Supplemental File D: Narrative summary of regression analyses

Author, Country,	Participants	PAE level	Covariates	Outcomes of Interest	Key Finding
Cohort, Outcome					
UK	Pregnant women follow-up of children at 8 years of age (n = 4,332).	4g/w; 1-6glasses/w	Sex, social class, parity, ethnicity, house ownership, crowding, maternal and paternal education.	Scale for Children (WISC-	In fully adjusted models there was no statistical association between PAE and IQ.
	Pregnant women	<1glass/w (light PAE) =	Sex, other parent's alcohol	National Curriculum Key	In fully adjusted models consumption
UK	follow-up of children at 11 years (<i>n</i> = 7,062).	4g/w; 1-6glasses/w (moderate PAE) = 28g/w; 1+glasses/day (moderate PAE) = 86g/w	consumption, maternal age, parity,	Stage 2 (KS2) tests – academic	of 4 units (32 grams of alcohol) on a single drinking occasion was associated with reduced educational outcomes. Drinking up to 1 unit a day was not associated with lower outcomes.
Bakhireva et al	Pregnant women	PAE (moderate PAE) =	Infant sex, birth weight, single vs two-		Adjusted model approached
2018	follow-up of children 5-8 months (<i>n</i> = 93)	86.24g/w	parent household, Beck Depression Inventory, maternal education, maternal age, medication assisted therapy (methadone, buprenorphine), marijuana, tobacco use, Perceived	Development-III (BSID-III) – cognitive, language and motor	significance for BSID-III Cognitive. Not significant for Language or Motor. Approached significance for IBQ Surgency. Significant for Negative
Functional Neuro			1 -	Questionnaire-R	Affect. Non-significant for Sensory Profile.
				processing	
		9.8g/w; Trajectory C	P	and head	Only trajectory E (very heavy PAE level) associated with reduced birth
	children at birth, 6		,		weight and length. No significant
	months, and 12 months (n = 471)	Trajectory D (moderate	(married, single, divorced or separated), maternal prenatal or		association for mean head circumference percentile. Trajectory E
Physical Size	inonuis (11 – 471)		multivitamin use, maternal smoking		(very heavy PAE) associated with reductions in MDI and PDI at 6 and 12

Head			status, socioeconomic status,		months. Trajectory D (moderate PAE)
Circumference			gestational age at enrolment.		associated with reduced MDI and PDI
Functional Neuro					at 6 and 12 months. Trajectory C
					(moderate PAE) associated with
					reduced PDI at 6months and MDI at
					12 months. Trajectory C (moderate
					PAE) not associated with
					neurodevelopmental deficits.
Bandoli et al 2020	Pregnant women	Trajectory B (moderate PAE)	Maternal prenatal vitamin use,	Dysmorphology score,	Infants with exposure in the top 3
			maternal age, socioeconomic status,	minor dysmorphic	trajectories (C-E i.e., moderate to very
			pregnancy smoking, infant age at	features, height, weight	heavy exposure) had increased total
CIFASD	•		dysmorphology examination.	& head circumference	dysmorphology scores in a dose-
	-	PAE) = 96.05g/w; Trajectory			response fashion. Infants in the
Dysmorphology &		E (very heavy PAE) =			highest exposure trajectory were at
Physical Size		367.41g/w (very heavy)			increased risk to fall below the 10 th
					percentile on height, weight, and head
					circumference.
	_			MRI – grey and white	Fully adjusted model demonstrated
			, , ,	matter regions of	associations with PAE in grey matter in
		PAE) = 96.38g/w; pFAS (very	concentration (ug/dl).	interest	the caudate and hippocampus. No
·	l' .	heavy PAE) = 215.45g/w;			association for corpus callosum in fully
Longitudinal		FAS (very heavy PAE) =			adjusted model.
