T-score	<b>e)</b> (1 study)	
	Very I	Heavy I	PAE	С	ontrol			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)								Control Very Heavy PAE	
Risk of bias legend (A) Overall RoB										
	Any P	AE ai	nd CE	BCL A	ggre	ssion	– Caro	egiver (T-score) (1	1 study)	
	A	ny PAE		Co	ntrol		S	itd. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD 1	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α

Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 4.86 (P < 0	.00001)		2518			7201	100.0%	0.11 [0.07, 0.16] - -	4 -2 0 2 Control Any PAE	
Risk of bias legend										

(A) Overall RoB

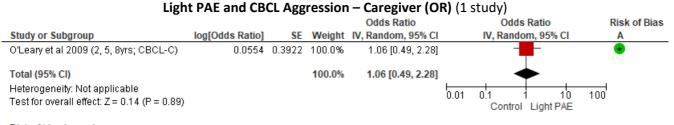
Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

### Confirmed PAE-Level Unguantifiable and CBCL Aggression – Caregiver (T-score) (2 studies)

Communeariae	LCVCIO	Iquunu	masic	una	CDC	- ~58	51 03310		score, (2 statics)	
	Confirme	l-Unquantii	fiable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.41; Chi <sup>2</sup> = 12.3	87, df = 1 (P =	0.0004); I <sup>2</sup>	= 92%							
Test for overall effect: Z = 3.47 (P = 0.0	005)								Control Confirmed-Un	quantifiable

Risk of bias legend (A) Overall RoB

## CBCL Aggression Caregiver Report (Frequency/OR)



Мос	derate PAE an	d CBCL	Aggre	ssion – Caregive	<b>r (OR)</b> (1 study)	
				Odds Ratio	Odds Ratio	<b>Risk of Bias</b>
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 = 1	0.41)				Control Moderate PAE	U
Risk of bias legend (A) Overall RoB						

Hear	Heavy PAE and CBCL Aggression – Caregiver (OR) (1 study)											
				Odds Ratio	Odds Ratio Risk of Bias							
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl A							
O'Leary et al 2009 (2, 5, 8yrs; CBCL-C)	0.6552	0.4879	100.0%	1.93 [0.74, 5.01]								
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.34 (P = 0.18)			100.0%	1.93 [0.74, 5.01]	0.01 0.1 1 10 100 Control Heavy PAE							
Risk of bias legend												

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> trimester was used. Sood et al 2001 also reports MD data and frequency data.

## CBCL Rule Breaking Behaviour (T-score)

Ai	ny PAE	E ar	nd CB	CL Ru	ıle-	Brea	king Be	ehaviour (T-scor	r <b>e)</b> (1	. study)	
	An	y PA	E	Co	ontro		-	Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% Cl	Α
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									-2		
Test for overall effect: Z = 3.69 (P = 0	.0002)								-2	Control Any PAE	Z
Risk of bias legend											
(A) Overall RoB											

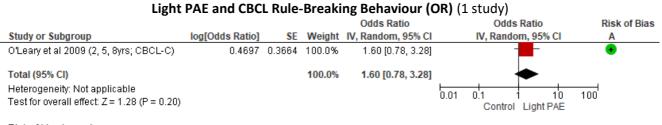
Note: Lees et al 2020 also reports multiple other subdomains that were not included in the meta-analyses.

## Confirmed PAE-Level Unquantifiable and CBCL Rule-Breaking Behaviour (T-score) (2 studies)

	Confirmed	-Unquantif	iable	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.05	i, df = 1 (P = 0	1.82); I <sup>z</sup> = 09	%					-4		4
Test for overall effect: Z = 8.68 (P < 0.0)	0001)							-4	Control Confirmed-Un	quantifiable

Risk of bias legend (A) Overall RoB

## CBCL Rule Breaking Behaviour (Frequency/OR)



				Odds Ratio	ur (OR) (1 study) Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 = 1	0.008)				0.01 0.1 1 10 Control Moderate PA	100 AE

## Heavy PAE and CBCL Rule-Breaking Behaviour (OR) (1 study)

				Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl A
O'Leary et al 2009 (2, 5, 8yrs; CBCL-C)	-1.2755	0.9915	100.0%	0.28 [0.04, 1.95]	••••••••••••••••••••••••••••••••••••••
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.29 (P = 0.20)			100.0%	0.28 [0.04, 1.95]	0.01 0.1 1 10 100 Control Heavy PAE
Risk of bias legend					

(A) Overall RoB

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> 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	. Hyj	pera	ctivity	– Caregiver (T-s	score) (1 study)
	Very I	leavy I	PAE	C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)								Control Very Heavy PAE
Risk of bias legend									

(A) Overall RoB

## SDQ Hyperactivity Caregiver Report (Mean Difference)

Lig	ht PAE and SD	Q Hyp	eractiv	ity – Caregiver (a	a <b>MD)</b> (1 study)	
				Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean Difference	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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	

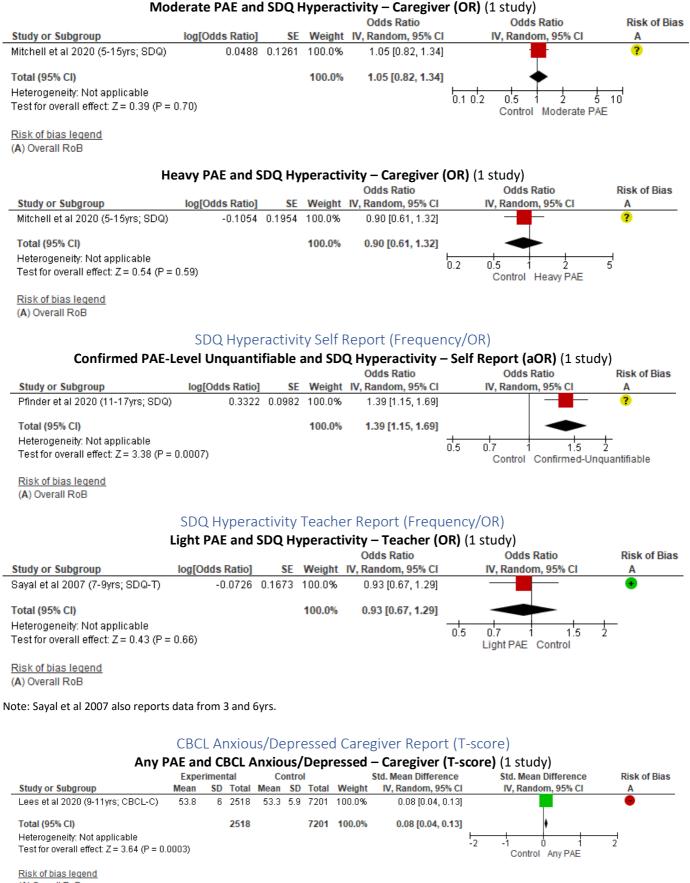
Risk of bias legend (A) Overall RoB

## SDQ Hyperactivity Caregiver Report (Frequency/OR)

				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 Control Light PAE	5 10

Risk of bias legend (A) Overall RoB

Note: Sayal et al 2007 also reports data from 3 and 6yrs.



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)

	Confirmed	l-Unquantif	iable	C	ontrol			Std. Mean Difference		Std. Mea	n Difference	R	lisk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rand	om, 95% Cl		Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.06 Test for overall effect: Z = 5.70 (P < 0.0		0.81); I² = 09	%						-4	-2 Contro	0 2 I Confirmed	4 -Unquan	tifiable

Risk of bias legend (A) Overall RoB

## CBCL Anxious/Depressed Caregiver Report (Frequency/OR)

		Mod	erate P	AE (1 study)		
				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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						<del></del>
Test for overall effect: Z = 1.40 (P = 0.	.16)				0.01 0.1 1 10 10 Control Moderate PAE	10
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)

	•		-	Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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						100
Test for overall effect: Z = 1.32 (P = 0.1	9)				Control Confirmed Un	
Disk of hiss langed						

Risk of bias legend (A) Overall RoB

#### Note: Pfinder et al 2020 reports SDQ emotional problems.

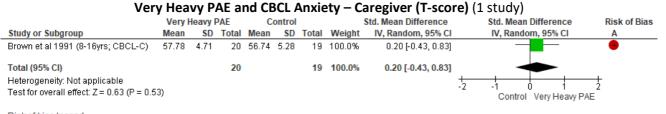
#### CBCL Anxious/Depressed Self-Report (T-score)

	Ligi	ht PA	E	Co	ontro	l i		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 = 0.0	2)							Control Light PAE	

Risk of bias legend (A) Overall RoB

## Moderate PAE and CBCL Anxious/Depressed Self-Report (T-score) (1 study)

	Moder	rate P	AE	Co	ontro	I I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									-1 -0.5 0 0.5 1	—
Test for overall effect: Z = 0.36	(P = 0.72	2)							Control Moderate PAE	



Risk of bias legend (A) Overall RoB

## CBCL Anxiety Caregiver Report (Frequency/OR)

Ligh	it PAE and C	BCL Ar	nxiety -	– Caregiver (OF	<b>R)</b> (1 study)	
				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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						100
Test for overall effect: Z = 2.40 (P = 0.02)					Control Light PAE	100
Risk of bias legend						

(A) Overall RoB

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> trimester was used.

#### Heavy PAE and CBCL Anxiety - Caregiver (OR) (1 study) Odds Ratio Odds Ratio Risk of Bias log[Odds Ratio] SE Weight IV, Random, 95% CI Study or Subgroup IV, Random, 95% CI ۸ 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 0.01 0.1 10 100 Test for overall effect: Z = 2.10 (P = 0.04) Control Heavy PAE Risk of bias legend (A) Overall RoB

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> trimester was used.

## CBCL Withdrawn/Depressed Caregiver Report (T-score)

Any PA	E and	CB	CL W	ithdr	aw	n/De	presse	d – Caregiver (1	T-score) (1 study)
	An	y PA	E	Co	ontro			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
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)								Control Any PAE
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)

	Confirmed-Unquantifiable Control		Std. Mean Difference		Std. Mean Difference		Risk of Bias				
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Rando	m, 95% Cl	Α
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		0.37); <b>i²</b> = 0%	Хо						-4 -2	2	4
Test for overall effect: Z = 6.24 (P < 0.0)	0001)								Control	Confirmed-Ur	nquantifiable

## Light PAE and Withdrawn/Depressed - Caregiver (OR) (1 study)

•		-	•	Odds Ratio	• •	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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]	I	•	
Heterogeneity: Not applicable							100
Test for overall effect: Z = 1.58 (P = 0.11)					0.01	0.1 1 10 Control Light PAE	100
Risk of bias legend							
(A) Overall RoB							

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> trimester was used.

				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
Sood et al 2001 (6-7yrs; CBCL-C)	0.2653	0.489	100.0%	1.30 [0.50, 3.40]	-	•
Fotal (95% CI)			100.0%	1.30 [0.50, 3.40]	•	
Heterogeneity: Not applicable						7
Fest for overall effect: Z = 0.54 (P = 0	.59)				0.01 0.1 1 10 10 Control Moderate PAE	J

Note: Sood et al 2001 also reports MD data and frequency data.

				Odds Ratio		Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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					0.01		100
Test for overall effect: Z = 0.47 (P = 0.64)					0.01	Control Heavy PAE	100

Risk of bias legend (A) Overall RoB

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> trimester was used.

## CBCL Somatic Complaints Caregiver Report (T-Score)

	Any F	ΡΑΕ	and	CBCL	So	mati	c Comp	plaints (T-score)	(1 study)
	An	y PA	E	Co	ontro			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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									-2 -1 0 1 2
Test for overall effect: Z = 4.99 (P < 0	.00001)								Control Any PAE
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.

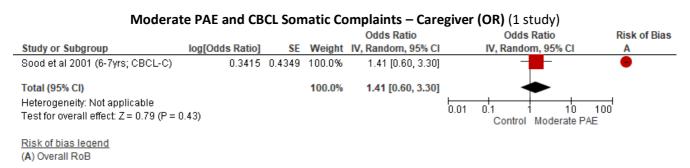
#### Confirmed PAE-Level Unquantifiable and CBCL Somatic Complaints (T-score) (2 studies) Std. Mean Difference Confirmed-Unquantifiable Control Std. Mean Difference **Risk of Bias** Total Mean SD Total Weight IV, Random, 95% CI Study or Subgroup Mean SD IV. Random, 95% CI Vaurio et al 2011 (6-16yrs; 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) 0.63 [0.08, 1.19] 107 188 100.0% Heterogeneity: Tau<sup>2</sup> = 0.13; Chi<sup>2</sup> = 4.92, df = 1 (P = 0.03); l<sup>2</sup> = 80% -4 $\frac{1}{2}$ 4 -2 ά Test for overall effect: Z = 2.23 (P = 0.03) Control Confirmed-Unquantifiable

## Light PAE and CBCL Somatic Complaints - Caregiver (OR) (1 study)

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio IV, Random, 95% Cl	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]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.24 (P = 0.81)			100.0%	1.07 [0.61, 1.88]	0.01 0.1 1 10 Control Light PAE	100
Risk of bias legend						

(A) Overall RoB

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> trimester was used.



#### Heavy PAE and CBCL Somatic Complaints – Caregiver (OR) (1 study)

			•	Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
O'Leary et al 2010 (2 5, 8yrs; CBCL-C)	1.0092	0.3183	100.0%	2.74 [1.47, 5.12]	
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 3.17 (P = 0.002)	)		100.0%	2.74 [1.47, 5.12]	0.01 0.1 1 10 100 Control Heavy PAE
Disk of biss is seed.					

Risk of bias legend (A) Overall RoB

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> 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)												
	An	y PA	E	Co	ontro	I I		Std. Mean Difference	Std. Mean Difference Risk of Bias			
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	I IV, Random, 95% CI 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]	ı] 🗧 👄			
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 5.95 (P < 0	.00001)		2518			7201	100.0%	0.14 [0.09, 0.18]	-2 -1 0 1 2 Control Any PAE			
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)

	Confirmed	l-Unquantif	iable	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.08 Test for overall effect: Z = 7.05 (P < 0.01		0.78); I² = 09	%						-4 -2 0 2 Control Confirmed-Un	4 Iquantifiable

## CBCL Thought Complaints Caregiver Report (Frequency/OR)

## Light PAE and CBCL Thought Complaints - Caregiver (OR) (1 study)

_		-	-	Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	Α
O'Leary et al 2010 (2 5, 8yrs; CBCL-C)	0.1154	0.4024	100.0%	1.12 [0.51, 2.47]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.29 (P = 0.77)			100.0%	1.12 [0.51, 2.47]	0.01 0.1 1 10 Control Light PAE	100
Risk of bias legend						

(A) Overall RoB

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> trimester was used.

#### Heavy PAE and CBCL Thought Complaints – Caregiver (OR) (1 study) Odds Ratio Odds Ratio **Risk of Bias** Study or Subgroup log[Odds Ratio] SE Weight IV, Random, 95% CI IV, Random, 95% CI Α 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 0.01 10 100 0.1 Test for overall effect: Z = 0.20 (P = 0.84) Control Heavy PAE Risk of bias legend (A) Overall RoB

Notes: O'Leary et al 2010 reports 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, data from the 1<sup>st</sup> trimester was used.

## BITSEA Maternal Report - Possible Problem (adjusted OR)

Modera	Moderate PAE and BITSEA Maternal Report – Possible Problem (1 study)												
				Odds Ratio	Odds Ratio	Risk of Bias							
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α							
Halliday et al 2017 (2yrs; BITSEA)	-0.5222	0.4834	100.0%	0.59 [0.23, 1.53]		•							
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.08 (P =	0.28)		100.0%	0.59 [0.23, 1.53]	0.01 0.1 1 10 Moderate PAE Control	100							
Risk of bias legend													

(A) Overal RoB

## BITSEA Maternal Report - Possible Competence Deficit (adjusted OR)

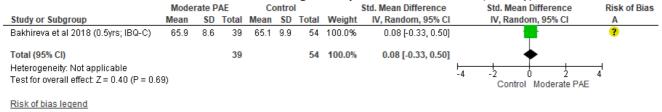
Moderate PAE and BITSEA Maternal Report – Possible Competence Deficit (1 study)												
				Odds Ratio	Odds Ratio	Risk of Bias						
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α						
Halliday et al 2017 (2yrs; BITSEA)	0.1548	0.4642	100.0%	1.17 [0.47, 2.90]	-#-	•						
Total (95% CI)			100.0%	1.17 [0.47, 2.90]	+							
Heterogeneity: Not applicable												
Test for overall effect: Z = 0.33 (P =	0.74)				Moderate PAE Control							
Risk of bias legend												
(A) Overal RoB												
	IBQ Caregive	er Rep	ort – N	egative Effect (	mean/SD)							

## Moderate PAE and IBQ Caregiver Report Negative Effect (1 study)

						-0			
	Moderate PAE		Control		Std. Mean Difference		Std. Mean Difference Risk of		
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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									-4 -2 0 2 4
Test for overall effect: Z = 2.58 (P = 0.0	J1U)								Control Moderate PAE
Risk of bias legend									

(A) Overal RoB

## Moderate PAE and IBQ Caregiver Report Effortful Control (1 study)



(A) Overal RoB

# **DIAGNOSED STUDIES**

# CBCL Total Behaviour Caregiver Report (Frequency/OR)

FASD and	CBCL	Total	Behav	viour	– Care	giver (Frequency	<b>/OR)</b> (1 study)	
	FAS	D	Contr	rol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 Heterogeneity: Not applicable Test for overall effect: Z = 2.22 (P = 0.03)	17		0			I	0.001 0.1 1 10 10 FASD Control	00

Risk of bias legend (A) Overal RoB

# CBCL Total Behaviour Caregiver Report (T-score)

		FASD		0	ontrol			Std. Mean Difference	Std. Mean	Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rando	om, 95% Cl	Α
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: Tau <sup>2</sup> = 0.26; Chi <sup>2</sup> = 36.11, df = 8 (P < 0.000	1); l <sup>2</sup> = 7(	8%							L_L_	<u> </u>	<u> </u>
Test for overall effect: Z = 7.82 (P < 0.00001)									-4 -2 Control	U 2	4

### 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)

		FAS		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	- <b>+</b>	•
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]	- <b>-</b>	•
Total (95% CI)			73			386	100.0%	0.62 [0.35, 0.89]	•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 1.74, df Test for overall effect: Z = 4.53 (P < 0.0000	•	0.42); I	²=0%					-4	-2 0 2 Control FAS	4

## pFAS and CBCL/PBCL-36 Total Behaviour – Caregiver (T-score) (2 studies)

•	pFAS		C	ontrol			Std. Mean Difference		Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.20; Chi <sup>2</sup> = 4.12, df = Test for overall effect: Z = 3.02 (P = 0.003)	= 1 (P = 0.04);	I² = 76%	b					-4	-2 0 2 Control pFAS	4

# Risk of bias legend

(A) Overal RoB

# TRF/PBCL-36 Total Behaviour Teacher Report (T-score)

Study or Subgroup         Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI         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]         Image: Comparison of the comparison of		F	ASD		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
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]	Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
	(alberg 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]		•
Total (95% CI) 155 75 100.0% 0.88 [0.58, 1.17]	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]		•
	otal (95% CI)			155			75	100.0%	0.88 [0.58, 1.17]	•	

### Risk of bias legend (A) Overal RoB

	FA	S	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
May et al 2013a (6-7yrs; TRF-Total)	50.2 4	2.6 66	29.1	29.1	87	41.5%	0.59 [0.26, 0.92]		•
May et al 2016 (6-7yrs; TRF-Total)	35.9 3	4.7 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 = 0.2 Test for overall effect: Z = 4.89 (P < 0.		? = 0.61); I <sup>2</sup>	= 0%					-4 -2 0 2 Control FAS	4

### Risk of bias legend (A) Overal RoB

## pFAS and TRF Total Behaviour – Teacher (2 studies)

•							· ·	,
p	FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bia
Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
45.1	42.2	51	29.1	29.1	87	34.5%	0.46 [0.11, 0.81]	
39.6	38.2	88	22.9	24	206	65.5%	0.58 [0.32, 0.83]	
		139			293	100.0%	0.54 [0.33, 0.74]	•
	(P = 0.	61); I²	= 0%					
00001)								Control pFAS
	Mean 45.1 39.6	45.1 42.2 39.6 38.2 7, df = 1 (P = 0.	Mean         SD         Total           45.1         42.2         51           39.6         38.2         88           139         139           7, df = 1 (P = 0.61); I <sup>2</sup> 100	Mean         SD         Total         Mean           45.1         42.2         51         29.1           39.6         38.2         88         22.9           139         139           7, df = 1 (P = 0.61); P = 0%         100	Mean         SD         Total         Mean         SD           45.1         42.2         51         29.1         29.1           39.6         38.2         88         22.9         24           139         7, df = 1 (P = 0.61); P = 0%         9%         9%	Mean         SD         Total         Mean         SD         Total           45.1         42.2         51         29.1         29.1         87           39.6         38.2         88         22.9         24         206           139         293           7, df = 1 (P = 0.61); P = 0%         26	Mean         SD         Total         Mean         SD         Total         Weight           45.1         42.2         51         29.1         29.1         87         34.5%           39.6         38.2         88         22.9         24         206         65.5%           139         293         100.0%         7, df = 1 (P = 0.61); P = 0%         293         100.0%	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           45.1         42.2         51         29.1         29.1         87         34.5%         0.46 [0.11, 0.81]           39.6         38.2         88         22.9         24         206         65.5%         0.58 [0.32, 0.83]           139         293         100.0%         0.54 [0.33, 0.74]           7, df = 1 (P = 0.61); P = 0%         56         56         56         56

### Risk of bias legend (A) Overal RoB

# ARND/Others and TRF Total Behaviour - Teacher (2 studies)

	ARND	)/Othe	ers	C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.06, df = 1	1 (P = 0.8	81); I <sup>z</sup> :	= 0%							
Test for overall effect: Z = 6.71 (P < 0.00001)									Control ARND/Others	4

# SSRS Total Behaviour Caregiver Report (mean/SD)

## FASD and SSRS Total Behaviour Caregiver Report (1 study)

		FASD		(	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	\$D	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									-4 -2 0 2 Control FASD	4

Risk of bias legend (A) Overal RoB

# SSRS Total Behaviour Teacher Report (mean/SD)

udy or Subgroup		FASD			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
auy or subgroup	Mean	SD	Total	Mean	SD.	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
reenbaum 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]		•
swang et al 2010 (9yrs; SSRS-Total)	122.8	7.4	12	92.5	9	12	46.8%	3.55 [2.19, 4.91]	<b>∎</b>	•
otal (95% CI)			42			42	100.0%	2.22 [-0.22, 4.66]		
eterogeneity: Tau <sup>2</sup> = 2.83; Chi <sup>2</sup> = 11.17, df = 1 (P	P = 0.00	008); I <sup>z</sup> = 9	1%					-		_

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)

P.		FAS			ontrol			-report (T-score Std. Mean Difference	-/ \-	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
_ynch et al 2017 (22yrs; ASR-Total)	53.14	1.44	47	49.51	1.33	58	100.0%	2.61 [2.08, 3.14]			•
Fotal (95% CI)			47			58	100.0%	2.61 [2.08, 3.14]		•	
Heterogeneity: Not applicable									4		
Fest for overall effect: Z = 9.71 (P < 0.0	00001)								-4	Control pFAS	4