Cohort		291.71g/w			
Structural Neuro					
	Pregnant women	Continuous measure of	Covariates varied based on outcome:	Attention, Executive	Following adjustment significant
	_		child age, SES, HOME, maternal	Function, Working	associations between PAE and digit
		_	education, child sex, PPVT, alcohol use		span cancellation omission, digit span,
	= 337).		7-yr, opiate/cocaine use 7-yr, children	ivicinory	tower of London, arithmetic, working
0.5	_ 557 j.		in household, maternal age, parity,		memory composite, category fluency.
Functional Neuro			opiates pregnancy, cocaine pregnancy,		line
			GSI, disruption, examiner effects,		
			cigarette use, lead, Beck, crowded,		
			marital status, marijuana pregnancy,		
			w. marijuana at 7-yrs.		
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U.S. n not reported. drinks/week (moderate PAE) = 28g/w; 4+ drinks/week (moderate PAE) = 28g/w; 4+ drinks/week (moderate PAE) = 77g/w significant at 4 or more drinks per week. Social engagement was significant at 1-3 drinks per week. Social engagement was significant at 1-3 drinks per week. Social engagement was significant at 1-3 drinks per week. Social engagement was significant at 1-3 drinks per week. Social engagement was significant at 1-3 drinks per week. Social engagement was significant at 1-3 drinks per week. Social engagement was significant at 1-3 drinks per week. Social engagement was significant at 1-3 drinks per week. Social engagement was significant at 1-3 drinks per week. Social engagement was significant at 1-3 drinks per week. PAE was associated with reduced be assessed: maternal eigarette smoking, circumference, 6.5-month and 12-month gender, socioeconomic status. PaE was associated with reduced be assessed: maternal eigarette smoking, circumference, 6.5-month and 12-month gender, socioeconomic status. PaE was associated with reduced be assessed: maternal age at delivery, infant gender, socioeconomic status. PaE was associated with reduced be assessed: maternal eigarette smoking, circumference. PaE was associated with reduced be assessed: maternal pacity, maternal education, infants exceptionally stong in iron deficient infants. Cannabis where the postnatal growth. After adjustment weight, height and head circumference were significant at 1-3 drinks per week. PaE was associated with PAE were generally strong in iron deficient infants. Cannabis where assessed: maternal parity, maternal education, infants exc, child's age in circumference PaE were generally strong in iron deficient infants. Cannabis where assessed: maternal parity, maternal education, infants exc, hidi's age in circumference PaE were generally strong in iron deficient infants. Cannabis when controlling for birth. PAE measurement, food security, maternal education, degree the page in the page in the page						
U.S. In not reported. drinks/week (moderate PAE) = 28g/w; 4+ drinks/week (moderate PAE) = 28g/w; 4+ drinks/week (moderate PAE) = 28g/w; 4+ drinks/week (moderate PAE) = 77g/w Functional Neuro Carter et al 2007 Pregnant women with children assessed at 6.5 and 12 months of age (n= 188) Cape Town Longitudinal Cohort Cape Town Longitudina	Brown et al 2010		<u> </u>	, ,		
PAE) = 28g/w; 4+ drinks/week (moderate PAE) = 77g/w Functional Neuro Pregnant women with children South Africa South Afri				race/ethnicity.	development, behaviour,	scores for successively higher levels of
Functional Neuro Functional Neuro Pregnant women with children assessed at 6.5 and 12 months of age (n= Physical Size Head Circumference Carter et al 2022 Pregnant women with children assessed at 6.5 and 12 months of age (n= Physical Size Head Circumference Carter et al 2022 Pregnant women with children assessed at 6.5 and 12 months of age (n= Physical Size Head Circumference Carter et al 2022 Pregnant women with children assessed at 6.5 and 12 months of age (n= Physical Size Head Circumference Carter et al 2012 Cape Town Longitudinal Cohort Physical Size Head Circumference Carter et al 2012 Cape Town Longitudinal Cohort Carter et al 2012 Pregnant women with children assessed at 6.5 months, 12 months, 5 months, 12 months, 6 months, 12 m	U.S	•	•		sensory regulation.	_
Functional Neuro Pregnant women with children assessed at 6.5 and 196g/w assessed: maternal cigarette smoking, parity, maternal age at delivery, infant gender, socioeconomic status. South Africa assessed at 6.5 and 196g/w assessed: maternal cigarette smoking, parity, maternal age at delivery, infant gender, socioeconomic status. Physical Size Head Circumference Carter et al 2012 Pregnant women with children assessed at 6.5 months, 12 months, 5 years, and 9 years (n = 148) Chort Physical Size Head Circumference Carter et al 2022 Pregnant women with children assessed at 2.8 weeks and 5 years (n = 158) Carter et al 2022 Pregnant women with children assessed at 2.8 weeks and 5 years (n = 158) Physical Size Head Circumference Carter et al 2022 Pregnant women with children assessed at 2.8 weeks and 5 years (n = 158) Physical Size Head Circumference Carter et al 2022 Pregnant women with children assessed at 2.8 weeks and 5 years (n = 158) Physical Size Head Circumference Carter et al 2022 Pregnant women with children assessed at 2.8 weeks and 5 years (n = 158) Cape Town Longitudinal Cohort Bhase of the control line of the weight, beight and the decircumference were significant at 1.3 drinks per week. Birth weight, birth head circumference, 6.5-month and 12-month weight, the decircumference. Carter et al 2012 Pregnant women with children assessed at 5.5 months, 5 years, and 9 years (n = 158) Cape Town Longitudinal Cohort Bhase of the control line of the weight, genth with children assessed at 2 weeks and 5 years (n = 158) Cape Town Longitudinal Cohort Bhase of the control line of the weight, genth with children assessed at 2 weeks and 5 years (n = 158) Cape Town Longitudinal Cohort Bhase of the control line of the control lin						subscales. Three sensory regulation
Functional Neuro Carter et al 2007 Pregnant women with children assessed at 6.5 and 12 moths of age (n= 12 moths) Cape Town (Circumference) Carter et al 2012 Pregnant women with children assessed at 6.5 and 12 moths of age (n= 148) Cape Town (Contort) Ca	ECLS-B		drinks/week (moderate			variables found to be statistically
Carter et al 2007			PAE) = 77g/w			significant at 4 or more drinks per
Pregnant women with children 196g/w	Functional Neuro					week. Social engagement was
with children assessed at 6.5 and 12 moths of age (n= 96) Cape Town Longitudinal Cohort Pregnant women with children assessed at 6.5 months, 12 months, 5 months, 12 months, 5 months, 12 months, 12 months, 5 months, 12 months, 5 months, 12 months, 13 months, 14 months, 15 months, 12 months, 15 months, 15 months, 15 months, 15 months, 16 months, 16 months, 17 mo						significant at 1-3 drinks per week.