(A) Overal RoB

## ARND/Others and ASR Total Behaviour - Self-report (T-score) (1 study)

ART D/ Others	ana		100			loui	JUI	-10010(1-3001		
	ARNE	)/Othe	ers	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									-4 -2 0 2 4	_
Test for overall effect: Z = 11.25 (P < 0.00001)									Control ARND/Others	
Disk of his stand										

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 CB0	CL Ext	ternali	sing	Beh	aviou	r – C	Caregi	ver (T-score) (	9 studies)	
		FASD	-		Control		_	Std. Mean Difference	Std. Mean Difference R	isk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.20; Chi <sup>2</sup> = 39.71, df = 8 ( $P < 0.0$ ) Test for overall effect: Z = 5.46 ( $P < 0.00001$ )	0001); I²	= 80%							-4 -2 0 2 4	
185101 0/erail ellect. Z = 0.40 (F < 0.00001)									Control FASD	

## FAS and CBCL Externalising Behaviour – Caregiver (T-score) (2 studies)

		FAS		Č (	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 1.20, df = Test for overall effect: Z = 1.12 (P = 0.26)	1 (P = 0.2	27); I <b>*</b> = 1	17%					-4	4 -2 0 2 Control FAS	4

Risk of bias legend (A) Overall RoB

## pFAS and CBCL Externalising Behaviour – Caregiver (T-score) (2 studies)

	-///		oo						scalares	
	1	<b>FAS</b>		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.80; Chi <sup>2</sup> = 9.84, df = 1 (P = 0.0	102); I <sup>z</sup> =	90%								
Test for overall effect: Z = 1.45 (P = 0.15)									Control pFAS	4

Risk of bias legend (A) Overall RoB

## ARND/Others and CBCL Externalising Behaviour – Caregiver (T-score) (3 studies)

	ARN	D/Othe	rs	0	Control			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	<b>_</b>	•
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: Tau <sup>2</sup> = 0.27; Chi <sup>2</sup> = 10.90, df = 2 (P =	0.004); I <sup>z</sup>	= 82%								÷.
Test for overall effect: Z = 2.81 (P = 0.005)									-4 -2 U 2 Control ARND/Others	ł
Disk of hiss lagand										

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)

	FAS	D	Cont	rol		Odds Ratio		Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.02, df = 1	(P = 0.90)	); l <sup>z</sup> = 0	%				0.001		<u>_</u>
Test for overall effect: Z = 3.11 (P = 0.002)							0.001	Control FASD	00

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)

	F	ASD		C	ontrol			Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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									-4	-2 0 2	4
Test for overall effect: Z = 0.06 (P = 0.95)										Control FASD	

(A) Overall RoB

# TRF Total Externalising Behaviour Teacher Report (T-score) FASD and CBCL/TRF Externalising Behaviour – Teacher (T-score) (5 studies)

FASD and Cl	BCL/TRI		nalis	sing		viour		cher (T-score)		
Study or Subgroup	Mear	FASD 1 SD	Total	Mean	Control SD	Total		d. Mean Difference IV, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl	Risk of Bias A
Greenbaum et al 2009 (6-13yrs; TRF-Ext-T)	69.8		33		10.4957		14.7%	1.33 [0.80, 1.86]		•
May et al 2020a (6-7yrs; CBCL-Ext-T)	56		38	50.2	8.8		22.8%	0.63 [0.28, 0.97]	-	•
May et al 2020b (6-7yrs; CBCL-Ext-T) May et al 2020a (6 Zuro; TBE Ext T)	53.8		47	48.9	8.4		24.8%	0.56 [0.25, 0.87]		
May et al 2020c (6-7yrs; TRF-Ext-T) Quattlebaum & O'Connor 2013 (6-12yrs; CBCL-E)	53.6 (t-T) 61.47		42 94	48.5 50.2	7.8 8.31		24.1% 13.6%	0.63 [0.31, 0.95] 1.15 [0.58, 1.72]		ĕ
Total (95% CI)			254			1132	100.0%	0.78 [0.52, 1.05]	•	
Heterogeneity: Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 8.94, df = 4 (P = Test for overall effect: $Z = 5.88$ (P < 0.00001)	: 0.06); I <b>²</b> = 5	5%						-4	-2 0 2 Control FASD	4
Risk of bias legend (A) Overall RoB										
FAS and	TRF F	derna	lising	7 Re	havio	ur – 1	Teach	er (T-score) (1	study)	
	FAS		-	ontro				an Difference	Std. Mean Difference	Risk of Bi
Study or Subgroup	Mean SI	D Total	Mean	SD	Total	Weight	t IV, F	andom, 95% Cl	IV, Random, 95% Cl	Α
Chambers et al 2019 (6-7yrs; TRF-Ext-T)	54.8	95	49	9	771	100.0%	6 0	.64 [-0.24, 1.52]	+	•
Total (95% CI)		5			771	100.0%	6 0.	.64 [-0.24, 1.52]	•	
Heterogeneity: Not applicable								-4		
Test for overall effect: Z = 1.43 (P = 0.15)								-4	Control FAS	4
Risk of bias legend										
(A) Overall RoB nFΔS an	4 TRE F	vtorna	alicin	σΒά	ahavi	our –	Teach	er (T-score) (1	study)	
pi As un	pFAS			ontrol		Jui		an Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean SE	) Total	Mean	SD	Total	Weight	IV, R	andom, 95% Cl	IV, Random, 95% CI	Α
Chambers et al 2019 (6-7yrs; TRF-Ext-T)	48.4 9.6	6 44	49	9	771	100.0%	-0.	07 [-0.37, 0.24]	-	•
Total (95% CI)		44			771	100.0%	-0.0	07 [-0.37, 0.24]	•	
Heterogeneity: Not applicable								-4	-2 0 2	
Test for overall effect: Z = 0.43 (P = 0.67)									Control pFAS	
Risk of bias legend										
(A) Overall RoB	rs and T	RE Evi	orna	licir	ng Ro	havio	ur – T	eacher (T-scor	<b>م)</b> (1 study)	
		ID/Others			ntrol			Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD T	otal N	lean	SD To	tal We	ight IV	/, Random, 95% Cl	IV, Random, 95% Cl	Α
Chambers et al 2019 (6-7yrs; TRF-Ext-T; ARN	D) 56.4	9.7	44	49	9 7	71 100	.0%	0.82 [0.51, 1.12]		•
Fotal (95% CI)			44		7	71 100	.0%	0.82 [0.51, 1.12]	•	
Heterogeneity: Not applicable								F.	-2 0 2	
Test for overall effect: $Z = 5.23$ (P < 0.00001)								-4	Control ARND/Other	4 'S
<u>Risk of bias legend</u>										
A) Overall RoB				6 C						
ote: Greenbaum et al 2009 reported	mean val	ues adj	usted	for S	ses, toi		exposur	e, abuse, adoptio	n / foster home history.	
CCBC	Total F	vtorn	alicir	og B	2 ehav	viour <sup>-</sup>	Toach	er Report (m	(cd)	
				<u> </u>				her (mean/SI		
FASD and S	FAS		-	Contr		Jui -		an Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup		SD Tota			D Total	Weigh		Random, 95% Cl	IV, Random, 95% Cl	A
Rasmussen et al 2011a (3-8yrs; SSRS-Ext-T)	4.06 3			5 4.0		100.09		.24 [-0.77, 0.28]	-	•
Fotal (95% CI)		23	3		37	100.0	% -0	.24 [-0.77, 0.28]	•	
Heterogeneity: Not applicable										÷
Fest for overall effect: Z = 0.91 (P = 0.36)								- 4	-2 0 2 Control FASD	4
<u>Risk of bias legend</u> A) Overall RoB										
	R Total	Fxterr	nalisi	ng	Beha	viour	Self F	Report (T-scor	e)	
				_						
pFAS and AS	SK EXte	ernalis	sing	вen	avio	ur – S	seit-re	eport (T-score	e <b>)</b> (1 study)	

ргаз а	nu As	DR E	xterr	Idlisi	ng I	Dena	viour	– Sen-report (1	-200	e) (1 SU	uuyj		
	p	FAS		Co	ontro	I		Std. Mean Difference		Std. Mean	Difference	е	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% Cl		Α
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]			-	F	•
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	0.00001;	)							-4	-2 ( Control	) 2 pFAS	4	ł

# ARND/Others and ASR Externalising Behaviour - Self-report (T-score) (1 study)

	ARN	D/Othe	ers	C	ontro	1		Std. Mean Difference	S	td. Mean	Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	- I	V, Rando	om, 95% Cl	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 10.86 (P < 0.00001)			34			58	100.0%	4.08 [3.34, 4.82]	-4	-2 Control	0 2 4 ARND/Other D	iagnosis
Risk of bias legend												

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)

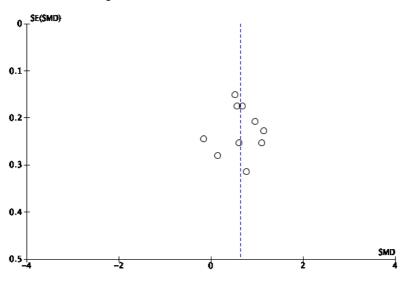
		FASD			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
Kerns et al 2016 (8-14yrs; CBCL-Int-C)	56.6	14.2	22	47.1	9.6	22	7.4%	0.77 [0.16, 1.38]		?
Fagerlund et al 2011 (8-21yrs; CBCL-Int-C)	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]		•
<rueger (8-16yrs;="" 2020="" al="" cbcl-int-c)<="" et="" td=""><td>63.08</td><td>11.78</td><td>39</td><td>50.29</td><td>11.1</td><td>34</td><td>9.1%</td><td>1.10 [0.61, 1.60]</td><td></td><td>•</td></rueger>	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]	- <b>-</b> -	•
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]	_ <b>_</b>	•
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: Tau <sup>2</sup> = 0.08; Chi <sup>2</sup> = 25.32, df = 9 (P = 0.0	03); <b> ²</b> =	64%						- ·	<u>    t                                </u>	<u> </u>
Test for overall effect: Z = 5.52 (P < 0.00001)	/1 '							-	4 -2 0 2 Control FASD	4

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.

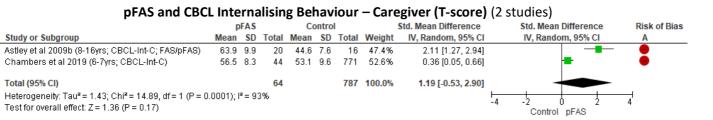


FAS and	CBCL	Inte	rnali	sing B	ehav	viour	– Care	egiver (T-score) (	2 studies)
	1	FAS		C	ontrol			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI

Chambers et al 2019 (6-7yrs; CBCL-Int-C)	50 14.3	55	3.1 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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.20, df =	1 (P = 0.65); I <sup>2</sup> =	0%					-	<u> </u>	-	<u> </u>		
Test for overall effect: Z = 0.66 (P = 0.51)							-4	-2 Cont	trol FAS	2	4	
<u> </u>	T (F = 0.65), F =	070					-4	-2 Cont	o trol FAS	ź	4	

Risk of bias legend (A) Overall RoB **Risk of Bias** 

Α



Risk of bias legend (A) Overall RoB

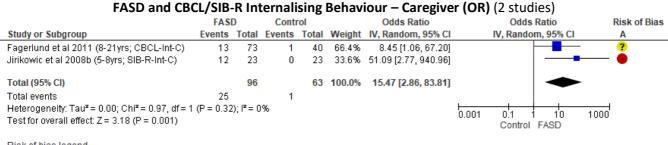
## ARND/Others and CBCL Internalising Behaviour – Caregiver (T-score) (3 studies)

		-			0				····	
	ARN	D/Oth	ег	0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 = Test for overall effect: Z = 1.81 (P = 0.07)	0.001); I	²= 859	%						-4 -2 0 2 Control ARND/Others	4

Risk of bias legend

(A) Overall RoB

# CBCL/SIB-R Total Internalising Behaviour Caregiver Report (Frequency/OR)



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 S	SSRS I	nter	nalis	ing B	Seha	aviou	ur – Ca	regiver (mean/	<b>SD)</b> (1 study)	
	F	ASD		Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable			37			23	100.0%	0.37 [-0.16, 0.89]	↓ ↓ ↓ -4 -2 0 2	
Test for overall effect: Z = 1.38 (P = 0.17)									Control FASD	-

Risk of bias legend (A) Overall RoB

#### TRF/CBCL Total Internalising Behaviour Teacher Report (T-score) nd TRE/CBCL Internalising Behaviour -Tooohow (Tooowa) (Footualiaa)

FASD and TRE	./CBC	L Inte	rnali	Ising	вепа	viou	r – 16	eacher (T-score	(5 studies)	
		FASD		(	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 3.11, df = 4 (P = 0.9 Test for overall effect: Z = 7.94 (P < 0.00001)	54); I² = (	)%							-4 -2 0 2 Control FASD	4

Risk of bias legend

(A) Overall RoB

# FAS and CBCL Internalising Behaviour – Teacher (T-score) (1 study)

					-			•			
	1	FAS		С	ontro	1		Std. Mean Difference		Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Random, 95% Cl	Α
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			774	100.0%	0.30 [-0.58, 1.18]			
			5			111	100.0%	0.30 [-0.36, 1.16]			
Heterogeneity: Not applicable									-4	-2 0 2	4
Test for overall effect: Z = 0.66 (P = 0.51)										Control FAS	
Risk of bias legend											
(A) Overall RoB											
pFAS an	d CB	CL Ir	ntern	alisi	ng B	eha	viour -	Teacher (T-scor	<b>e)</b> (1	. study)	
	p	FAS		Co	ontrol			Std. Mean Difference		Std. Mean Difference	Risk of Bia
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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			774	100.0%	0.09 [-0.21, 0.40]			
			44			111	100.0%	0.09 [-0.21, 0.40]		· · ·	
Heterogeneity: Not applicable									-4	-2 0 2	4
Test for overall effect: Z = 0.59 (P = 0.55)										Control pFAS	
Risk of bias legend											
(A) Overall RoB											
APND/Othor			<u></u>	+	ماند					(1, 1)	
ARND/Other	rs and	a CB	CL IN	itern	ansi	ing c	Sehavio	our – Teacher (T-	scor	' <b>e)</b> (1 stuay)	
ANND/ Other						-	Sehavio	our – Teacher (T-			Risk of Bi
Study or Subgroup			Others	;	Co	ntrol	otal Wei	Std. Mean Difference		CE) (L STUCIY) Std. Mean Difference IV, Random, 95% CI	Risk of Bi A
	М	ARND	Others SD T	i otal M	Co	ntrol SD T		Std. Mean Difference ht IV, Random, 95% C	1	Std. Mean Difference	-
Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-Int-T; ARN	М	ARND lean	Others SD T	i <mark>otal M</mark> 44	Co lean	ntrol SD T 9.7	otal Wei 771 100.0	Std. Mean Difference           IV, Random, 95% C           0%         0.48 [0.18, 0.79]	1 ]	Std. Mean Difference	-
Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-Int-T; ARN Total (95% CI)	М	ARND lean	Others SD T	i otal M	Co lean	ntrol SD T 9.7	otal Wei	Std. Mean Difference           IV, Random, 95% C           0%         0.48 [0.18, 0.79]	1 ]	Std. Mean Difference	-
Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-Int-T; ARN Total (95% CI) Heterogeneity: Not applicable	М	ARND lean	Others SD T	i <mark>otal M</mark> 44	Co lean	ntrol SD T 9.7	otal Wei 771 100.0	Std. Mean Difference           IV, Random, 95% C           0%         0.48 [0.18, 0.79]	1 ]	Std. Mean Difference IV, Random, 95% CI	• 
Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-Int-T; ARN Total (95% CI)	М	ARND lean	Others SD T	i <mark>otal M</mark> 44	Co lean	ntrol SD T 9.7	otal Wei 771 100.0	Std. Mean Difference           IV, Random, 95% C           0%         0.48 [0.18, 0.79]	ı ] ]	Std. Mean Difference IV, Random, 95% Cl	A • 
Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-Int-T; ARN Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 3.10 (P = 0.002)	М	ARND lean	Others SD T	i <mark>otal M</mark> 44	Co lean	ntrol SD T 9.7	otal Wei 771 100.0	Std. Mean Difference           IV, Random, 95% C           0%         0.48 [0.18, 0.79]	ı ] ]	Std. Mean Difference IV, Random, 95% CI	A • 
Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-Int-T; ARN Total (95% CI) Heterogeneity: Not applicable	М	ARND lean	Others SD T	i <mark>otal M</mark> 44	Co lean	ntrol SD T 9.7	otal Wei 771 100.0	Std. Mean Difference           IV, Random, 95% C           0%         0.48 [0.18, 0.79]	ı ] ]	Std. Mean Difference IV, Random, 95% CI	A • 

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)

	F	ASD		C	ontrol			Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	Α
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]		-	•
Fotal (95% CI)			37			23	100.0%	0.22 [-0.30, 0.74]		•	
Heterogeneity: Not applicable									-4	-2 0 2	

Risk of bias legend (A) Overall RoB

## pFAS and ASR Internalising Behaviour - Self-report (T-score) (1 study)

	р	FAS		С	ontrol			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	-	• <b>•</b>
Total (95% CI)			47			58	100.0%	3.56 [2.94, 4.19]	. <	Þ
Heterogeneity: Not applicable Test for overall effect: Z = 11.19 (P	< 0.0000	)1)							-4 -2 0 2 Control pFAS	4

Risk of bias legend (A) Overall RoB

## ARND/Others and ASR Internalising Behaviour – Self-report (T-score) (1 study)

	ARNI	D/Othe	ers	С	ontrol			Std. Mean Difference		Std. Mean	Difference		<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% Cl		Α
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]				٠	
Heterogeneity: Not applicable Test for overall effect: Z = 10.71 (P < 0.00001)									-4	-2 Control	0 2 ARND/Oth	4 ners	-

Risk of bias legend (A) Overall RoB

Note: Lynch et al 2017 also reports other minor CBCL subdomains.

FAS	SD and	d CBC	L Co	nduc	t Pro	blen	ns –	Caregiver (T-score	e) (4 studies)	
		FASD		С	ontrol			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean			Mean	SD		Weig			A
May et al 2020a (6-7yrs; CBCL-C)	57.1	8.8	38	52.9	5.2	273		• • •		
May et al 2020b (6-7yrs; CBCL-C)	55.5	7.2	49	53.3	5.2	444		• • •		
May et al 2020c (6-7yrs; CBCL-C) Popova et al 2019 (7-9yrs; CBCL-C)	56.9 56.6	7.1 16.26	37	53.8 52.24	5.7 6.04	331 39		• • •		
	50.0	10.20	15	52.24	0.34	39	10.3	0.40[-0.10, 0.90]	_	•
Total (95% CI)			143			1087	100.	0% 0.52 [0.35, 0.70]	•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.1	8, df = 3	(P = 0.5	4); l² =	0%					-4 -2 0 2	7
Test for overall effect: $Z = 5.78$ (P < 0.1	00001)								-4 -2 0 2 Control FASD	4
Risk of bias legend										
(A) Overall RoB	15 an			nduc	+ Dro	hlor	<b>m</b> c _	Caragivar (T. score	(1  study)	
E.	AS an		.L CO			bier	115 -	Caregiver (T-score		
Study or Subgroup	Me	FAS an SD	Tota	I Mean	ontrol	Total	Woir	Std. Mean Difference IN, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl	Risk of Bias A
Chambers et al 2019 (6-7yrs; CBCL-		6.8 8.7			6.7		100.0			
Chambers et al 2019 (0-7)(S, CBCE-	C) 0	0.0 0.7	5	0 00.0	0.7	701	100.0	0.19[-0.09, 1.07]		•
Total (95% CI)			5	5		761	100.	0% 0.19 [-0.69, 1.07]	-	
Heterogeneity: Not applicable										4
Test for overall effect: Z = 0.43 (P = 0.	67)								-4 -2 U 2 Control FAS	4
									Control 1710	
Risk of bias legend										
(A) Overall RoB								a · /=		
рі	AS ar					oble	ms –	· Caregiver (T-scor		
Study on Sylandy		pFAS			ontrol	T-4-1	14/	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup		an SD		l Mean						A
Chambers et al 2019 (6-7yrs; CBCL-	U) 5	6.4 7.3	44	55.5	6.7	761	100.0	0% 0.13 [-0.17, 0.44]		•
Total (95% CI)			44	ļ.		761	100.0	0% 0.13 [-0.17, 0.44]	•	
Heterogeneity: Not applicable								- / -		÷
Test for overall effect: Z = 0.86 (P = 0.3	39)								-4 -2 0 2 Control pFAS	4
	/Otho	rs and			nduc	t Dr	مالم	ms – Caregiver (T	-	
	oune		D/Othe			ntrol	Obic	Std. Mean Differend		Risk of Bias
Study or Subgroup		Mean		Total			otal V			A
Chambers et al 2019 (6-7yrs; CBCL-C;	ARND)	62.8		44	55.5		761 1			•
Total (95% CI)				44			761 1	1.06 [0.75, 1.3	▼	
Heterogeneity: Not applicable Test for overall effect: Z = 6.73 (P < 0.00	001\								-4 -2 0 2	4
restion overall ellect. 2 = 0.75 (F < 0.00	001)								Control ARND/Others	
<u>Risk of bias legend</u>										
(A) Overall RoB										
	-						-		<b>)</b>	
	Т	KF Co	วท่ดเ	uct Pr	oble	ems	lead	cher Report (T-so	core)	
F	ASD a	nd TR	F Co	nduc	t Pro	bler	ns –	Teacher (T-score)	(4 studies)	
	FA			Contr				Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean		al Me	ean SI		al W	eight	IV, Random, 95% CI	IV, Random, 95% CI	Α
May et al 2020a (6-7yrs; TRF-T)	57.3			3.2 5.0			9.9%	0.63 [0.29, 0.98]	-	•
May et al 2020b (6-7yrs; TRF-T)	56.5 8			2.9 5.4			4.0%	0.63 [0.33, 0.92]	-	•
May et al 2020c (6-7yrs; TRF-T)	56.3 7	<b>'.9</b> 3		2.5 4.8		1 2	9.9%	0.73 [0.39, 1.07]		•
May et al 2021 (6-7yrs; TRF-T)	50.5	1	4 5	3.3 5.1	15	0 1	6.2%	-0.56 [-1.58, 0.47]		•
T-4-1/054/ 00										
Total (95% CI)		12		_		8 10	0.0%	0.59 [0.32, 0.86]	,   ● .	
Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 5		3 (P = 1	0.14);1	I² = 45%				- -	4 -2 0 2	4
Test for overall effect: $Z = 4.27$ (P <	0.0001)								Control FASD	
Disk of hiss lases 1										
Risk of bias legend										
(A) Overall RoB										

CBCL Conduct Problems Caregiver Report (T-score)

# FAS and TRF Conduct Problems – Teacher (T-score) (1 study)

	I	FAS		C	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									-4 -2 0 2	4
Test for overall effect: Z = 0.08 (P = 0.94	)								Control FAS	
Risk of bias legend										