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12 moths of age (n=		with children	196g/w	assessed: maternal cigarette smoking,	circumference, 6.5-	weight after controlling for maternal
Cape Town Longitudinal Cohort Chort Child weight, and head circumference Chort Child weight, and head circumference Chort Child weight, and head circumference associated with PAE. BMI was not. The properties of PAE were generally strong in iron deficient infants. Cannabis wence associated with prenatal or postnatal growth. After adjustment weight, height and head circumference were significant associated with PAE. BMI was not. The properties of PAE were substantially diminished when controlling for bin weight and the effects on weight were substantially diminished when controlling for bin weight and the effect on length/height, weight and the effect on length/height are properties. Chort Child weight, length/height, and head circumference associated with PAE. BMI was not. offects on weight were substantially diminished when controlling for bin weight and the effect on length/height, weight and the effect on length/height, weight and the effects. Chort Chort Chort Chort Child weight, length, weight and head circumference associated with PAE. BMI was not. offects on weight were substantially diminished when controlling for bin weight and the effects on length/height, weight and the effects on length/height, weight and head circumference Chort Child weight, length, weight and head circumference associated with PAE. BMI was not. offects on weight and the effects on weight was not. offects	South Africa	assessed at 6.5 and		parity, maternal age at delivery, infant	month and 12-month	smoking. Effect of PAE on birth weight
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Physical Size Head Circumference Carter et al 2012 Carter et al 2012 Cape Town Longitudinal Chort Chort Physical Size Head Circumference Carter et al 2012 Cape Town Longitudinal Cohort Carter et al 2012 Carter et al 2022 Carter	Longitudinal				circumference.	months and length at 12 months
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Circumference have caused epigenetic changes that resulted in permanent effects. Carter et al 2022 Pregnant women with children assessed at 2 weeks and 5 years (n = 158) Pregnant (n = 158) have caused epigenetic changes that resulted in permanent effects. Birth weight, 2 week and 5-year length/height, weight and head overlapping associations with grow and neurobehavioural outcomes.	Physical Size					of PAE on growth were largely
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Carter et al 2022 Pregnant women with children assessed at 2 weeks and 5 years (n = 158) Pregnant women with children assessed at 2 weeks and 5 years (n = 158) Pregnant women with children assessed at 2 weeks and 5 years (n = 158) Pregnant women with children assessed at 2 weeks and 5 years (n = 158) Pregnant women with children education, cigarettes/day, marijuana use, methamphetamine use, gestation, infant sex, age at circumference resulted in permanent effects. PAE and maternal and infant iron measures had separate and overlapping associations with grow and neurobehavioural outcomes.	Circumference					have caused epigenetic changes that
Carter et al 2022 Pregnant women with children South Africa assessed at 2 weeks and 5 years (n = 158) Heavy exposure (heavy PAE) Maternal age, gravidity, maternal birth weight, 2 week and 5 years (n = 158) South Africa assessed at 2 weeks and 5 years (n = 158) South Africa beducation, cigarettes/day, marijuana use, methamphetamine use, gestation, infant sex, age at south africa birth weight, 2 week and page and maternal and infant iron weight, and head overlapping associations with grow and neurobehavioural outcomes.						
with children assessed at 2 weeks and 5 years (n = 158) = 178.60g/w education, cigarettes/day, marijuana use, methamphetamine use, gestation, infant sex, age at sequence of the control o	Carter et al 2022	Pregnant women	Heavy exposure (heavy PAE)	Maternal age, gravidity, maternal	Birth weight, 2 week and	·
South Africa assessed at 2 weeks and 5 years (n = 158) use, methamphetamine use, gestation, infant sex, age at circumference and neurobehavioural outcomes.		_			5-year length/height,	measures had separate and
and 5 years (n = 158) gestation, infant sex, age at circumference and neurobehavioural outcomes.	South Africa	assessed at 2 weeks	_	use, methamphetamine use,	weight and head	overlapping associations with growth
Physical size assessment		and 5 years (<i>n</i> = 158)		gestation, infant sex, age at	circumference	and neurobehavioural outcomes.
	Physical size			assessment		

_					
Head Circumference Functional neuro					
Chiodo et al 2009		Continuous measure of average ounces of alcohol		WPPSI, attention, VMI, Fine motor (Pegboard),	Following adjustment many WPPSI subtests, Digit span, Pegboard, Finger
U.S		, , ,	SES, the HOME total score, mother's age at initial prenatal screen, caregiver	Working memory (digit span), Personal	Tapping, VMI, Divided attention, Academic and Communication skills
Functional Neuro	,	PAE); Range from 0g/w (no PAE – 660.8g/w (very heavy PAE).	, ,	Behaviour Checklist	were associated with PAE.
Chiodo et al 2010		Continuous measure of average ounces of alcohol	Covariates varied based on the outcome being assessed: prenatal	Continuous performance test; ADHD Score – sum	Pregnancy drinking per drinking day was better predictor than the average
U.S	with children assessed at 7 years (n	per day during pregnancy	cocaine, 7-year-old blood lead levels, caregiver education, HOME score,	of T scores for different measures) and Teacher	across pregnancy. Following adjustment CPT errors of omission, d
Functional Neuro	= 462)		PPVT, child gender, caregiver marital status, prenatal marijuana, 7-year caregiver marijuana, prenatal nicotine, child age, SES.	Report Form (TRF).	prime change score were significantly associated with PAE.
Coles et al 2019	with children	(moderate PAE) = 44.30g/w;	status, gestational age, SES, child's sex,	•	Following adjustment PAE was associated with MDI and PDI. PAE had
Ukraine		Alcohol-exposed - pre-term (moderate PAE) = 49.98g/w	study site, number of cigarettes smoked, parity.	(MDI) and Psychomotor Development Index (PDI)	both a direct and indirect effect on MDI and PDI. Smoking was not
Functional Neuro					associated Gestational age was a mediating factor and SES was not. While PAE had a direct effect some of the impact was mediated through preterm birth.
Day et al 2013				Total behaviour, externalising and	After controlling for covariates PAE significantly predicted adult
U.S				internalising behaviour and attention problems.	behaviour. Effects were dose-response and significant at each trimester.
Functional Neuro	•	150.5g/w	maternal hostility, gender, 1 st trimester PAE, 2nd trimester PAE, 3 rd trimester PAE.	·	Duration across pregnancy was a better predictor than drinking during first trimester only. Binge drinking was not a better predictor compared to average daily volume.

Falgreen Eriksen	Birth cohort follow-	1-4 drinks/w (light PAE) =	Parental education, maternal IQ,	Wechsler Primary and	No difference in test performance at 1
et al 2012	up at 5 years (n =		•	Preschool Scales of	or 4 or between 5 to 8 drinks per week
et al 2012	1628)	G	drinking, maternal age, parity,	Intelligence-Revised	at any point in pregnancy. Was a
Denmark	1020)			(WPPSI-R) to determine	significant association for 9 or more
LDPS		120g/w	•	verbal IQ (VIQ),	drinks per week on FSIQ and verbal IQ
LDP3		120g/ W	pre-pregnancy BMI, child's gender and		but not performance IQ.
Functional Neuro				and full-scale IQ (FSIQ)	but not performance iq.
runctional Neuro			status on the day of testing,	scores. Visual and	
			family/home environment, tester.	hearing	
Fan et al 2016	Pregnant women	Diagnosed study (NR).	Maternal education, lead exposure,	Diffusion tensor imaging	Following adjustment all brain areas
rall et al 2016	with children	Continuous measure of	maternal smoking, maternal age.	(DTI) to determine	still significantly associated with PAE.
South Africa		average ounces of alcohol	-	fractional anisotropy (FA)	,
South Africa	1	_	omitting 3 children whose mothers	and higher mean	
Cape Town	- J4)	per day during pregnancy	used marijuana and one who used	diffusivity (MD)	
Longitudinal			cocaine.	diffusivity (IVID)	
Cohort			cocame.		
Conort					
Structural Neuro					
MRI					
Foroud et al 2012	Pregnant women	Diagnosed study (IOM	Covariates varied based on outcome	Ear length, lower facial	All measures, except palpebral fissure
	with children	, ,		depth, minimal frontal,	width, were negatively correlated with
South Africa			smoking.	and palpebral fissure.	the amount of alcohol consumed by
		alcohol per day during		' '	the mother both around the time of
Cape Town	l' '	pregnancy			conception and across pregnancy.
Longitudinal		i g ,			
Cohort					
Dysmorphology					
Forrest et al 1991	Pregnant women	1-49g/w (moderate PAE) =	Maternal cigarette consumption,	Mental development	PAE was not related to any outcome.