(A) Overall RoB

		SD SD	Total		ontro		S Weight	td. Mean Difference IV, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl	Risk of Bia A
Study or Subgroup Chambers et al 2019 (6-7yrs; TRF-Ext-T)	52.9		44		5.9		100.0%	0.02 [-0.29, 0.32]	IV, Kandolli, 95% Cl	•
							400.0%		T	-
Fotal (95% CI) Heterogeneity: Not applicable			44			/61	100.0%	0.02 [-0.29, 0.32]	<b>▼</b>	
Fest for overall effect: Z = 0.11 (P = 0.91)								-4	4 -2 Ó 2 Control pFAS	4
Risk of bias legend									Control - pr AG	
A) Overall RoB										
ARND/O			d TR Others	F Cor	ndu Con		oblems -	- Teacher (T-sco Std. Mean Difference	re) (1 study) Std. Mean Difference	Risk of Bia
Study or Subgroup	Mea			otal Me			tal Weight		IV, Random, 95% Cl	A
Chambers et al 2019 (6-7yrs; TRF-T; ARND)	57	.8	8.6	44 5	2.8 (	5.9 7	61 100.0%	0.82 [0.52, 1.13]		•
Fotal (95% CI)				44		7	61 100.0%	0.82 [0.52, 1.13]	•	
Heterogeneity: Not applicable Fest for overall effect: Z = 5.26 (P < 0.00001)									-4 -2 0 2 Control ARND/Others	4
<u>Risk of bias legend</u> A) Overall RoB										
								aregiver Report – Caregiver (T-se		
FASD and CD	FAS		JSILIU		ontrol			td. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup Mea			Fotal I				l Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
May et al 2020a (6-7yrs; CBCL-C) 58 May et al 2020b (6-7yrs; CBCL-C) 5		3.8 3.2	38 49	54 54.3	5.3 5.9			0.70 [0.36, 1.05]		2
Aay et al 2020b (6-7yrs, CBCL-C) 56		7	49 37	54.5 54.9	0.9 6			0.60 [0.30, 0.90] 0.33 [-0.01, 0.67]		ĕ
	3 11.	05	19 (	54.43	12.96	i 39	3 15.4%	0.00 [-0.55, 0.55]	-	•
otal (95% CI)			143			1087	7 100.0%	0.46 [0.20, 0.72]	•	
Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 5.92, df =	3 (P =	0.12)		9%						-
Test for overall effect: Z = 3.50 (P = 0.0005)									Control FASD	4
Risk of bias legend										
A) Overall RoB										
A) Overall RoB			ositic					– Caregiver (T-so		Diele of Die
A) Overall RoB FAS and CB	F	AS		Co	ontrol	l i	St	d. Mean Difference	Std. Mean Difference	
A) Overall RoB FAS and CB Study or Subgroup	F	AS SD		Co	ontrol SD	Total				Risk of Bia
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C)	F Mean	AS SD	Total 5	Co Mean	ontrol SD	Total 761	St Weight 100.0%	d. Mean Difference IV, Random, 95% CI 0.25 [-0.63, 1.13]	Std. Mean Difference	-
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Total (95% CI)	F Mean	AS SD	Total	Co Mean	ontrol SD	Total 761	St Weight	d. Mean Difference <u>IV, Random, 95% CI</u> 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] ⊢	Std. Mean Difference IV, Random, 95% CI	-
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Total (95% CI) Heterogeneity: Not applicable	F Mean	AS SD	Total 5	Co Mean	ontrol SD	Total 761	St Weight 100.0%	d. Mean Difference IV, Random, 95% CI 0.25 [-0.63, 1.13]	Std. Mean Difference IV, Random, 95% CI	
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend	F Mean	AS SD	Total 5	Co Mean	ontrol SD	Total 761	St Weight 100.0%	d. Mean Difference <u>IV, Random, 95% CI</u> 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] ⊢	Std. Mean Difference IV, Random, 95% CI	-
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Total (95% CI) Heterogeneity: Not applicable rest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB	F <u>Mean</u> 58.4	AS SD 8.6	Total 5 5	Co <u>Mean</u> 56.5	ntrol SD 7.6	<u>Total</u> 761 <b>761</b>	St Weight 100.0%	d. Mean Difference <u>IV, Random, 95% CI</u> 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4	Std. Mean Difference IV, Random, 95% CI	
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable "est for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB	F <u>Mean</u> 58.4 3CL C	AS SD 8.6	Total 5 5	Co <u>Mean</u> 56.5	ntrol SD 7.6	<u>Total</u> 761 761	St Weight 100.0% 100.0% Disorder	d. Mean Difference <u>IV, Random, 95% CI</u> 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] ⊢	Std. Mean Difference IV, Random, 95% CI	A 
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable "est for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB pFAS and CI Study or Subgroup	F Mean 58.4 3CL C pl Mean	AS SD 8.6 8.6	Total 5 5 Ositie	Co Mean 56.5 onal Co Mean	Def	Total 761 761 761 iant	St Weight 100.0% 100.0% Disorder St Weight	d. Mean Difference <u>IV, Random, 95% CI</u> 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI	Risk of Bia
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB pFAS and CI Study or Subgroup	F <u>Mean</u> 58.4 BCL C	AS SD 8.6 8.6	Total 5 5 ositie	Co <u>Mean</u> 56.5 onal	Def	Total 761 761 761 iant	St Weight 100.0% 100.0% Disorder St	d. Mean Difference <u>IV, Random, 95% CI</u> 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI	A 
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB pFAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C)	F Mean 58.4 3CL C pl Mean	AS SD 8.6 8.6	Total 5 5 Ositie	Co Mean 56.5 onal Co Mean	Def	Total 761 761 761 iant Total 761	St Weight 100.0% 100.0% Disorder St Weight	d. Mean Difference <u>IV, Random, 95% CI</u> 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI	A 
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB pFAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable	F Mean 58.4 3CL C pl Mean	AS SD 8.6 8.6	<u>Total</u> 5 <b>ositi</b> <u>Total</u> 44	Co Mean 56.5 onal Co Mean	Def	Total 761 761 761 iant Total 761	St           Weight           100.0%           100.0%           Disorder           St           Weight           100.0%	d. Mean Difference <u>IV, Random, 95% CI</u> 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI	A 
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB pFAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable	F Mean 58.4 3CL C pl Mean	AS SD 8.6 8.6	<u>Total</u> 5 <b>ositi</b> <u>Total</u> 44	Co Mean 56.5 onal Co Mean	Def	Total 761 761 761 iant Total 761	St           Weight           100.0%           100.0%           Disorder           St           Weight           100.0%	d. Mean Difference IV, Random, 95% CI 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI	A 
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB pFAS and CE Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 2.36 (P = 0.02) Risk of bias legend	F Mean 58.4 3CL C pl Mean	AS SD 8.6 8.6	<u>Total</u> 5 <b>ositi</b> <u>Total</u> 44	Co Mean 56.5 onal Co Mean	Def	Total 761 761 761 iant Total 761	St           Weight           100.0%           100.0%           Disorder           St           Weight           100.0%	d. Mean Difference IV, Random, 95% CI 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI	A 
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB pFAS and CI Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 2.36 (P = 0.02) Risk of bias legend A) Overall RoB	F <u>Mean</u> 58.4 3 <b>CL C</b> pi <u>Mean</u> 59.3	As <u>sD</u> 8.6 <b>SD</b> <b>FAS</b> <u>SD</u> 8.3	<u>Total</u> 5 5 0sitiu <u>Total</u> 44 44	Co Mean 56.5 Onal Co Mean 56.5	Defi ontrol SD 7.6 Defi ontrol SD 7.6	<u>Total</u> 761 761 761 <u>Total</u> 761	St Weight 100.0% 100.0% Disorder St Weight 100.0% 100.0%	d. Mean Difference IV, Random, 95% CI 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI	A 
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB  FAS and CI Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 2.36 (P = 0.02) Risk of bias legend A) Overall RoB  ARND/Others ar	F Mean 58.4 3CL C pi Mean 59.3	AS SD 8.6 Pppp FAS SD 8.3 8.3 8.3	Total 5 5 ositiu 44 44 Oppp /Others	onal Co Mean 56.5 Mean 56.5	Defi ontrol SD 7.6 7.6 7.6 7.6	Total 761 761 761 <u>Total</u> 761 761 761	St           Weight           100.0%           100.0%           Disorder           St           Weight           100.0%           100.0%           iant Disc	d. Mean Difference IV, Random, 95% CI 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI -2 Control FAS Score) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control pFAS	A Risk of Bia A A A A A A A A A A A A A
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB pFAS and CE Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 2.36 (P = 0.02) Risk of bias legend A) Overall RoB ARND/Others ar Study or Subgroup	Amena 58.4 BCL C pl Mean 59.3 MCCL	AS SD 8.6 Ppp AS SD 8.3 8.3 8.3 8.3	Total 5 5 ositiv Total 44 44 VOpp VOthers SD 1	Co Mean 56.5 Onal Co Mean 56.5 Ositic	Definition Definition Definition SD 7.6 7.6 Onal Co lean	iant 761 761 761 <u>Total</u> 761 761 761	St           Weight           100.0%           100.0%           Disorder           St           Weight           100.0%           100.0%           iant Disconter           otal Weight	d. Mean Difference IV, Random, 95% CI 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI -2 Control FAS Score) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control pFAS	A • 4 Risk of Bia A • 4
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB PFAS and CE Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 2.36 (P = 0.02) Risk of bias legend A) Overall RoB ARND/Others ar Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C; ARNE	Amena 58.4 BCL C pl Mean 59.3 MCCL	AS SD 8.6 Pppp FAS SD 8.3 8.3 8.3	Total 5 5 ositiu 44 44 Oppp /Others	Co Mean 56.5 Onal Co Mean 56.5 56.5	Defi ontrol SD 7.6 7.6 7.6 7.6	Total 761 761 761 761 761 761 761 761	St           Weight           100.0%           100.0%           Disorder           St           Weight           100.0%           100.0%           iant Disc           otal Weight           761	d. Mean Difference IV, Random, 95% CI 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI -2 Control FAS Score) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control pFAS	A Risk of Bia A A Risk of Bia
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend (A) Overall RoB PFAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 2.36 (P = 0.02) Risk of bias legend (A) Overall RoB ARND/Others an Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C; ARNE	Amena 58.4 BCL C pl Mean 59.3 MCCL	AS SD 8.6 Ppp AS SD 8.3 8.3 8.3 8.3	Total 5 5 ositiv Total 44 44 VOpp VOthers SD 1	Co Mean 56.5 Onal Co Mean 56.5 Ositic	Definition Definition Definition SD 7.6 7.6 Onal Co lean	Total 761 761 761 761 761 761 761 761	St           Weight           100.0%           100.0%           Disorder           St           Weight           100.0%           100.0%           iant Disconter           otal Weight	d. Mean Difference IV, Random, 95% CI 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI -2 Control FAS Score) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control pFAS r (T-score) (1 study) Std. Mean Difference IV, Random, 95% CI	A Risk of Bia A A A A A A A A A A A A A
A) Overall RoB FAS and CB Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 0.56 (P = 0.58) Risk of bias legend A) Overall RoB FAS and CE Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 2.36 (P = 0.02) Risk of bias legend A) Overall RoB ARND/Others ar Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C; ARNE	Amena 58.4 BCL C pl Mean 59.3 MCCL	AS SD 8.6 Ppp AS SD 8.3 8.3 8.3 8.3	Total 5 5 ositiv Total 44 44 VOpp VOthers SD 1	Co Mean 56.5 Onal Co Mean 56.5 56.5	Definition Definition Definition SD 7.6 7.6 Onal Co lean	Total 761 761 761 761 761 761 761 761	St           Weight           100.0%           100.0%           Disorder           St           Weight           100.0%           100.0%           iant Disc           otal Weight           761	d. Mean Difference IV, Random, 95% CI 0.25 [-0.63, 1.13] 0.25 [-0.63, 1.13] -4 -4 -4 -4 -4 -4 -4 -4 -4 -4	Std. Mean Difference IV, Random, 95% CI -2 Control FAS Score) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control pFAS	A Risk of Bia A A A A A A A A A A A A A

# Vanderbilt-C Oppositional Defiant Disorder Caregiver Report (m/SD)

## FASD and Vanderblit-C Oppositional Defiant Disorder – Caregiver (mean/SD) (1 study)

	F	ASD		Co	ontro	1		Std. Mean Difference	Std. Mean Difference Ri	sk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 4.28 (P < 0.0001	)		16			21	100.0%	1.67 [0.91, 2.44]	-4 -2 0 2 4 Control FASD	
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)

	F	ASD		Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias	
Study or Subgroup	Mean	<b>SD</b>	Total	Mean SD Total		Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α	
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: Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> = Test for overall effect: Z = 3.37 (P			9 = 0.20	0); I² = 35%				-4 -2 0 2 Control FASD	4	

Risk of bias legend (A) Overall RoB

## FAS and TRF Oppositional Defiant Disorder – Teacher (T-score) (1 study)

	F	FAS Control				I		Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 2.06 (P = 0.04)	)		5			761	100.0%	0.92 [0.04, 1.81]	-4 -2 0 2 Control FAS	

Risk of bias legend (A) Overall RoB

## pFAS and TRF Oppositional Defiant Disorder – Teacher (T-score) (1 study)

	pFAS Contr				ontro	1		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean SD Total		Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α	
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) Heterogeneity: Not applicable Test for overall effect: Z = 0.71 (P = 0.48)	)		44			761	100.0%	0.11 [-0.19, 0.41]	-4 -2 0 2 Control pFAS	4
Risk of bias legend										

(A) Overall RoB

## ARND/Others and TRF Oppositional Defiant Disorder – Teacher (T-score) (1 study)

	ARND/Others		Control				Std. Mean Difference	Std. Mean Difference Risk of Bias	
Study or Subgroup	Mean	ean SD Total Mean SD Total Weight IV, Random, 95% Cl IV, Random, 95% Cl				IV, Random, 95% CI 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)									-4 -2 0 2 4 Control ARND/Others

# CBCL Aggression Caregiver Report (T-score)

FASD and CBCL	$\Lambda$ agrossion $-C$	aragivar (T. coo	rol (E studios)
FASD and CBCL	Aggression – Ca	aregiver (1-sco	<b>prej</b> (5 studies)

			DCL	7651	2221011	1 – Ca	ICGIV	er (T-score) (5 s	studies)		
		FASD			Control			Std. Mean Difference		Difference	Risk of Bias
Study or Subgroup	Mea			I Mean		Total V	-	IV, Random, 95% CI	IV, Rand	om, 95% Cl	A
Mattson & Riley 2000 (4-16yrs; CBCL- May et al 2020a (6-7yrs; CBCL-C)	-C) 66 58						16.9% 21.7%	1.11 [0.59, 1.63]			
May et al 2020b (6-7yrs; CBCL-C)	57						23.2%	1.05 [0.70, 1.40] 0.74 [0.45, 1.04]			
May et al 2020c (6-7yrs; CBCL-C)		.0 0. 57 7.4					22.0%	0.50 [0.16, 0.84]			ĕ
Popova et al 2019 (7-9yrs; CBCL-C)		7 11.42		9 54.33			16.2%	-0.04 [-0.59, 0.50]	-	♣_	ĕ
Total (95% CI)			170			1120 1	00.0%	0.69 [0.36, 1.03]		•	
Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 14.		P = 0.001	6); I <b>*</b> = 7	73%					-4 -2	0 2	4
Test for overall effect: Z = 4.04 (P < 0.0	JUU1)								Contro	FASD	
Risk of bias legend											
(A) Overall RoB											
	FAS	and C	BCL	Aggre	ession	n – Ca	regiv	er (T-score) (1	studv)		
	-	FAS			ontrol		-	td. Mean Difference		Difference	Risk of Bias
Study or Subgroup	Mea	n SD	Total	Mean	SD To	otal We	eight	IV, Random, 95% CI	IV, Rando	m, 95% Cl	Α
Chambers et al 2019 (6-7yrs; CBCL-	·C) 57.	6 10.4	5	56.2	7.9 7	761 100	0.0%	0.18 [-0.70, 1.06]	-	-	•
T-t-1/05% CIV					-		0.00/	0 40 5 0 70 4 001			
Total (95% CI)			5			761 10	0.0%	0.18 [-0.70, 1.06]			
Heterogeneity: Not applicable Test for overall effect: Z = 0.39 (P = 0.	60)								-4 -2	0 <u>2</u>	4
Testion overall ellect. $\Sigma = 0.33$ (F = 0.	.03)								Control	FAS	
Risk of bias legend											
(A) Overall RoB											
	pFAS	and	CBCL	Aggr	essio	n – Ca	regiv	ver (T-score) (1	study)		
	P1710	pFAS			ntrol		-	d. Mean Difference		Difference	Risk of Bias
Study or Subgroup	Mea		Total		SD To	tal We		IV, Random, 95% CI		m, 95% Cl	A
Chambers et al 2019 (6-7yrs; CBCL		59 8.8	44	56.2		61 100	-	0.35 [0.05, 0.66]	,		
	•, •			00.2		000	.0 /0	0.00 [0.00] 0.00]			•
Total (95% CI)			44		7	61 100	).0%	0.35 [0.05, 0.66]		◆	
Heterogeneity: Not applicable									-4 -2	<u>+</u> +	
Test for overall effect: Z = 2.27 (P = 0	.02)								Control	pFAS 2	4
Risk of bias legend											
(A) Overall RoB					_		-				
Al	RND/O						– Ca	regiver (T-scor			
		ARND	Others		Contro	bl		Std. Mean Difference	Etd Moo	n Difference	Risk of Bias
Chudu on Cubaroup		Maan		otol M	CD	Total	Mainh				
		Mean			ean SD		-	t IV, Random, 95% C	I IV, Rand	lom, 95% Cl	A
	; ARND)	Mean 66.3	<u>SD T</u> 10		ean SD 6.2 7.9		Weigh 100.0%	t IV, Random, 95% C	I IV, Rand		
Chambers et al 2019 (6-7yrs; CBCL-C	; ARND)					761	-	t IV, Random, 95% C 5 1.26 (0.95, 1.57	I IV, Rand ]		
Chambers et al 2019 (6-7yrs; CBCL-C Total (95% CI)	; ARND)			44 5		761	100.0%	t IV, Random, 95% C 5 1.26 (0.95, 1.57	I IV, Rand	lom, 95% Cl	
Chambers et al 2019 (6-7yrs; CBCL-C Total (95% CI) Heterogeneity: Not applicable				44 5		761	100.0%	t IV, Random, 95% C 5 1.26 (0.95, 1.57	I IV, Rand	lom, 95% Cl	A • 
Chambers et al 2019 (6-7yrs; CBCL-C Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 7.95 (P < 0.0				44 5		761	100.0%	t IV, Random, 95% C 5 1.26 (0.95, 1.57	I IV, Rand	lom, 95% Cl	A • 
Chambers et al 2019 (6-7yrs; CBCL-C Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 7.95 (P < 0.0 <u>Risk of bias legend</u>				44 5		761	100.0%	t IV, Random, 95% C 5 1.26 (0.95, 1.57	I IV, Rand	lom, 95% Cl	A • 
Chambers et al 2019 (6-7yrs; CBCL-C Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 7.95 (P < 0.0 <u>Risk of bias legend</u>	0001)	66.3	10	44 5 44	6.2 7.9	761 <b>761</b>	100.0%	t IV, Random, 95% C 5 1.26 (0.95, 1.57 6 1.26 (0.95, 1.57	I IV, Rand I I -4 -2 Contro	lom, 95% Cl	A • 
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Chambers et al 2019 (6-7yrs; CBCL-C Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 7.95 (P < 0.0 <u>Risk of bias legend</u> (A) Overall RoB <u>Study or Subgroup</u> May et al 2020a (6-7yrs; TRF-T) May et al 2020b (6-7yrs; TRF-T) May et al 2020c (6-7yrs; TRF-T) May et al 2020c (6-7yrs; TRF-T) May et al 2020c (6-7yrs; TRF-T) May et al 2021 (6-7yrs; TRF-T) Total (95% CI) Heterogeneity: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> = 4 Test for overall effect: Z = 3.71 (P = <u>Risk of bias legend</u> (A) Overall RoB <u>Study or Subgroup</u>	0001) <b>FASI</b> <b>FAS</b> 59.1 11 55.8 7 55.5 50.3 0 5.69, df = 3 0.0002) <b>FA</b>	66.3 RF/C D and D SD Tota .6 3 .5 4 7 3 0.5 12 3 (P = 0. S and FAS	10 BCL. TRF a <u>l Me</u> 8 53 9 52 7 52 4 53 8 13); I <sup>2</sup> = 13); I <sup>2</sup> =	44 6 44 Aggre Aggre Contro an SD 3.9 6.5 2.9 5.5 2.6 4.7 3.6 5.7 = 47% Aggre Con	6.2 7.9 ession Total 273 444 331 50 1098 ession trol 50 Total	761 761 761 761 29.8% 33.9% 29.9% 6.4% 100.0%	ache std. IV	t IV, Random, 95% C 5 1.26 [0.95, 1.57 1.26 [0.95, 1.57 1.26 [0.95, 1.57 1.26 [0.95, 1.57 1.26 [0.95, 1.57 r (T-score) (4 st 1.27 [0.37, 1.05] 0.51 [0.21, 0.80] 0.58 [0.24, 0.92] -0.59 [-1.61, 0.44] 0.52 [0.25, 0.79] -4 r (T-score) (1 st 1. Mean Difference	I IV, Rand I -4 -2 Control re) udies) Std. Mean D IV, Randon -2 0 Control udy) Std. Mean	ifference h, 95% Cl ARND/Other FASD Difference	A 4 rs Risk of Bias A 4 Risk of Bias
Chambers et al 2019 (6-7yrs; CBCL-C Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 7.95 (P < 0.0 <u>Risk of bias legend</u> (A) Overall RoB <u>Study or Subgroup</u> May et al 2020a (6-7yrs; TRF-T) May et al 2020b (6-7yrs; TRF-T) May et al 2020c (6-7yrs; TRF-T) Heterogeneity: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> = 4 Test for overall effect: Z = 3.71 (P = <u>Risk of bias legend</u> (A) Overall RoB <u>Study or Subgroup</u> Chambers et al 2019 (6-7yrs; TRF-T)	0001) <b>FASI</b> <b>FAS</b> 59.1 11 55.8 7 55.5 50.3 0 5.69, df = 3 0.0002) <b>FA</b>	66.3 RF/C D and D SD Tota .6 3 .5 4 7 3 0.5 12 3 (P = 0. S and FAS SD T	10 BCL. TRF 8 53 9 52 7 52 4 53 8 13); I <sup>2</sup> = TRF 5	44 6 44 Aggre Aggre Contro an SD 3.9 6.5 2.9 5.5 2.6 4.7 3.6 5.7 = 47% Aggre Con Mean S	ession Total 273 444 331 50 1098 ession trol 50 Tota 344 331 50	761 761 761 761 29.8% 33.9% 29.9% 6.4% 100.0%	100.0%	t IV, Random, 95% C 1.26 [0.95, 1.57 1.26 [0.95, 1.57 1.26 [0.95, 1.57 1.26 [0.95, 1.57 r (T-score) (4 st Mean Difference Random, 95% CI 0.71 [0.37, 1.05] 0.51 [0.21, 0.80] 0.58 [0.24, 0.92] -0.59 [-1.61, 0.44] 0.52 [0.25, 0.79] -4 r (T-score) (1 st Mean Difference IV, Random, 95% CI 0.64 [-0.24, 1.52]	I IV, Rand I -4 -2 Control re) udies) Std. Mean D IV, Randon -2 0 Control udy) Std. Mean	ifference h, 95% Cl ARND/Other FASD Difference	A 4 rs Risk of Bias A 4 Risk of Bias
May et al 2020a (6-7yrs; TRF-T) May et al 2020b (6-7yrs; TRF-T) May et al 2020c (6-7yrs; TRF-T) May et al 2021 (6-7yrs; TRF-T) Total (95% CI) Heterogeneity: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> = 4 Test for overall effect: Z = 3.71 (P = <u>Risk of bias legend</u> (A) Overall RoB <u>Study or Subgroup</u> Chambers et al 2019 (6-7yrs; TRF-T Total (95% CI)	0001) <b>FASI</b> <b>FAS</b> 59.1 11 55.8 7 55.5 50.3 0 5.69, df = 3 0.0002) <b>FA</b>	66.3 RF/C D and D SD Tota .6 3 .5 4 7 3 0.5 12 3 (P = 0. S and FAS SD T	10 BCL. TRF a <u>l Me</u> 8 53 9 52 7 52 8 13); I <sup>2</sup> = 8 13); I <sup>2</sup> =	44 6 44 Aggre Aggre Contro an SD 3.9 6.5 2.9 5.5 2.6 4.7 3.6 5.7 = 47% Aggre Con Mean S	ession Total 273 444 331 50 1098 ession trol 50 Tota 344 331 50	761 761 761 761 29.8% 33.9% 29.9% 6.4% 100.0%	100.0%	t IV, Random, 95% C 5 1.26 [0.95, 1.57 6 1.26 [0.95, 1.57 7 1.26 [0.95, 1.57 8 1.26 [0.95, 1.57 8 1.26 [0.95, 1.57 1.26 [0.95, 1.57 8 1.26 [0.95, 1.57 9 1.26 [0.95, 1.57 1.26 [0.95, 1.57 9 1.26 [0.95, 1.57] 9 1.26 [0.	I IV, Rand I -4 -2 Control re) udies) Std. Mean D IV, Randon -2 0 Control udy) Std. Mean	ifference h, 95% Cl ARND/Other FASD Difference	A 4 rs Risk of Bias A 4 Risk of Bias
Chambers et al 2019 (6-7yrs; CBCL-C Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 7.95 (P < 0.0 <u>Risk of bias legend</u> (A) Overall RoB <u>Study or Subgroup</u> May et al 2020a (6-7yrs; TRF-T) May et al 2020b (6-7yrs; TRF-T) May et al 2020c (6-7yrs; TRF-T) Total (95% CI) Heterogeneity: Not applicable	0001) FASI FAS 59.1 11 55.5 50.3 0 5.69, df = 3 0.0002) FA Mean ) 57.2	66.3 RF/C D and D SD Tota .6 3 .5 4 7 3 0.5 12 3 (P = 0. S and FAS SD T	10 BCL. TRF 8 53 9 52 7 52 4 53 8 13); I <sup>2</sup> = TRF 5	44 6 44 Aggre Aggre Contro an SD 3.9 6.5 2.9 5.5 2.6 4.7 3.6 5.7 = 47% Aggre Con Mean S	ession Total 273 444 331 50 1098 ession trol 50 Tota 344 331 50	761 761 761 761 29.8% 33.9% 29.9% 6.4% 100.0%	100.0%	t IV, Random, 95% C 5 1.26 [0.95, 1.57 6 1.26 [0.95, 1.57 7 1.26 [0.95, 1.57 7 1.26 [0.95, 1.57 8 1.26 [0.95, 1.57 8 1.26 [0.95, 1.57 8 1.26 [0.95, 1.57 9 1.26 [0.95, 1.57] 9 1.26 [0.95, 1.57]	I IV, Rand I -4 -2 Control re) udies) Std. Mean D IV, Randon -2 0 Control udy) Std. Mean	ifference h, 95% Cl ARND/Other FASD Difference	A 4 rs Risk of Bias A A A A A A A A A A A A A
Chambers et al 2019 (6-7yrs; CBCL-C Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 7.95 (P < 0.0 <u>Risk of bias legend</u> (A) Overall RoB <u>Study or Subgroup</u> May et al 2020a (6-7yrs; TRF-T) May et al 2020b (6-7yrs; TRF-T) May et al 2020c (6-7yrs; TRF-T) Total (95% CI) Heterogeneity: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> = 4 Test for overall effect: Z = 3.71 (P = <u>Risk of bias legend</u> (A) Overall RoB <u>Study or Subgroup</u> Chambers et al 2019 (6-7yrs; TRF-T)	0001) FASI FAS 59.1 11 55.5 50.3 0 5.69, df = 3 0.0002) FA Mean ) 57.2	66.3 RF/C D and D SD Tota .6 3 .5 4 7 3 0.5 12 3 (P = 0. S and FAS SD T	10 BCL. TRF 8 53 9 52 7 52 4 53 8 13); I <sup>2</sup> = TRF 5	44 6 44 Aggre Aggre Contro an SD 3.9 6.5 2.9 5.5 2.6 4.7 3.6 5.7 = 47% Aggre Con Mean S	ession Total 273 444 331 50 1098 ession trol 50 Tota 344 331 50	761 761 761 761 29.8% 33.9% 29.9% 6.4% 100.0%	100.0%	t IV, Random, 95% C 5 1.26 [0.95, 1.57 6 1.26 [0.95, 1.57 7 1.26 [0.95, 1.57 7 1.26 [0.95, 1.57 8 1.26 [0.95, 1.57 8 1.26 [0.95, 1.57 8 1.26 [0.95, 1.57 9 1.26 [0.95, 1.57] 9 1.26 [0.95, 1.57]	I IV, Rand I -4 -2 Control re) udies) Std. Mean D IV, Randon -2 0 Control udy) Std. Mean 1 -2 0 Control	ifference h, 95% Cl ARND/Other ARND/Other FASD Difference m, 95% Cl ARND/Other 1 2 FASD	A 4 rs Risk of Bias A 4 Risk of Bias