Scotland	with children	25g/w; 50-99g/w (moderate	maternal age, social class, child's sex,	index and psychomotor	
	assessed at 18	PAE) = 74.5g/w; ≥100g/w	birth weight, gestational age.	development index.	
Functional Neuro	months (<i>n</i> = 592)	(heavy PAE) = 136.75g/w			
Fraser et al 2012	Pregnant Inuit	Continuous measure of	Covariates varied on the outcome	Visual acuity, Fagan Test	After controlling for confounding
		_		of Infant Intelligence	variables birth weight and visual acuity
Canada	assessed at 6 months			(FTII) novelty preference	was associated with AA per day. Birth
	(n = 180)		before delivery, gestational		

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Functional &			hypertension, maternal SES, infant	and FTII fixation	weight, head circumference and visual
Structural Neuro				duration.	acuity associated with binge exposure.
			smoked during pregnancy, Maternal		
Croops Frahart at	Dragnant waman	Continuous measure of	Raven Matrices. Covariates varied on the outcome	Language (Sequenced	After controlling for confounding
Greene Ernhart et al 1990	with children	average ounces of alcohol	being assessed: sex, race, parental	Inventory of	After controlling for confounding variables no significant relationships
	assessed at 1, 2 &	per day during pregnancy –	education, maternal age, maternal	Communication	found between PAE and language
U.S	3yrs (n = 359)	M = 13.86g/w (light PAE);	drug use, day of first antenatal visit,	Development [SICD],	indices.
0.3	5y15 (11 – 559)	Range – 0g/w to 414.75g/w		Mean Length of	indices.
Functional Neuro		(very heavy PAE)	psychosocial stress, maternal IQ,	Utterance [MLU]).	
i diletional Neuro		(very neavy FAL)	cigarette smoking, maternal parity,	Otterance [WILO]).	
			medical problems.		
Greene Ernhart et	Pregnant women	Continuous measure of		Birth weight, length, and	After covariate adjustment birth
al 1991a	with children	average ounces of alcohol	maternal parity, parental education,	head circumference.	weight was significant, trend for birth
		per day during pregnancy –	maternal age, gestational age at birth	nedd en cannerence.	length and non-significant association
	359)	M = 13.86g/w (light PAE);	(Ballard estimate), date of first		for head circumference.
		G	antenatal visit, duration of gestation at		
Physical Size		(very heavy PAE)	first antenatal visit, cumulative HOME		
Head		, , , ,	scores at ages 1, 2, 3, and 4-10, exact		
Circumference			age at testing, maternal substance use		
			(cigarettes/day, marijuana use),		
			parental size (maternal pre-pregnancy		
			weight, maternal height, maternal		
			head circumference, paternal size)		
Goldschmidt et al	Pregnant women	Continuous measure of	Covariates varied based on outcome	Academic achievement	After adjustment for significant
1996	with children	average ounces of alcohol	being assessed: Current maternal	(WRAT-R) and	covariates teacher ratings of
	assessed at 6.5yrs (n	per day during pregnancy	sociodemographic characteristics	intelligence (Stanford-	performance were related to PAE
U.S	= 522)		(education, marital status,	Binet Intelligence Scale	during 1st and 2nd trimester, WRAT and
			work/school status, Income, race),		PIAT-R were not. 2 nd trimester binge
Maternal Health			current maternal psychosocial		was a significant predictor of WRAT-R
Practices and			characteristics (depression, hostility,		reading subscale, PIAT-R reading
Child			life events, self-esteem, social support,	,	comprehension and teacher ratings.
Development			perception of child), family		1 st and 3 rd trimester binge were not
Project			configuration and environment (Home		associated with any outcomes.
			Screening Questionnaire [HSQ],		
Functional Neuro			number of siblings, age spread of		
			siblings), child characteristics (grade in		

school, gender, IQ, Illnesses), current maternal substance abuse (alcohol, tobacco, marijuana, other illicit drugs),	
prenatal substance uses for each trimester (alcohol, tobacco, marijuana, other illicit drugs)	15.5
Halliday et al Pregnant women Low in T1-abstinent in Covariates varied based on outcome BSID-III, ITSP, BITSEA Positive association with low le	
2017 with children T2&T3 (moderate PAE) = assessed: parity, exercise in T1, was attenuated following adjust assessed at 2 years (n 35.5g/w; Moderate/High in smoking in pregnancy, healthy diet in for environmental factors. Early	
Australia = 554) T1-abstinent in T2&T3 pregnancy, child sex, breastfeeding, and low level PAE were associa	_
AQUA (moderate PAE) = 76.13g/w maternal mental health (depression, with increased risk for sensory	cu
anxiety), folate supplements in T1, dysregulation.	
household income, healthy diet in	
Functional Neuro pregnancy, maternal age, pre-	
pregnancy BMI, folate supplements in T2/T3.	
Hannigan et al Pregnant women Continuous measure of Pregnancy marijuana use, WISC-III and TRF Following adjustment, no signif	cant
2010 with children average ounces of alcohol mother/caregiver education, SES, Birth weight, length, and association for IQ and head	
assessed at 14 years per day during pregnancy – HOME Total Score, number of children head circumference. circumference, was an associate to the house protection of the bound	
U.S (n = 288) M = 5.95-77.35g/w in the home, maternal IQ, 7-year-old with TRF subscales, birth weigh Detroit Cohort (antenatal – retrospective blood lead levels, maternal age at length.	and
report) conception, teen gender, teen age at	
Physical Size testing.	
Functional Neuro	
Head	
Circumference Children between 2- Unable to quantify to Covariates varied based on outcome Child behaviour checklist Following adjustment anxiety	
Ichikawa et al Children between 2- Unable to quantify to Covariates varied based on outcome Child behaviour checklist Following adjustment anxiety being assessed: child's sex, child's age, (CBCL) – total behaviour, subscale, internalising and total	
parent age, parent education level, internalizing and behaviour associated with PAE	
Japan parent working status, family income, externalizing.	
family number, domestic violence,	
J-SHINE prenatal smoking, baseline prenatal	
drinking status among siblings,	
Functional Neuro parent's age. Jacobson et al African American Continuous measure of Covariates varied on outcome being Visual recognition Following control for potential	
Jacobson et al African American Continuous measure of Covariates varied on outcome being Visual recognition Following control for potential pregnant women average ounces of alcohol assessed: maternal age, maternal memory (VRM), Cross-confounding variables PAE associated assessed.	riated
with children per day during pregnancy. education, welfare, number of modal transfer, Bayley	ciacca

U.S Functional Neuro	assessed at 6.5, 12 & 13 months (<i>n</i> = 403)		prenatal visits, maternal parity, sex of infant, maternal PPVT-R, maternal ISS, maternal HOME score, maternal cocaine/marijuana/ opiate/cigarette use during pregnancy, age at visit, examiner.	Scales of Infant Development (BSID).	with fixation duration and elicited play.
Jacobson et al 1994a U.S Physical size	ľ -	Continuous measure of average ounces of alcohol per day during pregnancy.	Covariates varied based on outcome: maternal age, pre-pregnancy weight, parity, number of prenatal visits, child sex, birth weight, birth head circumference, age at assessment, exposure to other substances	& head circumference	Regression analysis controlling for birth size found PAE was associated with a slower rate of growth. Smoking was associated with a faster weight gain. When pregnancy weight gain was added coefficients for PAE remained unchanged. Effects of PAE were seen primarily in infants exposed to at least 57 grams AA/day. Analyses indicated a persistent deficit in physical stature associated with PAE but not smoking.