## pFAS and TRF Aggression – Teacher (T-score) (1 study)

				Control			Std. Mean Difference	Std. Mean Difference Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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									-4 -2 0 2 4
Test for overall effect: Z = 0.81 (P = 0.42	)								Control pFAS
Risk of bias legend									
(A) Overall RoB									

## ARND/Others and TRF Aggression – Teacher (T-score) (1 study)

	ARND/Others			Control				Std. Mean Difference	Std. Mean Difference Ri	sk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	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) Heterogeneity: Not applicable Test for overall effect: Z = 5.02 (P < 0.00001)			44			761	100.0%	0.79 [0.48, 1.09]	-4 -2 0 2 4 Control ARND/Others	
Risk of bias legend										

(A) Overall RoB

# ASR Aggression Self-Report (T-score)

# pFAS and ASR Aggression - Self-Report (T-score) (1 study)

	1	pFAS Control					Std. Mean Difference		Std. Mean	Ri	sk of Bias		
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% Cl		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 (F	0.00 × 0	001)							-4	-2 Control	pFAS	4	

Risk of bias legend (A) Overall RoB

# ARND/Others and ASR Aggression - Self-Report (T-score) (1 study)

	ARND/Others			-	ontrol			Std. Mean Difference	Std. Mean	Risk of Bias	
Study or Subgroup	Mean	Mean SD Total		Mean	Mean SD Total		Weight IV, Random, 95% Cl		IV, Rando	m, 95% Cl	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									-4 -2		_
Test for overall effect: Z = 11.11 (P < 0.00001)									Control	ARND/Others	
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)

	FASD		Control				Std. Mean Difference	Std. Mean Difference	Risk of Bias	
Study or Subgroup	Mean	SD Total M		Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]	+ <b>-</b> -	•
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]	<b>+-</b> -	•
Total (95% CI)			176			1120	100.0%	0.48 [0.19, 0.77]	◆	
Heterogeneity: Tau² = 0.07; Chi² = 11.05, c Test for overall effect: Z = 3.24 (P = 0.001)	lf= 4 (P =	= 0.03);	l² = 649	%				⊢	-2 0 2 Control FASD	4

		FAS Control				Std. Mean Difference			Std. Mean	е	Risk of Bias		
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	6 CI IV, Random, 95% CI			Α	
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: Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> = 1.18, c	f=1 (P=	= 0.28)	; <b>I</b> ² = 16	5%					<u> </u>	<u> </u>	<u>t</u>		4
Test for overall effect: Z = 1.73 (P = 0.08)									-4	Control	FAS	4	•

Risk of bias legend (A) Overall RoB

## pFAS and CBCL Rule-Breaking Behaviour - Caregiver (T-score) (1 study)

	p	FAS		Co	ontro	I I		Std. Mean Difference	Std. Mean Difference Risk of Bia
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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									-4 -2 0 2 4
Test for overall effect: Z = 1.20 (P = 0.23)									Control pFAS
Disk of bios logand									

Risk of bias legend (A) Overall RoB

## ARND/Others and CBCL Rule-Breaking Behaviour – Caregiver (T-score) (2 studies)

	ARNI	D/Othe	ers	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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: Tau <sup>2</sup> = 0.13; Chi <sup>2</sup> = 4.57, df = 1 (P =	0.03); l <sup>e</sup> :	= 78%	,							<del>,</del>
Test for overall effect: Z = 2.67 (P = 0.007)									Control ARND/Others	4

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)

	FASI	)	Contr	rol		Odds Ratio	Odds Ratio Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.94, o	df = 1 (P =	0.33);	I <sup>2</sup> = 0%				
Test for overall effect: Z = 3.24 (P = 0.001	)						0.01 0.1 1 10 100 Control FASD

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)

						-		-		-	
	F	ASD		Co	ontro	I		Std. Mean Difference	Std. Mea	n Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rand	lom, 95% Cl	Α
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	53.2	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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = Test for overall effect: Z = 6.24 (P	•		(P = 0.9	13); <b>1²</b> = 1	)%				-4 -2 Contro	0 2 I FASD	4

			FAS	ale-		Cont	-			Teacher (T-scor	Std. Mean Diff	erence	Risk of Bia
Study or Subgroup	N	Nean		Total				al Wei		IV, Random, 95% Cl	IV, Random,		A
Chambers et al 2019 (6-7yrs; TF		52.8		5		8 5.		1 100.	-	0.00 [-0.88, 0.88]		-	ê
				_			_				T		
Fotal (95% CI)				5			76	1 100	.0%	0.00 [-0.88, 0.88]		-	
Heterogeneity: Not applicable Fest for overall effect: Z = 0.00 (F	2 - 1 00\									-	4 -2 0	2	4
restion overall ellect. Σ = 0.00 (F	1.00)										Control FA	S	
Risk of bias legend													
(A) Overall RoB													
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Study or Subgroup		l Nean	SD SD	Total		Conti		al Wei		I. Mean Difference IV, Random, 95% Cl	Std. Mean Diff IV, Random,		Risk of Bia
Chambers et al 2019 (6-7yrs; TF			5.6	44		8 5.		1 100.	<u> </u>	0.02 [-0.29, 0.32]	iv, italiaoni,	5577 61	ê
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Total (95% CI)				44			76	1 100	.0%	0.02 [-0.29, 0.32]	. 🔶		
Heterogeneity: Not applicable Teet for guerell offect: 7 – 0.42 /F	0 00									-	4 -2 0	2	4
Fest for overall effect: Z = 0.12 (F	<sup>2</sup> = 0.90)										Control pF	AS	
Risk of bias legend													
(A) Overall RoB													
	- /					_							
ARNE	D/Othe	ers a						-	navio	our – Teacher (1		• •	<b></b>
Study or Subgroup			ARND Iean	Other:	-		Control	Total	Wojab*	Std. Mean Difference IV, Random, 95% C	Std. Mean Di IV. Random		Risk of Bia A
Chambers et al 2019 (6-7yrs; TRF	F-T' ARND'		57.1	6.9	44		B 5.3		100.0%	0.80 [0.49, 1.10]	,	, 55% CI	
	, , , a (10)	<i>,</i>	01.1	0.0		01.	0.0						•
Total (95% CI)					44			761	100.0%	0.80 [0.49, 1.10]		<u>ب</u>	
Heterogeneity: Not applicable Test for overall effect: Z = 5.09 (P <	~ 0 00001)										-4 -2 0	2	4
restror overall ellect. Z = 5.03 (F -	~ 0.00001)										Control /	ARND/Others	5
Risk of bias legend													
A) Overall RoB													
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pF										elf Report (T-sc Self-report (T-sc			
pF	AS and					kin			ur – S	elf Report (T-sc Self-report (T-sc Mean Difference		erence	Risk of Bia
-	AS and	d AS F <mark>as</mark>	R R	ule-B	Brea Cont	king rol	g Beł		ur — S Std. N	elf-report (T-so	ore) (1 study)		Risk of Bia A
Study or Subgroup	AS and	d AS FAS SD	R R	ule-B	Brea Cont	king rol SD 1	g Beł Total	navio	ur — S Std. N t IV,	elf-report (T-so Mean Difference	ore) (1 study) Std. Mean Diffe		
Study or Subgroup Lynch et al 2017 (22yrs; ASR)	AS and pl Mean	d AS FAS SD	<b>Total</b> 47	ule-B <u>Mea</u> 3.7	Brea Cont	king rol SD 1	g Beł Total 58	Naviou Weight 100.0%	ur — S Std. N t IV,	elf-report (T-so lean Difference Random, 95% Cl 1.25 [0.82, 1.67]	ore) (1 study) Std. Mean Diffe		
Study or Subgroup Lynch et al 2017 (22yrs; ASR) Total (95% CI)	AS and pl Mean	d AS FAS SD	Total	ule-B <u>Mea</u> 3.7	Brea Cont	king rol SD 1	g Beł Total 58	navio Weight	ur — S Std. N t IV,	Self-report (T-so Mean Difference Random, 95% Cl	ore) (1 study) Std. Mean Diffe		
Study or Subgroup Lynch et al 2017 (22yrs; ASR) Total (95% CI) Heterogeneity: Not applicable	FAS and pl <u>Mean</u> 4.38	SD 0.5	<b>Total</b> 47	ule-B <u>Mea</u> 3.7	Brea Cont	king rol SD 1	g Beł Total 58	Naviou Weight 100.0%	ur — S Std. N t IV,	elf-report (T-so lean Difference Random, 95% Cl 1.25 [0.82, 1.67]	sore) (1 study) Std. Mean Diffe IV, Random, 9	5% CI → 2	
pF <u>Study or Subgroup</u> Lynch et al 2017 (22yrs; ASR) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 5.79 (	FAS and pl <u>Mean</u> 4.38	SD 0.5	<b>Total</b> 47	ule-B <u>Mea</u> 3.7	Brea Cont	king rol SD 1	g Beł Total 58	Naviou Weight 100.0%	ur — S Std. N t IV,	Gelf-report (T-sc           Mean Difference           Random, 95% CI           1.25 [0.82, 1.67]           1.25 [0.82, 1.67]	sore) (1 study) Std. Mean Diffe IV, Random, 9	5% CI → 2	
<b>Study or Subgroup</b> Lynch et al 2017 (22yrs; ASR) <b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 5.79 (	FAS and pl <u>Mean</u> 4.38	SD 0.5	<b>Total</b> 47	ule-B <u>Mea</u> 3.7	Brea Cont	king rol SD 1	g Beł Total 58	Naviou Weight 100.0%	ur — S Std. N t IV,	Gelf-report (T-sc           Mean Difference           Random, 95% CI           1.25 [0.82, 1.67]           1.25 [0.82, 1.67]	sore) (1 study) Std. Mean Diffe IV, Random, 9	5% CI → 2	
Study or Subgroup Lynch et al 2017 (22yrs; ASR) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 5.79 ( <u>Risk of bias legend</u>	FAS and pl <u>Mean</u> 4.38	SD 0.5	<b>Total</b> 47	ule-B <u>Mea</u> 3.7	Brea Cont	king rol SD 1	g Beł Total 58	Naviou Weight 100.0%	ur — S Std. N t IV,	Gelf-report (T-sc           Mean Difference           Random, 95% CI           1.25 [0.82, 1.67]           1.25 [0.82, 1.67]	sore) (1 study) Std. Mean Diffe IV, Random, 9	5% CI → 2	
Study or Subgroup Lynch et al 2017 (22yrs; ASR) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 5.79 ( <u>Risk of bias legend</u> (A) Overall RoB	FAS and p <u>Mean</u> 4.38 (P < 0.000	<b>J AS</b> FAS 5D 0.5	Total 47 47	ule-B <u>  Mea</u>   3.7	Grea Cont n 8 0.	king so 1 46	g Beł Total 58 58	Weight 100.0% 100.0%	ur — S Std. N t IV,	Self-report (T-sc           Mean Difference           Random, 95% CI           1.25 [0.82, 1.67]           1.25 [0.82, 1.67]	sore) (1 study) Std. Mean Diffe IV, Random, 9	5% CI	
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Study or Subgroup Lynch et al 2017 (22yrs; ASR) Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 5.79 ( Risk of bias legend (A) Overall RoB ARND/ Study or Subgroup Lynch et al 2017 (22yrs; ASR; Cog Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 5.33 (P < Risk of bias legend A) Overall RoB Dte: Lynch et al 2017 also re Study or Subgroup	FAS and pi <u>Mean</u> 4.38 (P < 0.000 /Others (n Affected) < 0.00001) < 0.00001) reports o FASI Mea	d AS FAS SD 0.5 0001) s an N V	Total 47 47 47 47 47 47 47 47 47 47 47 47 47	Ule-E <u>Mea</u> 3.7 SR Ru Others <u>SD 1</u> 0.7 or CBC G Hyp BRS-	Grea Contin 18 0. 18 0. 19 0. 10 0. 10 0. 10 0. 10 0. 10 0.	king rol <u>SD</u> 1 <u>46</u> Brea <u>Mean</u> 3.76 bdor activ ype contro si	s Beł <u>fotal</u> 58 58 58 58 58 58 58 58 58 58	Weight 100.0% 100.0% 3 Beh 100.0% 58 58 58 58 Careg vity – al Wei	ur – S std. N t IV, aviou Weight 100.0% 100.0%	Self-report (T-sc           Random, 95% CI           1.25 [0.82, 1.67]           1.25 [0.82, 1.67]           1.25 [0.82, 1.67]           -4           IT - Self-report           Std. Mean Difference           IV, Random, 95% CI           1.26 [0.79, 1.72           1.26 [0.79, 1.72           1.26 [0.79, 1.72           Mean Difference           IV, Random, 95% CI           Mean Difference           IV, Random, 95% CI	core) (1 study) Std. Mean Diffe IV, Random, 9 -2 Control pF/ (T-score) (1 study) (T-score) (1 study) (1 study)	5% CI	A Risk of Bia A A
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Study or Subgroup Lynch et al 2017 (22yrs; ASR) Total (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 5.79 ( Risk of bias legend (A) Overall RoB Cutode Subgroup Lynch et al 2017 (22yrs; ASR; Cog Total (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 5.33 (P < Risk of bias legend (A) Overall RoB Dote: Lynch et al 2017 also ro Study or Subgroup Way et al 2012 (5-14yrs; CBRS-I	FAS and pi <u>Mean</u> 4.38 (P < 0.000 /Others (n Affected) < 0.00001) < 0.00001) reports o FASI Mea	d AS FAS SD 0.5 0001) s an N V	Total 47 47 47 47 47 47 47 47 47 47 47 47 47	SR Ru SR Ru ST Contents SD 1 0.7 Or CBC S Hyp BRS- 25	Grea Contin 18 0. 18 0. 19 0. 10 0. 10 0. 10 0. 10 0. 10 0.	king rol <u>SD</u> 1 <u>46</u> Brea <u>Mean</u> 3.76 bdor activ ype contro si	s Beł <u>fotal</u> 58 58 58 58 58 58 58 58 58 58	Weight           100.0%           100.0%           100.0%           58	ur – S Std. N t IV, aviou <u>Weight</u> 100.0% 100.0% Std giver Care Std ght I	Gelf-report (T-score         Random, 95% CI         1.25 [0.82, 1.67]         1.25 [0.82, 1.67]         1.25 [0.82, 1.67]         1.25 [0.82, 1.67]         1.25 [0.82, 1.67]         -4         std. Mean Difference         IV, Random, 95% CI         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         Mean Difference         IV, Random, 95% CI         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72	core) (1 study) Std. Mean Diffe IV, Random, 9 -2 Control pF/ (T-score) (1 study) Std. Mean Diffe IV, Random IV, Random Control pF/ (1 study) Std. Mean Diffe	5% CI	A Risk of Bia
Study or Subgroup Lynch et al 2017 (22yrs; ASR) Fotal (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 5.79 ( Risk of bias legend (A) Overall RoB Lynch et al 2017 (22yrs; ASR; Cog Fotal (95% CI) Heterogeneity: Not applicable Fest for overall effect: Z = 5.33 (P < Risk of bias legend A) Overall RoB Dote: Lynch et al 2017 also re Study or Subgroup	FAS and pi <u>Mean</u> 4.38 (P < 0.000 /Others (n Affected) < 0.00001) < 0.00001) reports o FASI Mea	d AS FAS SD 0.5 0001) s an N V	Total 47 47 47 47 47 47 47 47 47 47 47 47 47	Ule-E <u>Mea</u> 3.7 SR Ru Others <u>SD 1</u> 0.7 or CBC G Hyp BRS-	Grea Contin 18 0. 18 0. 19 0. 10 0. 10 0. 10 0. 10 0. 10 0.	king rol <u>SD</u> 1 <u>46</u> Brea <u>Mean</u> 3.76 bdor activ ype contro si	s Beł <u>fotal</u> 58 58 58 58 58 58 58 58 58 58	Weight 100.0% 100.0% 3 Beh 100.0% 58 58 58 58 Careg vity – al Wei	ur – S Std. N t IV, aviou <u>Weight</u> 100.0% 100.0% Std giver Care Std ght I	Gelf-report (T-sc         Random, 95% CI         1.25 [0.82, 1.67]         1.25 [0.82, 1.67]         1.25 [0.82, 1.67]         -4         Ir - Self-report         Std. Mean Difference         IV, Random, 95% CI         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72         1.26 [0.79, 1.72	core) (1 study) Std. Mean Diffe IV, Random, 9 -2 Control pF/ (T-score) (1 study) Std. Mean Diffe IV, Random IV, Random Control pF/ (1 study) Std. Mean Diffe	5% CI	A Risk of Bia

# CBCL Hyperactivity Caregiver Report (Frequency/OR)

FASD and CBCL Hyperactivity – Caregiver (OR) (1 study)

	FAS	D	Contr	ol		Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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 Heterogeneity: Not applicable Test for overall effect: Z = 2.93 (P = 0.00	16 )3)		10				0.005 0.1 1 10 200 Control FASD	
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)

			•	•		•	•		. ,,	
	F	ASD		С	ontrol			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									-4 -2 0 2 -	-  4
restion overall ellect. 2 = 2.75 (F = 0.000)									FASD Control	
Risk of bias legend										

(A) Overall RoB

## pFAS and DBD Hyperactivity – Caregiver (mean/SD) (2 studies)

		pFAS		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
vragon 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: Tau <sup>2</sup> = 0.20; Chi <sup>2</sup> = 4.19, df = 1 (P = 0.04 Test for overall effect: Z = 1.13 (P = 0.26)	4); I² = 78	6%							-4 -2 0 2 Control pFAS	4

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)

						-				
	F	FASD		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									-4 -2 0 2 FASD Control	4

Risk of bias legend (A) Overall RoB

## pFAS and DBD Hyperactivity – Teacher (mean/SD) (2 studies)

		<b>FAS</b>	_	-	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	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: Tau <sup>2</sup> = 0.11; Chi <sup>2</sup> = 2.75, df = 1 (P = 0.1 Test for overall effect: $Z = 1.32$ (P = 0.19)	0); I <b>²</b> = 6	4%							-4 -2 0 2	4
reation overall ellect. 2 = 1.32 (r = 0.13)									Control pFAS	

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)

		FASD		С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.2 Test for overall effect: $Z = 5.30$ (P < 0.0	•	(P = 0.5	2); <b>I</b> ² =	0%					-4 -2 0 2 Control FASD	4

Risk of bias legend (A) Overall RoB

## FAS and CBCL Attention/Hyperactivity – Caregiver (T-score) (1 study)

		FAS		Co	ontro			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
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)									-4 -2 0 2 Control FAS	4

Risk of bias legend (A) Overall RoB

# pFAS and CBCL Attention/Hyperactivity - Caregiver (T-score) (1 study)

	р	FAS		Co	ontro	1		Std. Mean Difference	Std.	Mean Differen	се	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, F	Random, 95% (	CI	Α
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)									-4 -2	0	2 4	-  1
									C	ontrol pFAS		

Risk of bias legend (A) Overall RoB

## ARND/Others and CBCL Attention/Hyperactivity – Caregiver (T-score) (1 study)

	ARNI	D/Othe	rs	Co	ontro	I	:	Std. Mean Difference		Std. Mea	n Differend	ce	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI		IV, Ran	dom, 95% (	1	Α
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)									-4	-2 Contro	0 0 ARND/0	l 2 Others	<b>⊣</b> 4

Risk of bias legend (A) Overall RoB

## TRF Attention/Hyperactivity Teacher Report (T-score)

## FASD and TRF Attention/Hyperactivity – Teacher (T-score) (3 studies)

	E	ASD		Co	ontro	1		Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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 = Test for overall effect: Z = 6.73 (P			(P = 0.4	6); I² = (	)%				-4 -2 0 2 4 Control FASD

F	AS		С	ontro	ol		- Teacher (T-scor Std. Mean Difference	Std. Mean Difference	Risk of Bia
Mean		Total			Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
59.6	6.9	5	53.6	6.1	761	100.0%	0.98 [0.10, 1.86]		•
		5			761	100.0%	0.98 (0.10, 1.86)		
		5			701	100.0%	0.50 [0.10, 1.00]		
								-4 -2 0 2	4
								Control PAS	
	DE	<b>^++</b> ~	ation	./ц	mora	ativity	Toochor (T coo	rol(1 ctudy)	
		Alle				ictivity	-		Diak of Di
		Total	-			Weight			Risk of Bi
						-			-
								T.	-
		44			761	100.0%	0.23 [-0.08, 0.53]	🕈 .	
								-4 -2 0 2	4
								Control pFAS	
					-	peract	•		
									Risk of Bi
									A
"	10.9	1.1	44	03.0	0.1	/01 100	0.80 0.80 [0.00, 1.10	'' <b></b>	
			44			761 100	.0% 0.85 [0.55, 1.16	1 🔶	
								-4 -2 0 2	4
)								Control ARND/Other	5
				-				/	
CL/C	BRS	S An	kious	s/De	epres	sed C	aregiver Report	(T-score)	
СВС	L/C	BRS	Anxi	ous	/Dep	ressed	– Caregiver (T-so	ore) (7 studies)	
					-				Risk of Bi
									A
								-	
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63.6	10	.0	24 4	r.5	5.0	17 7.	0%0 1.19[0.51, 1.87		•
		2	39		1	171 100	.0% 0.60 [0.40, 0.80	1 ♦	
	0.17)	; <b>I²</b> = 3	4%					-4 -2 0 2	4
)								Control FASD	·
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and		LAN		-	•	sed – (	• ·	• • • • •	
Moa		Tota				l Woigh			Risk of Bi
						-			A
50.,	2 O.C		) 50.	з <i>г</i> .		100.0%	-0.01[-0.08, 0.07]	_	•
		!	5		771	100.09	-0.01 [-0.89, 0.87]	-	
								-4 -2 0 2	4
								Control FAS	
								Control FAS	
								Control FAS	
								Control FAS	
and	CBC	Ί Δr	viou	c / D	onro	sed –	Caregiver (T-scor		
and					-	ssed –	Caregiver (T-scor	<b>e)</b> (1 study)	Pisk of Pi
	pFAS			Cont	rol		Std. Mean Difference	<b>e)</b> (1 study) Std. Mean Difference	Risk of Bi A
Mear	pFAS	Tota	l Mea	Cont	rol D Tota	l Weigh	Std. Mean Difference IV, Random, 95% CI	<b>e)</b> (1 study)	-
Mear	pFAS 1 SD	Tota	l Mea	Cont n S	rol D Tota	l Weigh	Std. Mean Difference IV, Random, 95% Cl	<b>e)</b> (1 study) Std. Mean Difference	
Mear	pFAS 1 SD	Tota	I Mea 56.	Cont n S	rol D Tota	I Weigh	Std. Mean Difference           IV, Random, 95% CI           0.18 [-0.12, 0.49]	<b>e)</b> (1 study) Std. Mean Difference	-
Mear	pFAS 1 SD	Tota 4	I Mea 56.	Cont n S	rol <u>D Tota</u> 1 771	I Weigh	Std. Mean Difference           IV, Random, 95% CI           0.18 [-0.12, 0.49]	e) (1 study) Std. Mean Difference IV, Random, 95% Cl	-
Mear	pFAS 1 SD	Tota 4	I Mea 56.	Cont n S	rol <u>D Tota</u> 1 771	I Weigh	Std. Mean Difference           IV, Random, 95% CI           0.18 [-0.12, 0.49]	e) (1 study) Std. Mean Difference IV, Random, 95% Cl	•
Mear	pFAS 1 SD	Tota 4	I Mea 56.	Cont n S	rol <u>D Tota</u> 1 771	I Weigh	Std. Mean Difference           IV, Random, 95% CI           0.18 [-0.12, 0.49]	e) (1 study) Std. Mean Difference IV, Random, 95% CI	A ●
	ers a <u>Mean</u> 55 ers a <u>M</u> <u>Mean</u> 55 ers a <u>M</u> <u>Mean</u> 55 ers a <u>64.56</u> 59.5 55.2 56.3 57.35 63.6 57.35 63.6 57.35 63.6 57.35 63.6 57.35 63.6 57.35 63.6 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 64.9 65.9 55.2 57.35 63.6 64.9 64.9 64.9 64.9 65.2 57.35 63.6 64.9 64.9 64.9 65.2 57.35 63.6 64.9 64.9 64.9 65.2 57.35 63.6 64.9 64.9 64.9 64.9 65.2 57.35 63.6 64.9 64.9 64.9 65.2 57.35 63.6 64.9 64.9 64.9 64.9 64.9 65.2 57.35 63.6 64.9 64.9 64.9 65.2 57.35 63.6 64.9 64.9 64.9 65.2 57.35 63.6 64.9	ers and <u>Solution</u> Solution Solut	Sand TRF Atter         pFAS         Mean       SD       Total         55       7       44         44       44         ers and TRF /         Mean       SD       Total         Mean       SD       7         Mean       SD       Total         Sold (BCL/CBRS)       Choile       Science         Sold (BCL/CBRS)       Total       Science         Mean       SD       Total         Mean       SD       Total         Mean       SD       Total	$\frac{5}{5}$	$5$ $\frac{\text{and TRF Attention/Hi}}{pFAS} Control Mean SD Total Mean SD} 55 7 44 53.6 6.1 44$ $\frac{44}{44}$ $\frac{\text{and CBCL Anxious/Deters}}{FASD} Color Mean SD Total Mean SD}$	$5   761$ $\frac{pFAS}{5}   Control}$ $\frac{pFAS}{5}   Control}   Control$ $\frac{Mean   SD   Total   Mean   SD   Total}{55   7   44   53.6   6.1   761}$ $\frac{44   761}{44   761}$ $\frac{44   761}{56   7   44   53.6   6.1   761}$ $\frac{Mean   SD   Total   Mean   SD   Total   Mean   SD   Total}{56   7   44   53.6   6.1   761}$ $\frac{Mean   SD   Total   Mean   SD   Total   Mean   SD   Total   44   761}$ $\frac{Mean   SD   Total   Mean   SD   Total   Mean   SD   Total   44   761}$ $\frac{Mean   SD   Total   Mean   SD   Total   Mean   SD   Total   44   761}$ $\frac{Mean   SD   Total   Mean   SD   Total   Mean   SD   Total   44   761}$ $Mean   SD   Total   Mean   SD   Total   Mean   SD   Total   56.5   7.43   55.5  $	5       761 100.0%         Ind TRF Attention/Hyperactivity         Jotal Mean SD Total Weight         55       7       44       50       Total Weight         55       7       44       Total Mean SD Total Weight         55       7       44       761       100.0%         ARND/Others       Control         Mean SD Total Mean SD Total Weight         0)       58.9       7.7       44       53.6       6.1       761       100.0%         ARND/Others       Control         Mean SD Total Mean       SD Total Weight         0)       58.9       7.7       44       53.6       6.1       761       100.0%         Control         Mean       SD Total Mean       SD Total Weight         Control         Mean       SD Total Mean       SD Total Weight         SD Total Mean       SD Total Weight         64.56       11.19       39       5.5       7.43 </td <td>5         761         100.0%         0.98 [0.10, 1.86]           and TRF Attention/Hyperactivity – Teacher (T-scoop           Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           55         7         44         53.6         6.1         761         100.0%         0.23 [-0.08, 0.53]           44         761         100.0%         0.23 [-0.08, 0.53]           Attention/Hyperactivity – Teacher (T           Annotation of the main SD         Total Weight         IV, Random, 95% CI           Attention/Hyperactivity – Teacher (T           Annotation SD           Total Mean         SD           Opticit Mean         Std. Mean Difference           Mean         SD         Total Mean         SD           Control         Std. Mean Difference           FAS         Control         Std. Mean Difference           Control         Std. Mean Difference           Control         Std. Mean Difference           FAS         Contro</td> <td>5 761 100.0% 0.98 [0.10, 1.86] 4 2 Control FAS Total Mean SD Total Mean SD Total Weight IV, Random, 95% CI 44 761 100.0% 0.23 [-0.08, 0.53] 44 761 100.0% 0.23 [-0.08, 0.51] 44 761 100.0% 0.85 [0.55, 1.16] 44 761 100.0% 0.85 [0.55, 1.16] 55 7 10.84 33 545 8.22 33 11.7% 0.85 [0.35, 1.16] 55 7 10.84 33 545 8.22 33 11.7% 0.85 [0.35, 1.16] 55 7 10.84 33 545 8.22 33 11.7% 0.85 [0.35, 1.16] 55 7 10.84 33 545 8.22 33 11.7% 0.52 [0.38, 0.51] 55 7 10.84 33 545 8.22 33 11.7% 0.52 [0.38, 0.51] 55 7 10.84 33 545 8.22 33 11.7% 0.52 [0.38, 0.51] 55 7 10.84 33 545 8.22 33 11.7% 0.52 [0.38, 0.51] 56 7 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 56 3 7.6 39 52.5 1.144 21.9% 0.38 [0.09, 0.88] 56 3 7.6 39 52.5 1.144 21.9% 0.58 [0.32, 100] 56 7 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 57 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 56 7 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 57 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 56 3 7.6 39 52.5 1.144 21.9% 0.68 [0.32, 100] 57 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 56 3 7.6 39 52.5 1.144 21.9% 0.58 [0.30, 0.88] 57 7 1 19 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 57 7 1 19 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 58 1.0 Mean Difference 58 1.0 Mean Difference 59 7.6 Control Kadom Difference 59 7.6 Control Kadom Difference 59 7.6 Control Kadom Difference 50 7.6 Mean Difference 50 7.6 Me</td>	5         761         100.0%         0.98 [0.10, 1.86]           and TRF Attention/Hyperactivity – Teacher (T-scoop           Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           55         7         44         53.6         6.1         761         100.0%         0.23 [-0.08, 0.53]           44         761         100.0%         0.23 [-0.08, 0.53]           Attention/Hyperactivity – Teacher (T           Annotation of the main SD         Total Weight         IV, Random, 95% CI           Attention/Hyperactivity – Teacher (T           Annotation SD           Total Mean         SD           Opticit Mean         Std. Mean Difference           Mean         SD         Total Mean         SD           Control         Std. Mean Difference           FAS         Control         Std. Mean Difference           Control         Std. Mean Difference           Control         Std. Mean Difference           FAS         Contro	5 761 100.0% 0.98 [0.10, 1.86] 4 2 Control FAS Total Mean SD Total Mean SD Total Weight IV, Random, 95% CI 44 761 100.0% 0.23 [-0.08, 0.53] 44 761 100.0% 0.23 [-0.08, 0.51] 44 761 100.0% 0.85 [0.55, 1.16] 44 761 100.0% 0.85 [0.55, 1.16] 55 7 10.84 33 545 8.22 33 11.7% 0.85 [0.35, 1.16] 55 7 10.84 33 545 8.22 33 11.7% 0.85 [0.35, 1.16] 55 7 10.84 33 545 8.22 33 11.7% 0.85 [0.35, 1.16] 55 7 10.84 33 545 8.22 33 11.7% 0.52 [0.38, 0.51] 55 7 10.84 33 545 8.22 33 11.7% 0.52 [0.38, 0.51] 55 7 10.84 33 545 8.22 33 11.7% 0.52 [0.38, 0.51] 55 7 10.84 33 545 8.22 33 11.7% 0.52 [0.38, 0.51] 56 7 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 56 3 7.6 39 52.5 1.144 21.9% 0.38 [0.09, 0.88] 56 3 7.6 39 52.5 1.144 21.9% 0.58 [0.32, 100] 56 7 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 57 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 56 7 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 57 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 56 3 7.6 39 52.5 1.144 21.9% 0.68 [0.32, 100] 57 7 1 9 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 56 3 7.6 39 52.5 1.144 21.9% 0.58 [0.30, 0.88] 57 7 1 19 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 57 7 1 19 54, 9 11.05 33 9 9.9% 0.1 [0.90, 0.88] 58 1.0 Mean Difference 58 1.0 Mean Difference 59 7.6 Control Kadom Difference 59 7.6 Control Kadom Difference 59 7.6 Control Kadom Difference 50 7.6 Mean Difference 50 7.6 Me

	ARND	/Othe	rs	Co	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 3.81 (P = 0.0001)			44			771	100.0%	0.59 [0.29, 0.90]	-4 -2 0 2 Control ARND/Others	4

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)

	E	ASD		Co	ontro	1		Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)									-4 -2 0 2 4 Control FASD

Risk of bias legend (A) Overall RoB

## TRF Anxious/Depressed Teacher Report (T-score) **FASD and TRF Anxious/Depressed – Teacher (T-score)** (3 studies)

	FASD a	mu	1 K F /	AIIXIO	usy	Debu	esseu -	- reacher (r-scor	ej (S studies)	
	E.	ASD		Co	ontro	1		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.02; Chi <sup>2</sup> :	= 3.26, df	f = 2 i	(P = 0.2)	20); <b>I<sup>2</sup> =</b> 3	39%					<u> </u>
Test for overall effect: Z = 5.42 (P	< 0.0000	01)							-4 -2 U 2 Control FASD	4
Risk of bias legend										

(A) Overall RoB

### FAS and TRF Anxious/Depressed – Teacher (T-score) (1 study)

June				,	.p. co	564		(+ 5000)	
1	FAS		Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
55.4	6.2	5	52.8	5.6	771	100.0%	0.46 [-0.42, 1.34]		•
		5			771	100.0%	0.46 [-0.42, 1.34]	-	
)								4 -2 0 2 Control FAS	4
	Mean	FAS <u>Mean SD</u> 55.4 6.2	FAS           Mean         SD         Total           55.4         6.2         5           55.4         5         5	FAS         Common	FAS     Contro       Mean     SD     Total     Mean     SD       55.4     6.2     5     52.8     5.6       5     5     5     5     5	FAS         Control           Mean         SD         Total         Mean         SD         Total           55.4         6.2         5         52.8         5.6         771           5         771         771         771         771	FAS         Control           Mean         SD         Total         Mean         SD         Total         Weight           55.4         6.2         5         52.8         5.6         771         100.0%           5         771         100.0%         771         100.0%	FAS         Control         Std. Mean Difference           Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% CI           55.4         6.2         5         52.8         5.6         771         100.0%         0.46 [-0.42, 1.34]           5         5         771         100.0%         0.46 [-0.42, 1.34]         100.0%	Mean         SD         Total         Mean         SD         Total         Weight         IV, Random, 95% Cl         IV, Random, 95% Cl           55.4         6.2         5         52.8         5.6         771         100.0%         0.46 [-0.42, 1.34]

Risk of bias legend (A) Overall RoB

## pFAS and TRF Anxious/Depressed – Teacher (T-score) (1 study)

									· · · · //	
	p	FAS		Co	ontro	l i		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 1.24 (P = 0.21)	)		44			771	100.0%	0.19 [-0.11, 0.50] -4	-2 0 2 Control pFAS	4

Risk of bias legend (A) Overall RoB

## ARND/Others and TRF Anxious/Depressed – Teacher (T-score) (1 study)

	ARND	/Othe	ers	Co	ontro	I	1	Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									-4 -2 0 2 Control ARND/Others	4

# ASR Anxious/Depressed Self Report (T-score)

## pFAS and ASR Anxious/Depressed – Self Report (1 study)

		pFAS		C	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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) Heterogeneity: Not applicable			47			58	100.0%	3.62 [2.99, 4.25]	<b>→</b>
Test for overall effect: Z = 11.26	(P < 0.0	0001)							-4 -2 0 2 4 Control pFAS
Risk of bias legend									

(A) Overall RoB

## ARND/Others and ASR Anxious/Depressed – Self Report (1 study)

	ARNI	D/Othe	ers	С	ontrol			Mean Difference		Mean	Differenc	e	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Fixed, 95% CI		IV, Fix	ed, 95% (	1	Α
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									-4	-2		2 4	
Test for overall effect: Z = 16.17 (P < 0.00001)										Contr	ol ARND	/Others	
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)

	1	FASD		C	Control			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 6.59, df Test for overall effect: Z = 5.20 (P < 0.0000		0.16); I	<b>≃</b> = 39%	6				⊢ -4	-2 0 2 Control FASD	4

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)

	1	FAS		Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									Control FAS	4
Risk of bias legend										

(A) Overall RoB

## pFAS and CBCL Anxiety - Caregiver (T-score) (1 study)

	р	FAS		Co	ontro	1		Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.98 (P = 0.05)			44			771	100.0%	0.31 [0.00, 0.61]  - -	4 -2 0 2 Control pFAS	<b>⊣</b> 4

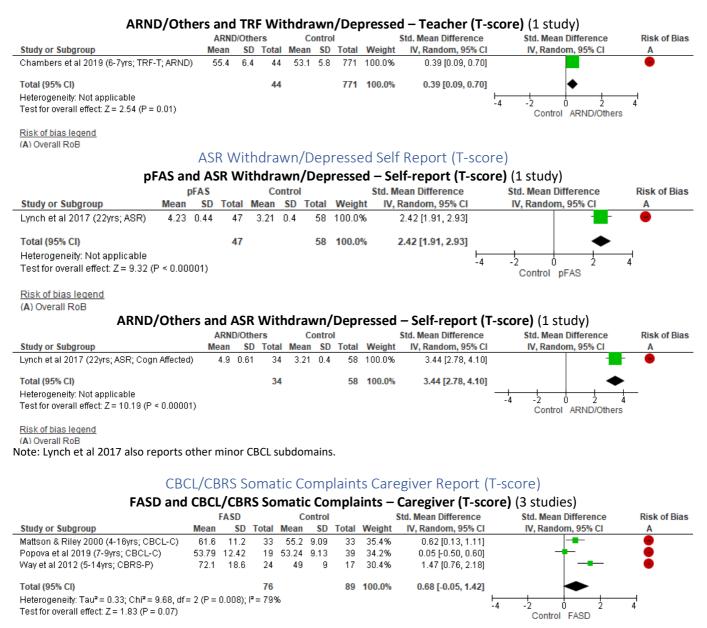
Chudu an Subanaun		D/Others		Contro		14/4:-1	Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C; ARND	Mean ) 60.4	<u>SD 10</u> 8.5		ean SD 6.5 7.1	771	Weight 100.0%		IV, Random, 95% CI	A
Chambers et al 2019 (0-7915, CBCL-C, ARNE	9 00.4	0.0	44 0	10.0 7.1		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)							1	-4 -2 0 2	4
								Control ARND/Others	
Risk of bias legend									
(A) Overall RoB	г		viot		chor	Done	ort (Ticcoro)		
				·			ort (T-score)	1	
				-	- Tea	-	<b>T-score)</b> (3 studie		
	ASD SD Tot		Control		Weight		ean Difference Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl	Risk of Bia A
May et al 2020a (6-7yrs; TRF-T) 57.7			2 5.6	273	32.1%		0.76 [0.42, 1.11]	-	Ô
May et al 2020b (6-7yrs; TRF-T) 54.9		9 52.2		444	36.1%		0.52 [0.22, 0.82]	-	ě
May et al 2020c (6-7yrs; TRF-T) 56.5	7.2 3	7 51.9	34	331	31.8%	)	1.04 [0.69, 1.39]	-	•
Total (95% CI)	12	4		1048	100.0%		0.76 [0.46, 1.06]	▲	
Heterogeneity: Tau <sup>2</sup> = 0.04; Chi <sup>2</sup> = 4.97, d			60%	1040	100.07		L	<u> </u>	-
Test for overall effect: Z = 4.99 (P < 0.000							-4	-2 0 2 Control FASD	4
								0011101 17100	
<u>Risk of bias legend</u> ( <b>A</b> ) Overall RoB									
	FAS a	nd TRI	FΔny	vietv -	- Tea	cher (	T-score) (1 study	4	
	FAS		Cont	-	icu	-	Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup M	ean SD	Total M	ean S	SD Tota	l Wei		V, Random, 95% Cl	IV, Random, 95% Cl	Α
Chambers et al 2019 (6-7yrs; TRF-T) 🤤 🤅	57.2 11	5 :	53.1 5	.8 77	1 100.	0%	0.70 [-0.18, 1.58]	┼╋╌	•
Total (95% CI)		5		77	1 100.	.0%	0.70 [-0.18, 1.58]		
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.56 (P = 0.12)							-4	-2 0 2 Control FAS	4
Diele of hisseland									
<u>Risk of bias legend</u> (A) Overall RoB									
	pFAS a	nd TR	FAn	xietv	– Tea	cher	(T-score) (1 study	v)	
	pFAS		Con	-			Mean Difference	Std. Mean Difference	Risk of Bia
	ean SD					-	V, Random, 95% Cl	IV, Random, 95% Cl	A
Chambers et al 2019 (6-7yrs; TRF-T) 5	53.9 6.4	44	53.1 5	6.8 77	1 100.	0%	0.14 [-0.17, 0.44]	-	-
Total (95% CI)		44		77	1 100	.0%	0.14 [-0.17, 0.44]	•	
Heterogeneity: Not applicable							-4	-2 0 2	4
Test for overall effect: Z = 0.88 (P = 0.38)							-4	Control pFAS	4
Risk of bias legend									
(A) Overall RoB									
ARN	ND/Oth	ers an	d TR	F Anx	iety -	- Teac	cher (T-score) (1	study)	
		Others		Control	-		Std. Mean Difference	Std. Mean Difference	Risk of Bia
Study or Subgroup Chambers et al 2019 (6-7yrs; TRF-T; ARND)	Mean 55.6		al Mea 14 53	an SD 1.1 5.8		Weight 100.0%	IV, Random, 95% Cl 0.42 [0.12, 0.73]	IV, Random, 95% Cl	A
onambers et al 2018 (0-7918, TRF-1, ARND)	0.00	1.3 4	•+ 33	0.1 0.8	(11)	100.0%	0.42 [0.12, 0.73]		•
Total (95% CI)		4	14		771	100.0%	0.42 [0.12, 0.73]	◆	
Heterogeneity: Not applicable Fest for overall effect: Z = 2.71 (P = 0.007)								4 -2 0 2	4
(Corror overall energy 2 = 2.71 (F = 0.007)								Control ARND/Others	
Risk of bias legend									
A) Overall RoB									
CBO	CL Witł	ndraw	n/De	epres	sed (	Careg	iver Report (T-s	core)	
FASD and		Nithd	rawn	/Dep	resse	d – Ca	aregiver (T-score	) (6 studies)	
	FASE			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bi
, , ,		D Total			Total V		IV, Random, 95% CI	IV, Random, 95% Cl	A
Krueger et al 2020 (8-16yrs; CBCL-C)	50.92 9.1		53.94			14.1%	0.91 [0.42, 1.39]		
Mattson & Riley 2000 (4-16yrs; CBCL-C)	61.6 11	.2 33	65 0	9.09	33	13.8%	0.62 [0.13, 1.11]		

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]	<del>-</del>	
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: Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 11.23, c Test for overall effect: Z = 5.22 (P < 0.0000	•	= 0.05); l <sup>a</sup>	'= 559	6					-4 -2 0 2 4 Control FASD	

<sup>&</sup>lt;u>Risk of bias legend</u> (A) Overall RoB

Note: Krueger et al 2020 also reports other minor subdomains.

FAS a		FAS			ontrol			Std. Mean Difference	Std. Mean Difference	Dick of Dis
Study or Subgroup	Mea		Total	Mean		otal V	Neiaht	IV, Random, 95% Cl	IV, Random, 95% Cl	Risk of Bia A
Chambers et al 2019 (6-7yrs; CBCL-C)		2 6.4				771 1	-	-0.11 [-0.99, 0.77]		ê
			-							-
Fotal (95% CI)			5			771 1	100.0%	-0.11 [-0.99, 0.77]	· · · · ·	
Heterogeneity: Not applicable								H	4 -2 0 2	4
Test for overall effect: Z = 0.25 (P = 0.80)	1								Control FAS	
Risk of bias legend										
(A) Overall RoB										
pFAS a	and C					pres		- Caregiver (T-sco		
Study or Subgroup	Moa	pFAS n SD		C Mean	ontrol	otal N		Std. Mean Difference	Std. Mean Difference IV, Random, 95% Cl	Risk of Bi
Study or Subgroup Chambers et al 2019 (6-7yrs; CBCL-C)		3 7.6					00.0%	IV, Random, 95% Cl 0.32 [0.01, 0.62]	IV, Kalluolli, 95% Cl	A
	50.	, ,,,		50	1.2		00.070	0.32 [0.01, 0.02]		•
Fotal (95% CI)			44			771 1	100.0%	0.32 [0.01, 0.62]	◆	
Heterogeneity: Not applicable								ŀ	4 -2 0 2	4
fest for overall effect: Z = 2.05 (P = 0.04)	I								Control pFAS	
<u>Risk of bias legend</u> A) Overall RoB										
R) Overlain (OD										
ARND/Oth	ers a	nd C	BCL	With	draw	n/De	press	sed – Caregiver (T	<b>-score)</b> (1 study)	
		ARN	D/Othe	rs	Cont	rol	-	Std. Mean Difference	Std. Mean Difference	Risk of Bi
Study or Subgroup		Mean		Total M						Α
Chambers et al 2019 (6-7yrs; CBCL-C; AF	(ND)	59.5	8.7	44	56 7	.2 77	1 100.	0% 0.48 [0.18, 0.78]		-
Total (95% CI)				44		77	1 100.	.0% 0.48 [0.18, 0.78]	♦	
leterogeneity: Not applicable									-4 -2 0 2	4
est for overall effect: Z = 3.09 (P = 0.002)									Control ARND/Othe	rs
<u>tisk of bias legend</u> A) Overall RoB										
A) Overall ROB										
	TRE	۸/i+	hdra	wn/r	onro	ccod	ΙΤροί	cher Report (T-s	core	
				-				cher Report (T-s	· ·	
	and 1	RF		draw	n/De		sed –	Teacher (T-score	) (3 studies)	
FASD	and T FASD	RF	With	draw Contro	n/De N	press	ed – Std	Teacher (T-score Mean Difference	) (3 studies) Std. Mean Difference	-
FASD Study or Subgroup Me	and T FASE an SE	RF V	With al Me	draw Contro	n/De ol Total	press Weig	sed – Std ght I	Teacher (T-score . Mean Difference V, Random, 95% Cl	) (3 studies) Std. Mean Difference IV, Random, 95% Cl	Risk of Bia
FASD Study or Subgroup Me May et al 2020a (6-7yrs; TRF-T) 5	and T FASE an SE 5.8 5.6	Tot	With al Me	draw Contro an SD 53 5.7	n/De ol <u>Total</u> 273	press <u>Weig</u> 31.0	sed – Std pht i 0%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83]	) (3 studies) Std. Mean Difference	-
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5	and T FASE an SE 5.8 5.6 6.1 7.7	Tot	With <u>al Me</u> 38 49 5:	<b>draw</b> Contro an <u>SD</u> 53 5.7 2.2 4.6	n/De ol <u>Total</u> 273 444	<b>Weig</b> 31.0 38.6	sed – Sta <u>sta</u> <u>sta</u> 3 5%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08]	) (3 studies) Std. Mean Difference IV, Random, 95% Cl	-
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5	and T FASE an SE 5.8 5.6	Tot	With <u>al Me</u> 38 49 5:	draw Contro an SD 53 5.7	n/De ol <u>Total</u> 273 444	press <u>Weig</u> 31.0	sed – Sta <u>sta</u> <u>sta</u> 3 5%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83]	) (3 studies) Std. Mean Difference IV, Random, 95% Cl	-
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         May et al 2020c (6-7yrs; TRF-T)       5	and T FASE an SE 5.8 5.6 6.1 7.7	Tot	With al Me 38 49 5: 37 5:	<b>draw</b> Contro an <u>SD</u> 53 5.7 2.2 4.6	n/De Total 273 444 331	<b>Weig</b> 31.0 38.6	sed – Sta <u>pht 1</u> 0% 5% 5%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08]	) (3 studies) Std. Mean Difference IV, Random, 95% Cl	-
FASD           Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           May et al 2020c (6-7yrs; TRF-T)         5           Total (95% CI)         1           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4-	and T FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2	<b>RF</b> V Tot	With al Me 38 49 5: 37 5: 24	<b>Contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contr</b>	n/De Total 273 444 331 1048	<b>Weig</b> 31.0 38.6 30.6	sed – Sta <u>pht 1</u> 0% 5% 5%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92]	) (3 studies) Std. Mean Difference IV, Random, 95% Cl	-
FASD           Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           May et al 2020c (6-7yrs; TRF-T)         5           Fotal (95% CI)         -           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4-	and T FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2	<b>RF</b> V Tot	With al Me 38 49 5: 37 5: 24	<b>Contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contr</b>	n/De Total 273 444 331 1048	<b>Weig</b> 31.0 38.6 30.6	sed – Sta <u>pht 1</u> 0% 5% 5%	Teacher (T-score Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20]	) (3 studies) Std. Mean Difference IV, Random, 95% Cl	-
FASD           Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           May et al 2020c (6-7yrs; TRF-T)         5           Fotal (95% CI)         1           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4           Test for overall effect: Z = 6.70 (P < 0.00)	and T FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2	<b>RF</b> V Tot	With al Me 38 49 5: 37 5: 24	<b>Contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contr</b>	n/De Total 273 444 331 1048	<b>Weig</b> 31.0 38.6 30.6	sed – Sta <u>pht 1</u> 0% 5% 5%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92]	) (3 studies) Std. Mean Difference IV, Random, 95% CI 	-
FASD           Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           May et al 2020c (6-7yrs; TRF-T)         5           Total (95% CI)         5           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4           Test for overall effect: Z = 6.70 (P < 0.02)	and T FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2	<b>RF</b> V Tot	With al Me 38 49 5: 37 5: 24	<b>Contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contr</b>	n/De Total 273 444 331 1048	<b>Weig</b> 31.0 38.6 30.6	sed – Sta <u>pht 1</u> 0% 5% 5%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92]	) (3 studies) Std. Mean Difference IV, Random, 95% CI 	-
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FASD           Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           May et al 2020c (6-7yrs; TRF-T)         5           Total (95% CI)         5           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4           Test for overall effect: Z = 6.70 (P < 0.02)	and T FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2	<b>RF</b> V Tot	With al Me 38 49 5: 37 5: 24	<b>Contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contro</b> <b>contr</b>	n/De Total 273 444 331 1048	<b>Weig</b> 31.0 38.6 30.6	sed – Sta <u>pht 1</u> 0% 5% 5%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92]	) (3 studies) Std. Mean Difference IV, Random, 95% CI 	-
FASD           Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           Total (95% CI)         5           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         2.4.           Fest for overall effect: Z = 6.70 (P < 0.0)	and 1 FASE an <u>SE</u> 5.8 5.5 6.1 7.7 6.2 7.8 4, df = 2 00001)	<b>Tot</b> <b>Tot</b> <b>1</b> (P = 1	With <u>al Me</u> 38 49 5: 37 5: 24 0.30); F	drawn <u>Contro</u> <u>an SD</u> 53 5.7 2.2 4.6 2.2 4.2 <sup>2</sup> = 18%	n/De 0 773 444 331 1048	97ess Weig 31.0 38.6 30.6 100.0	sed – Std <u>ght 1</u> 0% 5% 5%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4	) (3 studies) Std. Mean Difference IV, Random, 95% CI 	-
FASD           Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           Total (95% CI)         5           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         2.4.           Fest for overall effect: Z = 6.70 (P < 0.0)	and 1 FASE 5.8 5.5 6.1 7.7 6.2 7.8 4, df = 2 00001)	TRF 1	With <u>al Me</u> 38 49 5: 37 5: 24 0.30); F	drawn <u>contro</u> <u>san</u> <u>SD</u> <u>53</u> 5.7 2.2 4.6 2.2 4.2 <sup>2</sup> = 18% drawn	n/De <u>Total</u> 273 444 331 1048	97ess Weig 31.0 38.6 30.6 100.0	sed – std <u>9ht 1</u> 0% 5% 5% 0%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4	) (3 studies) Std. Mean Difference IV, Random, 95% CI 	A ••• •• 4
Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           Total (95% CI)         6           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         2.4.           Test for overall effect: Z = 6.70 (P < 0.0)	and 1 FASE an SE 5.8 5.5 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1	Tot           12           (P = 1)           (P = 1)           (As)	With al Me 38 49 5: 37 5: 24 0.30); F With	drawi <u>contro</u> <u>san</u> <u>SD</u> <u>53</u> 5.7 <u>2.2</u> 4.6 <u>2.2</u> 4.2 <u>*</u> = 18% drawi <u>control</u>	n/De <u>Total</u> 273 444 331 1048 n/De	veig 31.0 38.6 30.6 100.0	sed – <u>Std</u> <u>pht 1</u> 0% 5% 0% sed –	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4	) (3 studies) Std. Mean Difference IV, Random, 95% CI 	A A 4 Risk of Bia
Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           Total (95% CI)         -           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         -           Test for overall effect: Z = 6.70 (P < 0.0)	and 1 FASE 5.8 5.5 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean	Tot           10           11           (P = 1)           (P = 1)           (As           SD	With al Me 38 49 5: 37 5: 24 0.30); F With Total	drawn Contro san SD 53 5.7 2.2 4.6 2.2 4.2 *= 18% drawn Control Mean	n/De <u>Total</u> 273 444 331 1048 n/De ntrol <u>SD To</u>	Weig           31.0           38.6           30.6           100.0	sed – Sta jht 1 0% 5% 5% 0%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl	) (3 studies) Std. Mean Difference IV, Random, 95% CI 	Risk of Bia
Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           Total (95% CI)         -           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         -           Test for overall effect: Z = 6.70 (P < 0.0)	and 1 FASE 5.8 5.5 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean	Tot           12           (P = 1)           (P = 1)           (As)	With al Me 38 49 5: 37 5: 24 0.30); F With	drawi <u>contro</u> <u>san</u> <u>SD</u> <u>53</u> 5.7 <u>2.2</u> 4.6 <u>2.2</u> 4.2 <u>*</u> = 18% drawi <u>control</u>	n/De <u>Total</u> 273 444 331 1048 n/De ntrol <u>SD To</u>	Weig           31.0           38.6           30.6           100.0	sed – <u>Std</u> <u>pht 1</u> 0% 5% 0% sed –	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4	) (3 studies) Std. Mean Difference IV, Random, 95% CI 	A A 4 Risk of Bia
FASD           Study or Subgroup         Me           May et al 2020a (6-7yrs; TRF-T)         5           May et al 2020b (6-7yrs; TRF-T)         5           May et al 2020c (6-7yrs; TRF-T)         5           Fotal (95% CI)         6           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.           Test for overall effect: Z = 6.70 (P < 0.0)	and 1 FASE 5.8 5.5 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean	Tot           10           11           (P = 1)           (P = 1)           (As           SD	With al Me 38 49 5: 37 5: 24 0.30); F With Total	drawn Contro san SD 53 5.7 2.2 4.6 2.2 4.2 *= 18% drawn Control Mean	n/De 0 <u>Total</u> 273 444 331 1048 1048 n/De ntrol <u>SD To</u> 5.8 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71         10	sed – Sta jht 1 0% 5% 5% 0%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl	) (3 studies) Std. Mean Difference IV, Random, 95% CI 	A A A Risk of Bi
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         Fotal (95% CI)       6         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Test for overall effect: Z = 6.70 (P < 0.02)	and 1 FASE san <u>SE</u> 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 <u>Mean</u> 52	Tot           10           11           (P = 1)           (P = 1)           (As           SD	With <u>al Me</u> 38 49 5: 37 5: 24 0.30); F With <u>Total</u> 5	drawn Contro san SD 53 5.7 2.2 4.6 2.2 4.2 *= 18% drawn Control Mean	n/De 0 <u>Total</u> 273 444 331 1048 1048 n/De ntrol <u>SD To</u> 5.8 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71         10	sed – <u>std</u> <u>3ht 1</u> 0% 5% 0% <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u>	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI	A A A Risk of Bi
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         Fotal (95% CI)       6         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Test for overall effect: Z = 6.70 (P < 0.02)	and 1 FASE san <u>SE</u> 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 <u>Mean</u> 52	Tot           10           11           (P = 1)           (P = 1)           (As           SD	With <u>al Me</u> 38 49 5: 37 5: 24 0.30); F With <u>Total</u> 5	drawn Contro san SD 53 5.7 2.2 4.6 2.2 4.2 *= 18% drawn Control Mean	n/De 0 <u>Total</u> 273 444 331 1048 1048 n/De ntrol <u>SD To</u> 5.8 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71         10	sed – <u>std</u> <u>3ht 1</u> 0% 5% 0% <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u>	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI	A • • • • • •
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         May et al 2020c (6-7yrs; TRF-T)       5         Fotal (95% CI)       1         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.44         Fest for overall effect: Z = 6.70 (P < 0.02	and 1 FASE san <u>SE</u> 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 <u>Mean</u> 52	Tot           10           11           (P = 1)           (P = 1)           (As           SD	With <u>al Me</u> 38 49 5: 37 5: 24 0.30); F With <u>Total</u> 5	drawn Contro san SD 53 5.7 2.2 4.6 2.2 4.2 *= 18% drawn Control Mean	n/De 0 <u>Total</u> 273 444 331 1048 1048 n/De ntrol <u>SD To</u> 5.8 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71         10	sed – <u>std</u> <u>3ht 1</u> 0% 5% 0% <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u>	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI	A A A Risk of Bi
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         May et al 2020c (6-7yrs; TRF-T)       5         Total (95% CI)       1         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.44       1         Test for overall effect: Z = 6.70 (P < 0.00)	and 1 FASE san <u>SE</u> 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 <u>Mean</u> 52	Tot           10           11           (P = 1)           (P = 1)           (As           SD	With <u>al Me</u> 38 49 5: 37 5: 24 0.30); F With <u>Total</u> 5	drawn Contro san SD 53 5.7 2.2 4.6 2.2 4.2 *= 18% drawn Control Mean	n/De 0 <u>Total</u> 273 444 331 1048 1048 n/De ntrol <u>SD To</u> 5.8 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71         10	sed – <u>std</u> <u>3ht 1</u> 0% 5% 0% <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u>	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI	A A A Risk of Bi
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         Fotal (95% CI)       1         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Fest for overall effect: Z = 6.70 (P < 0.0	and 1 FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean 52	Tot           12           (P = 1)           (P = 1)           (As           SD           3.1	With <u>al Me</u> 38 49 5: 37 5: 24 0.30); F With <u>Total</u> 5 5	drawn <u>contro</u> <u>san</u> <u>SD</u> <u>53</u> 5.7 2.2 4.6 2.2 4.2 <sup>2</sup> = 18% drawn <u>Con</u> <u>Mean</u> <u>53.3</u>	n/De <u>Total</u> 273 444 331 1048 n/De ntrol <u>SD To</u> 5.8 7 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71           71           71	sed – <u>sta</u> <u>jht 1</u> 0% 5% 5% 0% sed – <u>s</u> <u>/eight</u> 00.0% 00.0%	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66] -2.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FASD	A A A Risk of Bi
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         Fotal (95% CI)       1         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Fest for overall effect: Z = 6.70 (P < 0.0	and 1 FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean 52	Tot           1           1           2           3           12           (P = 1)	With <u>al Me</u> 38 49 5: 37 5: 24 0.30); F With <u>Total</u> 5 5	drawn 53 5.7 2.2 4.6 2.2 4.2 <sup>2</sup> = 18% drawn Con <u>Mean</u> 53.3	n/De <u>Total</u> 273 444 331 1048 n/De ntrol <u>SD</u> To 5.8 7 7 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71           71           71	sed – <u>sta</u> <u>jht 1</u> 0% 5% 5% 0% 5% 0% 5% 5% 0% 5% 5% 0% 5% 5% 5% 0% 5% 5% 5% 5% 5% 5% 5% 5% 5% 5	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FASD 4 -2 Control FAS e) (1 study)	A B Risk of Bi A 4
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         Total (95% CI)       Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.44         Test for overall effect: Z = 6.70 (P < 0.02	and 1 FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 100001) and 1 Mean 52	Tot           10           12           (P = 1)           (P = 1)           (As           SD           3.1	With <u>al Me</u> 38 49 5: 37 5: 24 0.30); F With <u>Total</u> 5 5 With	drawn <u>Contro</u> <u>53</u> 5.7 2.2 4.6 2.2 4.2 <sup>2</sup> = 18% drawn <u>Control</u> <u>Mean</u> <u>53.3</u>	n/De <u>Total</u> 273 444 331 1048 n/De ntrol 5.8 7 7 7 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71           71           71           71           71           71	sed – <u>sta</u> <u>jht 1</u> 0% 5% 0% sed – <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed – s</u>	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FASD 4 -2 Control FAS -2 Control FAS	A Risk of Bi A A Risk of Bi
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         Fotal (95% CI)       -         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Fest for overall effect: Z = 6.70 (P < 0.0	and 1 FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean 52 ) and 2 Mean	Tot           12           (P = 1)           (P = 1)<	With <u>al Me</u> <u>38</u> <u>39</u> 5: <u>37</u> 5: <u>24</u> 0.30); F With <u>Total</u> 5 5 With <u>Total</u>	drawn <u>contro</u> <u>san SD</u> <u>53</u> 5.7 2.2 4.6 2.2 4.2 <sup>2</sup> = 18% drawn <u>Control</u> <u>Mean</u> <u>Control</u> <u>Mean</u> <u>Control</u> <u>Mean</u> <u>Control</u> <u>Mean</u>	n/De <u>Total</u> 273 444 331 1048 1048 n/De ntrol <u>SD To</u> 5.8 7 7 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71           71           71           71           71           30.6	sed – <u>sta</u> <u>jht 1</u> 0% 5% 0% sed – <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u>	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FASD 4 -2 Control FAS e) (1 study)	A B Risk of Bi A 4
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         Fotal (95% CI)       -         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Fest for overall effect: Z = 6.70 (P < 0.0	and 1 FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 100001) and 1 Mean 52	Tot           10           12           (P = 1)           (P = 1)           (As           SD           3.1	With <u>al Me</u> 38 49 5: 37 5: 24 0.30); F With <u>Total</u> 5 5 With	drawn <u>Contro</u> <u>53</u> 5.7 2.2 4.6 2.2 4.2 <sup>2</sup> = 18% drawn <u>Control</u> <u>Mean</u> <u>53.3</u>	n/De <u>Total</u> 273 444 331 1048 1048 n/De ntrol <u>SD To</u> 5.8 7 7 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71           71           71           71           71           30.6	sed – <u>sta</u> <u>jht 1</u> 0% 5% 0% sed – <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed –</u> <u>sed – s</u>	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FASD 4 -2 Control FAS -2 Control FAS	A Risk of Bi A A Risk of Bi
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         Fotal (95% CI)       -         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Test for overall effect: Z = 6.70 (P < 0.00)	and 1 FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean 52 ) and 2 Mean	Tot           12           (P = 1)           (P = 1)<	With <u>al Me</u> <u>38</u> <u>39</u> 5: <u>37</u> 5: <u>24</u> 0.30); F With <u>Total</u> 5 5 With <u>Total</u>	drawn <u>contro</u> <u>san SD</u> <u>53 5.7</u> <u>2.2 4.6</u> <u>2.2 4.2</u> <u>2 = 18%</u> <u>a</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>c</u>	n/De <u>Total</u> 273 444 331 1048 n/De ntrol <u>SD To</u> 5.8 7 7 7 7 7	Weig           31.0           38.6           30.6           100.0           press           tal           W           71           71           71           71           71           30.6	sed – <u>std</u> <u>jht 1</u> 0% 5% 5% 0% 0% sed – <u>sed</u> <u>sed</u> <u>sed</u> <u>sed</u> <u>sed</u>	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FASD 4 -2 Control FAS -2 Control FAS	A Risk of Bia A A A A A A A A A A A A A
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         May et al 2020c (6-7yrs; TRF-T)       5         Fotal (95% CI)       -         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Fest for overall effect: Z = 6.70 (P < 0.0	and 1 FASE an SE 5.8 5.6 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean 52 ) and 2 Mean	Tot           12           (P = 1)           (P = 1)<	With al Me 38 49 5: 37 5: 24 0.30); F With Total 5 5 With Total 44	drawn <u>contro</u> <u>san SD</u> <u>53 5.7</u> <u>2.2 4.6</u> <u>2.2 4.2</u> <u>2 = 18%</u> <u>a</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>c</u>	n/De <u>Total</u> 273 444 331 1048 n/De ntrol <u>SD To</u> 5.8 7 7 7 7 7	Weig           31.0           38.6           30.6           100.0           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71	sed – <u>std</u> <u>jht 1</u> 0% 5% 5% 0% 0% sed – <u>sed</u> <u>sed</u> <u>sed</u> <u>sed</u> <u>sed</u>	Teacher (T-score         . Mean Difference         V, Random, 95% Cl         0.49 [0.15, 0.83]         0.78 [0.48, 1.08]         0.85 [0.51, 1.20]         0.71 [0.50, 0.92]         -4    Teacher (T-score          Std. Mean Difference         IV, Random, 95% Cl         -0.22 [-1.10, 0.66]         -0.22 [-1.10, 0.66]         -0.22 [-1.10, 0.66]         -0.22 [-1.10, 0.66]         -0.3 [-0.34, 0.27]         -0.03 [-0.34, 0.27]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FAS e) (1 study) Std. Mean Difference IV, Random, 95% CI	A Risk of Bi A A Risk of Bi
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         May et al 2020c (6-7yrs; TRF-T)       5         Fotal (95% CI)       -         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Fest for overall effect: Z = 6.70 (P < 0.0	and 1 FASE san SE 5.8 5.5 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean 52 ) 5 and p <u>Mean</u> 53.1	Tot           12           (P = 1)           (P = 1)<	With al Me 38 49 5: 37 5: 24 0.30); F With Total 5 5 With Total 44	drawn <u>contro</u> <u>san SD</u> <u>53 5.7</u> <u>2.2 4.6</u> <u>2.2 4.2</u> <u>2 = 18%</u> <u>a</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>c</u>	n/De <u>Total</u> 273 444 331 1048 n/De ntrol <u>SD To</u> 5.8 7 7 7 7 7	Weig           31.0           38.6           30.6           100.0           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71	sed – <u>std</u> <u>jht 1</u> 0% 5% 5% 0% 0% sed – <u>sed</u> <u>sed</u> <u>sed</u> <u>sed</u> <u>sed</u>	Teacher (T-score . Mean Difference V, Random, 95% Cl 0.49 [0.15, 0.83] 0.78 [0.48, 1.08] 0.85 [0.51, 1.20] 0.71 [0.50, 0.92] -4 Teacher (T-score Std. Mean Difference IV, Random, 95% Cl -0.22 [-1.10, 0.66] -0.22 [-1.10, 0.66]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FAS e) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FAS	A Risk of Bi A A Risk of Bi
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         May et al 2020c (6-7yrs; TRF-T)       5         Fotal (95% CI)       Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Test for overall effect: Z = 6.70 (P < 0.02)	and 1 FASE san SE 5.8 5.5 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean 52 ) 5 and p <u>Mean</u> 53.1	Tot           12           (P = 1)           (P = 1)<	With al Me 38 49 5: 37 5: 24 0.30); F With Total 5 5 With Total 44	drawn <u>contro</u> <u>san SD</u> <u>53 5.7</u> <u>2.2 4.6</u> <u>2.2 4.2</u> <u>2 = 18%</u> <u>a</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>c</u>	n/De <u>Total</u> 273 444 331 1048 n/De ntrol <u>SD To</u> 5.8 7 7 7 7 7	Weig           31.0           38.6           30.6           100.0           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71	sed – <u>std</u> <u>jht 1</u> 0% 5% 5% 0% 0% sed – <u>sed</u> <u>sed</u> <u>sed</u> <u>sed</u> <u>sed</u>	Teacher (T-score         . Mean Difference         V, Random, 95% Cl         0.49 [0.15, 0.83]         0.78 [0.48, 1.08]         0.85 [0.51, 1.20]         0.71 [0.50, 0.92]         -4    Teacher (T-score          Std. Mean Difference         IV, Random, 95% Cl         -0.22 [-1.10, 0.66]         -0.22 [-1.10, 0.66]         -0.22 [-1.10, 0.66]         -0.22 [-1.10, 0.66]         -0.3 [-0.34, 0.27]         -0.03 [-0.34, 0.27]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FAS e) (1 study) Std. Mean Difference IV, Random, 95% CI	A Risk of Bi A A Risk of Bi
FASD         Study or Subgroup       Me         May et al 2020a (6-7yrs; TRF-T)       5         May et al 2020b (6-7yrs; TRF-T)       5         Total (95% CI)       -         Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 2.4.         Test for overall effect: Z = 6.70 (P < 0.0	and 1 FASE san SE 5.8 5.5 6.1 7.7 6.2 7.8 4, df = 2 00001) and 1 Mean 52 ) 5 and p <u>Mean</u> 53.1	Tot           12           (P = 1)           (P = 1)<	With al Me 38 49 5: 37 5: 24 0.30); F With Total 5 5 With Total 44	drawn <u>contro</u> <u>san SD</u> <u>53 5.7</u> <u>2.2 4.6</u> <u>2.2 4.2</u> <u>2 = 18%</u> <u>a</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>control</u> <u>c</u>	n/De <u>Total</u> 273 444 331 1048 n/De ntrol <u>SD To</u> 5.8 7 7 7 7 7	Weig           31.0           38.6           30.6           100.0           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71           71	sed – <u>std</u> <u>jht 1</u> 0% 5% 5% 0% 0% sed – <u>sed</u> <u>sed</u> <u>sed</u> <u>sed</u> <u>sed</u>	Teacher (T-score         . Mean Difference         V, Random, 95% Cl         0.49 [0.15, 0.83]         0.78 [0.48, 1.08]         0.85 [0.51, 1.20]         0.71 [0.50, 0.92]         -4    Teacher (T-score          Std. Mean Difference         IV, Random, 95% Cl         -0.22 [-1.10, 0.66]         -0.22 [-1.10, 0.66]         -0.22 [-1.10, 0.66]         -0.22 [-1.10, 0.66]         -0.3 [-0.34, 0.27]         -0.03 [-0.34, 0.27]	) (3 studies) Std. Mean Difference IV, Random, 95% CI -2 Control FASD ) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FAS e) (1 study) Std. Mean Difference IV, Random, 95% CI -2 Control FAS	A Risk of Bia A A A A A A A A A A A A A



### ASR Somatic Complaints Self Report (T-score)

	pFAS	and	ASR S	Somat	tic Co	ompl	aints –	Self-report (T-sco	re) (1 study)	
	1	DFAS		C	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
Lynch et al 2017 (22yrs; ASR)	4.26	0.55	47	3.32	0.51	58	100.0%	1.77 [1.31, 2.22]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 7.60	(P < 0.00	001)	47			58	100.0%	1.77 [1.31, 2.22]	-4 -2 0 2 Control pFAS	

Risk of bias legend (A) Overall RoB

## ARND/Others and ASR Somatic Complaints - Self-report (T-score) (1 study)

	ARND	)/Othe	ers	С	ontrol	-		Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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]	
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 6.99 (P < 0.00001)			34			58	100.0%	1.78 [1.28, 2.28]	-4 -2 0 2 4 Control ARND/Others
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)

		FASD		0	Control			Std. Mean Difference	Std. Mean Diff	erence	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 9	95% CI	Α
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: Tau <sup>2</sup> = 1.33; Chi <sup>2</sup> = 12.3	35, df = 1	(P = 0.	0004);	l² = 929	6			F.		<u> </u>	4
Test for overall effect: Z = 1.34 (P = 0.1	8)							-4	Control FA	SD	4

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)

	1	pFAS		С	ontrol			Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI 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 (f	P < 0.00	01)							-4 -2 0 2 4 Control pFAS
Risk of higs legend									

(A) Overall RoB

## ARND/Others and ASR Thought Complaints - Self-report (T-score) (1 study)

	ARNI	)/Othe	ers	С	ontrol			Std. Mean Difference	Std. Me	an Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Ran	dom, 95% Cl	Α
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									-4 -2		
Test for overall effect: Z = 10.36 (P < 0.00001)									Contr	ol ARND/Others	
Distant in the second											

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)

	Tot	al FAS	D	0	Control		1	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>z</sup> = 0.04; Chi <sup>z</sup> = 6.0 Test for overall effect: Z = 5.82 (P < 0.0		(P = 0.	11); I² =	= 50%					-4 -2 0 2 Control FASD	4

Risk of bias legend (A) Overall RoB

## FAS and CBCL Affective Problems – Caregiver (T-score) (1 study)

	F	AS		Co	ontro			Std. Mean Difference	Std. Mean Difference	<b>Risk of Bias</b>
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 0.23 (P = 0.82)			5			771	100.0%	0.10 [-0.78, 0.98]	-4 -2 0 2 Control FAS	] 4

	p	FAS		Co	ontro	I	:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
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)									Control pFAS	4
Risk of bias legend										
(A) Overall RoB										

# ARND/Others and CBCL Affective Problems - Caregiver (T-score) (1 study)

	ARND	/Othe	ers	Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 3.08 (P = 0.002)			44			771	100.0%	0.48 [0.17, 0.78]	-4 -2 0 2 Control ARND/Others	4
Pick of bioc logond										

Risk of bias legend (A) Overall RoB

# CBCL Affective Problems Teacher Report (T-score)

	F	ASD		Co	ontro	1	:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> =	= 0.40, dt	f = 2 (	(P = 0.8	(2); <b>I</b> <sup>2</sup> = (	0%			۱.		<u> </u>
Test for overall effect: Z = 8.60 (P				-/1 -				-4	-2 0 2 Control FASD	4

# Risk of bias legend

(A) Overall RoB

## FAS and TRF Affective Problems – Teacher (T-score) (1 study)

					•••			Caence (1. 2001.0)	( + 00000 ) /	
	1	FAS		Co	ontro	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
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)	)								-4 -2 0 2 Control FAS	4

Risk of bias legend (A) Overall RoB

## pFAS and TRF Affective Problems – Teacher (T-score) (1 study)

	p	FAS		C	ontro	1		Std. Mean Difference	Std. M	lean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Ra	andom, 95% Cl	Α
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									4 -2		
Test for overall effect: Z = 1.11 (P = 0.27)	)								Cor	ntrol pFAS	4
Risk of bias legend											

(A) Overall RoB

## ARND/Others and TRF Affective Problems – Teacher (T-score) (1 study)

	ARND	/Othe	ers	Co	ontrol	I		Std. Mean Difference		Std. Mea	n Difference	1	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rand	om, 95% Cl		Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 4.16 (P < 0.0001)			44			771	100.0%	0.65 [0.34, 0.95]	-4	-2 Contro	ARND/Oth	4 ers	

# Summary of available outcomes for **social**

	5	ocial	
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	<b>3 studies:</b> 2 confirmed unquantifiable, 1 Any PAE, 1 light, 1 moderate
	Social Problems – Caregiver Report: CBCL, SDQ	OR/Frequency	<b>4 studies:</b> 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	<b>1 study:</b> 1 very heavy PAE, 1 confirmed unquantifiable
	Social Problems – Teacher Report: SDQ	OR/Frequency	1 study: 1 moderate
	Social – Self Report: YSR, SPSI,	mean/SD	3 studies: 1 light, 1 moderate, 2
	SRM-SF		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	<b>3 studies:</b> 2 FASD, 1 FAS
	Social Problems/Skills- Caregiver Report: CBCL, SRS	T-score	<b>7 studies:</b> 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

		Certainty	assessment			Nº of p	atients		Effect	Certainty
Nº of	Risk of	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative	Absolute	
studies	bias RE STUDIE	s						(95% CI)	(95% CI)	
		SID-III (mean/S	(ח							
		tifiable PAE	01							
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	very serious <sup>d,e,f</sup>	none	28	45	-	SMD 0.79 lower	000
				,					(1.28 lower to 0.3 lower)	Very low
Social Pr	roblems – (	Caregiver Repor	t (T-score)						· · · · · · · · · · · · · · · · · · ·	
Light										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	93	6669	-	SMD 0.04 lower (0.25 lower to 0.16 higher)	⊕⊕⊖⊖ Low
Modera	te									
1	serious <sup>a</sup>	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 <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	2518	7201	-	SMD 0.04 higher (0.00 lower to 0.09 higher)	⊕⊕⊖⊖ Low
Confirm	ed unquan	tifiable PAE								
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	140	188	-	<b>SMD 1.76 higher</b> (0.81 higher to 2.71 higher)	⊕○○○ Very low
Social Pr	roblems – C	Caregiver Repor	t (Odds of scor	ing in the 'clinic	al range	e'/scorin	g 'border	line or abno	ormal'/cut-off unclea	ır)
Light										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	208	690	<b>OR 1.54</b> (0.61 to 3.89)	2 fewer per 1,000 (from 4 fewer to 1 fewer)	⊕⊕⊖⊖ Low
Modera	te			_						
2	seriousª	not serious	not serious	serious <sup>d</sup>	none	584	875	<b>OR 1.12</b> (0.67 to 1.88)	<b>1 few per 1,000</b> (from 2 fewer to 1 fewer)	⊕⊕⊖⊖ Low
Heavy			1				1		1	
1	serious <sup>a</sup>	not serious	not serious	Serious <sup>d,e</sup>	none	57	690	<b>OR 2.20</b> (0.60 to 8.03)	2 fewer per 1,000 (from 8 fewer to 1 fewer)	⊕⊕⊖⊖ Low
		s – Self-report (d	cut-off unclear	)						
	ed unquan		1				1		1	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	850	5299	<b>aOR 1.20</b> (1.00 to 1.44)	1 fewer per 1,000 (from 1 fewer to 1 fewer)	⊕⊕⊖⊖ Low
Social Pr	roblems: So	cial Competend	cy Sum – Careg	iver Report (me	an/SD)					
Very He	avy									
1	seriousª	not serious	not serious	serious <sup>e,f</sup>	none	23	22	-	<b>SMD 0.96 lower</b> (1.58 lower to 0.34 lower)	⊕⊕⊖⊖ Low
Social Co	ommunicat	ion: Social Skills	s Improvement	: System – Careg	giver Re	port (me	ean/SD)			
Confirm	ed Unquar	ntifiable								

1		not conieve	nat agricus	e e ri e u e f		21	20	1	CNAD 0 70 Januar	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	31	39	-	SMD 0.78 lower (1.31 lower to	$\oplus \oplus \bigcirc \bigcirc$
									0.26 lower)	Low
Social P	roblems – 1	eacher Report	(Odds of scori	ng 'borderline or	abnorr	nal' scor	e)		,	
Modera		·	•	0						
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d</sup>	none	195	758	aOR 1.07		$\Theta \Theta O O$
								(0.50 to 2.30)		Low
Social –	Self Report	: (mean/SD)						/		
Light										
1	serious <sup>s</sup>	not serious	not serious	serious <sup>d</sup>	none	2536	2530	-	SMD 0.00 (0.06	$\Theta \Theta O O$
									lower to 0.06	Low
									higher)	
Modera	te		T			-		1		
1	serious <sup>s</sup>	not serious	not serious	serious <sup>d</sup>	none	66	2530	-	SMD 0.09 higher	$\oplus \oplus \bigcirc \bigcirc$
									(0.16 lower to 0.33 higher)	Low
Confirm	ed unquan	tifiable							0.55 fligher)	
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e,f</sup>	none	51	44		SMD 1.12 lower	000
2	Serious	Serious	not senous	Serious /	none	51	44	_	(2.19 lower to	Very low
									0.06 lower)	very low
DIAGNO	SED STUD	IES	•				•	•		
Theory	of Mind Me	asures: NEPSY-	II ToM Total (r	nean/SD)						
FASD										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	69	51	-	SMD 0.6 lower	000
									(1.73 lower to	Very Low
									0.52 higher)	
	of Mind Me	asures: NEPSY-	II ToM Contex	tual (mean/SD)						
FASD							-			
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	37	21	-	SMD 0.66 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.21 lower to	Low
FAS									0.11 lower)	
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	serious <sup>e,f</sup>	none	8	19		SMD 0.88 lower	*
T	serious	not senous	serious	serious	none	0	19	-	(1.74 lower to	⊕○○○ Very low
									0.01 lower)	very low
Theory	of Mind Me	asures: NEPSY-	II ToM Verbal	(mean/SD)						
FASD										
2	serious <sup>a</sup>	serious <sup>b</sup>	not serious	very serious <sup>d,e,f</sup>	none	69	51	-	SMD 0.65 lower	000
									(1.63 lower to	Very low
									0.32 higher)	,
-	ot Mind Me	asures: Readin	g of the Mind'	s Eye (mean/SD)						
FASD			1					1		
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	35	21	-	SMD 0.97 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.55 lower to 0.4	Low
				1					lower)	
F۵s						0	19		SMD 2.16 lower	000
	coriouca	not corious	corious	Soriousef	nono					
FAS 1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	Serious <sup>e, f</sup>	none	8	19			
	serious <sup>a</sup>	not serious	serious <sup>c</sup>	Serious <sup>e,f</sup>	none	8	15		(3.20 lower to 1.13 lower)	Very low
1		not serious Scores Favoure		Serious <sup>e,f</sup>	none	8	19		(3.20 lower to	

	-	-		-			-	-		
2	serious <sup>a</sup>	not serious	not serious	serious <sup>e, f</sup>	none	46	50	-	SMD 0.81 lower	$\oplus \oplus \bigcirc \bigcirc$
									(1.22 lower to	Low
									0.39 lower)	
FAS										
1	serious <sup>a</sup>	not serious	serious <sup>c</sup>	very serious <sup>d,e,f</sup>	none	34	34	-	SMD 0.24 lower	$\oplus O O O$
									(0.72 lower to	Very low
									0.24 higher)	, ,
Social P	roblems/Sk	ills – Caregiver	Report (T-scor	re)						
FASD										
5	serious <sup>a</sup>	serious <sup>b</sup>	not serious	Serious <sup>e, f</sup>	none	153	154	-	SMD 1.84 higher	$\oplus O O O$
									(0.87 higher to	Very low
									2.82 higher)	,
pFAS										
1	serious <sup>a</sup>	not serious	not serious	Serious <sup>e, f</sup>	none	20	16	-	SMD 1.85 higher	$\oplus \oplus \bigcirc \bigcirc$
									(1.05 higher to	Low
									2.64 higher)	
ARND/C	Others									
1	serious <sup>a</sup>	not serious	not serious	Serious <sup>e,f</sup>	none	24	16	-	SMD 1.91 higher	$\oplus \oplus \bigcirc \bigcirc$
									(1.14 higher to	Low
									2.68 higher)	
Social P	roblems/Sk	ills – Caregiver	Report (mean	/SD)						
FASD										
3	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>e, f</sup>	none	111	110	-	SMD 0.74 lower	⊕000
									(1.25 lower to	Very low
									0.23 lower)	,
Social Sl	kills – Teacl	ner Report (mea	an/SD)							
FASD										
3	serious <sup>a</sup>	not serious	not serious	very serious <sup>d,e,f</sup>	none	91	81	-	SMD 0.38 lower	$\oplus \bigcirc \bigcirc \bigcirc$
									(0.79 lower to	Very Low
									0.02 higher)	,

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<sup>2</sup> >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.

Exposure studies

# Theory of Mind Scores

N/A

#### Social-Emotional: BSID-III Confirmed PAE-Level Unguantifiable and BSID-III Social-Emotional Score (1 study) Confirmed Unquantifiable Control Std. Mean Difference Std. Mean Difference **Risk of Bias** Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Study or Subgroup Mean SD Donald et al 2016 (6mnths; BSID-III) 28 113.7 17 45 100.0% -0.79 [-1.28, -0.30] 101.25 13.15 Total (95% CI) 28 45 100.0% -0.79 [-1.28, -0.30] Heterogeneity: Not applicable -4 4 Test for overall effect: Z = 3.15 (P = 0.002) Confirmed Unquantifiable Control Risk of bias legend (A) Overall RoB Social Problems: CBCL – Caregiver Report (T-score) Light PAE and CBCL Social Problems (T-scores) (1 study) Std. Mean Difference Light PAE Control Std. Mean Difference **Risk of Bias** Mean SD Total Mean SD Total Weight Study or Subgroup IV, Random, 95% CI IV, Random, 95% CI 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] ⊢ -4 Heterogeneity: Not applicable -5 'n 4 Test for overall effect: Z = 0.42 (P = 0.68) Control Light PAE Risk of bias legend (A) Overall RoB Moderate PAE and CBCL Social Problems (T-scores) (1 study) Std. Mean Difference Moderate PAF Std. Mean Difference Control Risk of Bias Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI 0.13 [0.05, 0.20] Lees et al 2020 (9-11yrs; CBCL-C) 53.2 755 526 46 6669 100.0% 5.1 Total (95% CI) 755 6669 100.0% 0.13 [0.05, 0.20] Heterogeneity: Not applicable -4 -5 ń Δ Test for overall effect: Z = 3.36 (P = 0.0008) Control Moderate PAE Risk of bias legend (A) Overall RoB Any PAE and CBCL Social Problems (1 study) Std. Mean Difference Std. Mean Difference Any PAE Control **Risk of Bias** Mean SD Total Mean SD Total IV, Random, 95% CI IV. Random, 95% CI Study or Subgroup Weight A 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] 2518 7201 100.0% 0.04 [-0.00, 0.09] Total (95% CI) Heterogeneity: Not applicable -4 -2 ń 4 Test for overall effect: Z = 1.88 (P = 0.06) Control Any PAE Risk of bias legend (A) Overall RoB Confirmed PAE-Level Unguantifiable and CBCL Social Problems (2 studies) Std. Mean Difference **Confirmed Unguantifiable** Control Std. Mean Difference **Risk of Bias** Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI 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: Tau<sup>2</sup> = 0.43; Chi<sup>2</sup> = 12.56, df = 1 (P = 0.0004); l<sup>2</sup> = 92% ⊢ -4 5 Λ -2 Ó Test for overall effect: Z = 3.62 (P = 0.0003) Control Confirmed Unguantifiable

# 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% Cl		Odds Ratio IV, Random, 95% Cl	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]			•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.91 (P = 0.36)			100.0%	1.54 [0.61, 3.89]	↓ 0.01	0.1 1 10 Control Light PAE	100

Risk of bias legend (A) Overall RoB

## Moderate PAE and CBCL/SDQ Social Problems (Frequency/OR) (2 studies)

				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.2 Test for overall effect: Z = 0.44 (P = 0.		; I² = 0%			0.1 0.2 0.5 1 2 5 Control Moderate PAE	10

Risk of bias legend (A) Overall RoB

## Heavy PAE and CBCL/SDQ Social Problems (Frequency/OR) (1 study)

				Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
O'Leary et al 2010 (2, 5, 8yrs; CBCL-C)	0.7862	0.6617	100.0%	2.20 [0.60, 8.03]		•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 1.19 (P = 0.23)			100.0%	2.20 [0.60, 8.03]	0.1 0.2 0.5 1 2 5 10 Control Heavy PAE	H I

Risk of bias legend (A) Overall RoB

Note: O'Leary et al 2010 reports data from 1<sup>st</sup> trimester and 3<sup>rd</sup> trimester exposure, 1<sup>st</sup> 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)

		Odds Ratio Risk of Bia			
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% Cl 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)					Control Confirmed Unquantifiable
Risk of bias legend					
(A) Overall RoB					

# CBCL Social Competency Sum – Caregiver Report (mean/SD)

Very	Heavy	PAE	and	CBCI	. Soc	ial C	ompete	ency Sum (meai	n <b>/SD)</b> (1 study)	
-	Very I	leavy I	PAE	С	ontrol			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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									-4 -2 0 2	
Test for overall effect: Z = 3.02 (P = 0	.002)								Very Heavy PAE Control	4
Risk of bias legend										
(A) Overall RoB										

# Social Communication: SSIS – Caregiver Report (mean/SD)

	Confirmed	d Unquantif	fiable	0	Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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]		•
Fotal (95% CI)			31			29	100.0%	-0.78 [-1.31, -0.26]	•	
leterogeneity: Not applicable								H		
Fest for overall effect: Z = 2.91 (P =	0.004)							Confirme	ed Unquantifiable Control	4

(A) Overall RoB

# Social Problems: SDQ – Teacher Report (aOR/Frequency)

Moderate PAE and CBCL Social Problems (aOR/Frequency) (1 study)												
				Odds Ratio	Odds Ratio	Risk of Bias						
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α						
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						5 10						
Test for overall effect: Z = 0.18 (P = 0.8	36)				Control Moderate F							

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)

	Ligh	nt P/	AE an	d Self	f Re	port :	Social P	Problems (mean/	(1 study)
	Lig	ht PA	E	Co	ontro	I		Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl A
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 = 1.0	10)							-4 -2 U 2 4 Control Light PAE
Risk of bias legend (A) Overall RoB									

## Moderate PAE and YSR Social Problems (mean/SD) (1 study)

	Mode	rate P	AE	Co	ontro	l i	:	Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl A
Alati et al 2009 (14yrs; YSR)	4.2	2.2	66	4	2.3	2530	100.0%	0.09 [-0.16, 0.33]	•
<b>Total (95% CI)</b> Heterogeneity: Not applicable Test for overall effect: Z = 0.70	(P = 0.49	3)	66			2530	100.0%	0.09 [-0.16, 0.33]	-4 -2 0 2 4 Control Moderate PAE

Risk of bias legend (A) Overall RoB

## Confirmed unquantifiable PAE and SPSI/SRM-SF Self Report Social Problems (mean/SD) (2 studies)

	Confirmed U	nquantifiabl	e PAE	C	ontrol			Std. Mean Difference		Std. Mean D	Difference	Risk of	f Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Randor	n, 95% Cl	Α	
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: Tau <sup>2</sup> = 0.48; Chi <sup>2</sup> = 5.30, df = Test for overall effect: $Z = 2.06$ (P = 0.04)	1 (P = 0.02); I <sup>2</sup>	= 81%						Confirm	-4 ed Ungu	-2 0 Iantifiable	2 Control	4	
······ ,								Coniirm	ea Unqu	lanullable	Control		

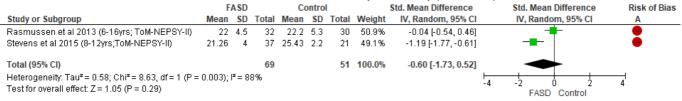
Risk of bias legend (A) Overall RoB

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)



Risk of bias legend (A) Overall RoB

# Theory of Mind Scores: NEPSY-II ToM Contextual (mean/SD)

FA	SD ar	nd M	NEPS	Y-II T	οM	Con	textua	I (mean/SD) (1	study)
	E	ASD		Co	ontro	I I		Std. Mean Difference	Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A
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)									-4 -2 0 2 4
Test for overall effect. $Z = 2.30$ (P = 0.02)									FASD Control
Risk of bias legend									

(A) Overall RoB

## FAS and NEPSY-II ToM Contextual (mean/SD) (1 study)

F	FAS		Co	ontro	1		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
3.5	1.2	8	4.4	0.9	19	100.0%	-0.88 [-1.74, -0.01]		•
		8			19	100.0%	-0.88 [-1.74, -0.01]	-	
								-4 -2 0 2	4
								FAS Control	
	Mean	FAS <u>Mean SD</u> 3.5 1.2	Mean SD Total	Mean SD Total Mean	Mean SD Total Mean SD	Mean         SD         Total         Mean         SD         Total           3.5         1.2         8         4.4         0.9         19	Mean SD Total Mean SD Total Weight	Mean         SD         Total         Weight         IV, Random, 95% CI           3.5         1.2         8         4.4         0.9         19         100.0%         -0.88 [-1.74, -0.01]	Mean         SD         Total         Weight         IV, Random, 95% CI         IV, Random, 95% CI           3.5         1.2         8         4.4         0.9         19         100.0%         -0.88 [-1.74, -0.01]         -           8         19         100.0%         -0.88 [-1.74, -0.01]         -         -         -           -4         -2         0         2         0         2

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)

FAS			EPSY				•	ean/SD) (2 studie	·	
	F	ASD		Co	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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: Tau <sup>2</sup> = 0.42; Chi <sup>2</sup> = 6.55, df = 1 (P = Test for overall effect: Z = 1.31 (P = 0.19)	0.01); I²	= 85	%					-4	-2 0 2 FASD Control	4

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)

	E	ASD		Co	ontrol	I		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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)									-4 -2 0 2	4
Piekofikieskoesed									FASD Control	

Risk of bias legend (A) Overall RoB

Note: Stevens et al 2017 also reports ToM-RMET subdomains.

	FAS	and	d Rea	ding	of t	he M	lind's E	<b>ye (mean/SD)</b> (1 s	study)	
	F	AS		Co	ontro			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	<b>SD</b>	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								H		<u> </u>
Test for overall effect: Z = 4.09 (P < 0.0	0001)							-4	FAS Control	4
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)

	ana	50010	1 381	1.5.11	SILCI	3001	c3 i av			.37	
	1	FASD		0	Control			Std. Mean Difference	Std. Me	an Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rai	idom, 95% Cl	Α
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]	-	F	•
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: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.00	), df = 1 (	P = 0.9	5); I <sup>z</sup> = (	0%					<u>⊢</u>		
Test for overall effect: Z = 3.78 (P = 0.0	002)								-4 -2 FAS	SD Control	4

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)

		FAS			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD.	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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) Heterogeneity: Not applicable Test for overall effect: Z = 0.98 (P = 0.33)			34			34	100.0%	-0.24 [-0.72, 0.24]	-4 -2 0 2 FAS Control	4
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) FASD Control Std. Mean Difference Std. Mean Difference Risk of Bias Mean Study or Subgroup Mean SD Total SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Δ de Water et al 2021 (8-16yrs; CBCL-C) 64.15 8.99 52.4 3.33 21.1% 1.73 [1.23, 2.24] 41 43 Mattson & Riley 2000 (4-16yrs; CBCL-C) 0.92 [0.41, 1.43] 9.55 55.6 21.0% 64.6 33 9.77 33 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: Tau<sup>2</sup> = 1.11; Chi<sup>2</sup> = 48.83, df = 4 (P < 0.00001); l<sup>2</sup> = 92% -'4 -2 Ó Test for overall effect: Z = 3.71 (P = 0.0002) Control FASD

Risk of bias legend (A) Overall RoB

Note: Way et al 2012 also reports SRS-C subdomains.

	p	FAS		Co	ontro	I	:	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								F		-
Test for overall effect: Z = 4.54 (P ≤ 0.00001)									Control pFAS	4

#### ARND/Others and Social Problems: CBCL/SRS – Caregiver Report (T-score) (1 study) Std. Mean Difference ARND/Others Control Std. Mean Difference Risk of Bias SD Total Mean SD Total Weight IV, Random, 95% CI Study or Subgroup Mean IV, Random, 95% CI Δ Astley et al 2009b (8-16yrs; CBCL-C; SE/AE) 66.8 24 52.3 4.6 16 100.0% 1.91 [1.14, 2.68] 8.8 Total (95% CI) 24 16 100.0% 1.91 [1.14, 2.68] ⊢ -4 Heterogeneity: Not applicable -2 4 Test for overall effect: Z = 4.86 (P < 0.00001) Control ARND/Others Risk of bias legend

(A) Overall RoB

# Social Problems/Skills: SSRS/BASC – Caregiver Report (mean/SD)

		FASD			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	Α
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: Tau <sup>2</sup> = 0.14; Chi <sup>2</sup> = 6.41, df = 3	2 (P = 0.0	(4); l <sup>2</sup> = 69	%							
Test for overall effect: Z = 2.85 (P = 0.004)									-4 -2 U 2 FASD Control	4

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)

	FASD								
	FASD			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
81.7	33.8929	33	101.3	16.9098	34	36.2%	-0.73 [-1.22, -0.23]		•
96.8	14.4	21	101.3	10.5	24	29.5%	-0.35 [-0.95, 0.24]		•
91.89	18.02	37	92.75	21.14	23	34.3%	-0.04 [-0.56, 0.48]	-+-	•
		91			81	100.0%	-0.38 [-0.79, 0.02]	•	
2 (P = 0.	18); I <sup>z</sup> = 43	3%					ł		-,
								FASD Control	4
2	81.7 96.8 91.89	81.7 33.8929 96.8 14.4 91.89 18.02	81.7         33.8929         33           96.8         14.4         21           91.89         18.02         37	81.7         33.8929         33         101.3           96.8         14.4         21         101.3           91.89         18.02         37         92.75           91         91         91         91	81.7         33.8929         33         101.3         16.9098           96.8         14.4         21         101.3         10.5           91.89         18.02         37         92.75         21.14           91         91         91         91         91	81.7         33.8929         33         101.3         16.9098         34           96.8         14.4         21         101.3         10.5         24           91.89         18.02         37         92.75         21.14         23           91         91         81         81         81         81	81.7         33.8929         33         101.3         16.9098         34         36.2%           96.8         14.4         21         101.3         10.5         24         29.5%           91.89         18.02         37         92.75         21.14         23         34.3%           91         81         100.0%	81.7       33.8929       33       101.3       16.9098       34       36.2%       -0.73 [-1.22, -0.23]         96.8       14.4       21       101.3       10.5       24       29.5%       -0.35 [-0.95, 0.24]         91.89       18.02       37       92.75       21.14       23       34.3%       -0.04 [-0.56, 0.48]         91       81       100.0%       -0.38 [-0.79, 0.02]       *         *(P = 0.18); I* = 43%       *       *       *       *	81.7 33.8929 33 101.3 16.9098 34 36.2% -0.73 [-1.22, -0.23] 96.8 14.4 21 101.3 10.5 24 29.5% -0.35 [-0.95, 0.24] 91.89 18.02 37 92.75 21.14 23 34.3% -0.04 [-0.56, 0.48] 91 81 100.0% -0.38 [-0.79, 0.02] • (P = 0.18); P = 43%

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.



# Summary of available outcomes for Sensory Processing and Soft Neurological

# Signs

	Sensory Processing	and Soft Neurologica	I 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

		Certainty	assessment			Nº of p	oatients		Effect	Certainty
Nº of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	PAE	Control	Relative (95% Cl)	Absolute (95% Cl)	
Exposur	e Studies									
Infant-To	oddler Sen	sory Profile (adj	usted odds of s	scoring <1SD be	elow the	mean):	Low Regi	stration		
Moderat	te PAE									
1	not serious	not serious	not serious	serious <sup>d,f</sup>	-	74	126	<b>aOR 1.21</b> (0.65 to 2.25)	-	⊕⊕⊕⊖ Moderate
Infant-To	oddler Sen	sory Profile (adj	usted odds of s	scoring <1SD be	elow the	mean):	Sensation	n Seeking		
Moderat	te PAE									
1	not serious	not serious	not serious	serious <sup>d,f</sup>	-	74	126	<b>aOR 0.52</b> (0.24 to 1.11)	-	⊕⊕⊕⊖ Moderate
Infant-To	oddler Sen	sory Profile (adj	usted odds of s	scoring <1SD be	elow the	mean):	Sensory S	Sensitivity		
Moderat	te PAE									
1	not serious	not serious	not serious	serious <sup>d,f</sup>	-	74	126	<b>aOR 1.36</b> (0.71 to 2.60)	-	⊕⊕⊕⊖ Moderate
Infant-To	oddler Sen	sory Profile (adj	usted odds of s	scoring <1SD be	elow the	mean):	Sensation	n Avoiding		
Moderat	te PAE									
1	not serious	not serious	not serious	serious <sup>d,f</sup>	-	74	126	<b>aOR 1.32</b> (0.70 to 2.49)	-	⊕⊕⊕⊖ Moderate
Infant-To	oddler Sen	sory Profile (Fre	quency of 'typ	ical' scores): Lo	w Regis	tration				
Modera	te PAE									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	-	22/39	25/54	<b>OR 1.50</b> (0.66 to 3.44)	-	⊕⊕⊖⊖ Low
Infant-To	oddler Sen	sory Profile (Fre	equency of 'typ	ical' scores): Se	nsation	Seeking				
Moderat	te PAE									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	-	24/39	32/54	<b>OR 1.10</b> (0.47 to 2.56)	-	⊕⊕⊖⊖ Low
Infant-To	oddler Sen	sory Profile (Fre	equency of 'typ	ical' scores): Se	nsory Se	ensitivity	/			

Modera	ate PAE									
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	-	21/39	39/54	<b>OR 0.45</b> (0.19 to 1.07)	-	⊕⊕⊖⊖ Low
		sory Profile (Fre	equency of 'typi	cal' scores): Se	ensation	Avoiding	g			
Modera	1				1					
1	serious <sup>a</sup>	not serious	not serious	serious <sup>d,f</sup>	-	25/39	40/54	<b>OR 0.63</b> (0.26 to 1.53)	-	⊕⊕⊖⊖ Low
Diagno	sed Studies									
Short Se	ensory Profi	le (mean/SD)								
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	25	23	-	<b>SMD 1.45 lower</b> (2.09 lower to 0.8 lower)	⊕⊕⊖⊖ Low
	ensory Profi	le (Frequency/	OR) (<1SD on SS	P)						
FASD					1					
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	11	12	<b>OR 175.0</b> (6.43 to 4764.19)	-	⊕⊕⊖⊖ Low
Sensory	Processing	Measure (Freq	Juency/OR) (<19	D on SPM)						
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	11	12	OR 95.0 (4.07 to 2219.98)	-	⊕⊕⊖⊖ Low
	leurological	Screen Test (Fr	equency/OR) (<	24 <sup>th</sup> centile or	n QNST-I	1)				
FASD						-				
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	21	42	<b>OR 2.40</b> (0.67 to 8.65)	-	⊕⊕⊖⊖ Low
Quick N	leurological	Screen Test (m	ean/SD)							
FASD										
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	25	26	-	SMD 1.44 higher (0.82 higher to 2.06 higher)	⊕⊕⊖⊖ Low
FAS/pF	AS		· ·		•	-	-	•	·	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	20	16	-	SMD 1.47 higher (0.72 higher to 2.22 higher)	⊕⊕⊖⊖ Low
ARND/	Others		•					•	-	
1	serious <sup>a</sup>	not serious	not serious	serious <sup>e,f</sup>	none	24	16	-	SMD 1.89 higher (1.12 higher to 2.66 higher)	⊕⊕⊖⊖ Low

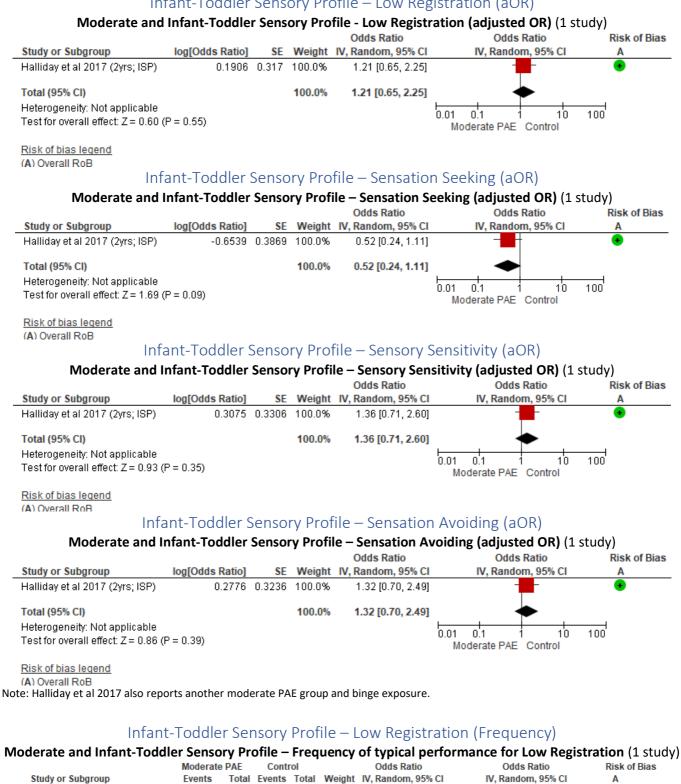
Notes: CI: confidence interval; SMD: standardized mean difference; OR: odds ratio.

**Explanations:** a) >50% of studies were rated as moderate or high risk of bias; b) High heterogeneity ( $l^2 >50\%$  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**

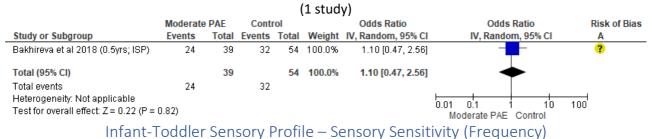
## Infant-Toddler Sensory Profile – Low Registration (aOR)



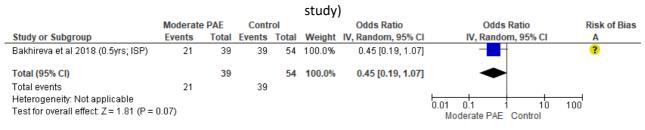
(A) Overall RoB

# Infant-Toddler Sensory Profile – Sensation Seeking (Frequency)

# Moderate and Infant-Toddler Sensory Profile – Frequency of typical performance for Sensation Seeking



# Moderate and Infant-Toddler Sensory Profile – Frequency of typical performance for Sensory Sensitivity (1



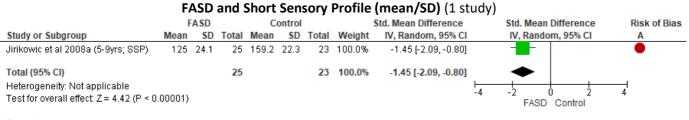
# Infant-Toddler Sensory Profile – Sensation Avoiding (Frequency)

## Moderate and Infant-Toddler Sensory Profile – Frequency of typical performance for Sensation Avoiding (1

study) Moderate PAE Odds Ratio Odds Ratio Control Risk of Bias Study or Subgroup Total Events Total Weight IV, Random, 95% CI IV, Random, 95% C Events Α 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 0.01 0.1 100 10 Test for overall effect: Z = 1.03 (P = 0.30) Moderate PAE Control

# **Diagnosed studies**

# Short Sensory Profile (mean/SD)



Risk of bias legend (A) Overall RoB

# Short Sensory Profile (Frequency/OR)

## FASD and Short Sensory Profile (Frequency/OR) (1 study)

Study or Subgroup         Events         Total         Events         Total         Weight         IV, Random, 95% CI         A           Hanson & Jirikowic 2013 (5-11yrs; SSP)         10         11         0         12         100.0%         175.00 [6.43, 4764.19]         Image: Constant of the second		FASI	D	Contr	ol		Odds Ratio	Odds Ratio Risk of Bia
Total (95% Cl)         11         12         100.0%         175.00 [6.43, 4764.19]           Total events         10         0           Heterogeneity: Not applicable         0.001         0.1         1         10         1000	Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl A
Total events         10         0           Heterogeneity: Not applicable         0.001         0.1         1         10         1000	Hanson & Jirikowic 2013 (5-11yrs; SSP)	10	11	0	12	100.0%	175.00 [6.43, 4764.19]	
Heterogeneity: Not applicable         Image: Constraint of the second secon	Total (95% CI)		11		12	100.0%	175.00 [6.43, 4764.19]	
	Heterogeneity: Not applicable	10		0				

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)

				,			
	FAS	D	Contr	ol		Odds Ratio	Odds Ratio Risk of
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI 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)							0.001 0.1 1 10 1000 FASD Control
Risk of bias legend							

(A) Overall RoB

# Note: Frequency of atypical score on SSP (<1SD).

# Quick Neurological Screen Test (Frequency/OR)

	FASD		Control			Odds Ratio	Odds Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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								400
Test for overall effect: Z = 1.34 (P =	0.18)						0.01 0.1 1 10 Control FASD	100

Risk of bias legend (A) Overall RoB

Note: Frequency of atypical score on SNS (<24<sup>th</sup> centile).

# Quick Neurological Screen Test (mean/SD)

Study or Subgroup	ASD and Quick			Control				Std. Mean Difference	Std. Mean Difference	Risk of Bias
	Mean SD		) Total	Mean	SD T	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	Α
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 ≤ 0.0	0001)								Control FASD	4

Risk of bias legend (A) Overall RoB

# pFAS and Quick Neurological Screen Test (mean/SD) (1 study)

•		FAS	•	Control				Std. Mean Difference	• •	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean						IV, Random, 95% Cl	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									-4	-2 0 2	4
Test for overall effect: Z = 3.84 (P = 0	.0001)								-4	Control pFAS	4
Disk of his states and											

Risk of bias legend (A) Overall RoB

Note: Astley 2009 reports FAS/pFAS.

Study or Subgroup	ARND	Control				Std. Mean Difference	Std. Mean Difference		Risk of Bias		
	Mean	<b>SD</b>	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		Α
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									H	<u> </u>	
Test for overall effect: Z = 4.82 (P ≤ 0.	00001)								-4 -2 Contro	I ARND/Others	4

(A) Overall RoB

Note: Astley 2009 reports SE/AE. Astley 2009 also reports ND/AE.