Jacobson et al 1998 U.S Physical Size Functional Neuro	i. O	Continuous measure of average ounces of alcohol per day during pregnancy	sex and age at assessment, maternal smoking and drug use (days/month), examiner, measures of intellectual	(walking and balance), elicited play (IQ/cognition), cognitive	
Jacobson et al 2004 U.S		Continuous measure of average ounces of alcohol per day during pregnancy	Demographics (SES, marital and welfare status, parity, education, and age of child's primary caregiver, crowded living conditions in child's home, child's gender, Number of	WISC-III	Arithmetic and Digit Span were the only 2 subtests associated with PAE after controlling for confounding variables. Each additional ounce of AA/day was associated with a 2.9

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Functional Neuro			children in the household),other prenatal exposures (maternal cocaine and marijuana use, smoking during pregnancy), child-rearing environment (HOME inventory, caregiver's verbal IQ, depression, psychopathology, perceived life stress for the caregiver and child, Family Environment Scale, Quality of social support, disruption in caregiving [separation from the mother ≥ 4 months]), current use of alcohol, hard drugs and marijuana and		decrease in FSIQ and 5.6-point decrease on FD after adjustment for confounders. Cocaine and tobacco were not associated. Cannabis use was associated with picture completion and backwards digit span.
			smoking by the primary caregiver, postnatal lead exposure, situational variables (examiner, child's age at the laboratory visit).		
Jacobson et al 2017	pregnant women with children	PAE (moderate PAE) = 46.78g/w	Total intracranial volume, maternal education, prenatal exposure to smoking, marijuana, and	Corpus callosum area measured by volumetric structural MRI	Corpus callosum was smaller in alcohol exposed infants compared to controls. Was unrelated to sex,
South Africa Structural Neuro	assessed at birth (<i>n</i> = 43)		methamphetamine.		gestational age, age at scan, smoking, cannabis, or methamphetamine use during pregnancy.
Lees et al 2020 ABCD Study	years)	No PAE = 0g; Light-reducer = 32.48g/w (moderate); Stable-light = 15.4g/w	Birth weight, prematurity, child sex, race, age at assessment, maternal age at birth, maternal depression, other	Wide range of psychological, behavioural and	Covariate-adjusted models found that all exposure groups had greater psychopathology and behavioural
U.S		(light); Heavy-reducer = 74.48g/w (moderate)	substances during pregnancy, parental education used as an indicator of SES.		problems, increased mental disorder diagnoses. When youths were
Functional Neuro					demographically matched results generally remained consistent, expect positive effect of PAE on cognition were no longer found.
Lewis et al 2015	pregnant women		Weschler Intelligence Scale for Children IQ (WISC-IV), total learning.	CVLT-C	Cape Town: After controlling for IQ Total learning, short delay recall and
South Africa & U.S	assessed at 10.3	of average ounces of alcohol per day during			recognition discriminated were significant and immediate and long
Functional Neuro	years (n = 151) African American	pregnancy			delay approached significance. After

	pregnant women with children assessed at 14.4 years (n = 291).				controlling for total learning none of the measures remained significant. Detroit: After controlling for IQ long and recognition remained significant. After controlling for total learning recognition remained significant and long delay approached significance.
New Zealand,	with children assessed at 2 and 5	Occasional-Low (moderate PAE) = 32g/w; Moderate-	Maternal age, maternal education, marital status, family income, maternal body mass index, maternal smoking status at 15 weeks gestation and infant sex.	K-BIT & CBCL	Adjusted regression found that first trimester moderate-high PAE was associated with lower verbal intelligence scores and lower internalising scores on the CBCL.
	Pregnant women with children assessed at 1 year (n = 1,331)	No PAE (0g); Low (moderate = 40g); Moderate (moderate = 50g); Heavy (heavy = 110g)		Bayley Scales of Infant Development-III (BSID- III)	After controlling for confounding variables no association found for low exposure on development.
Noland 2003 U.S Functional Neuro	Rural pregnant women with children assessed at 4 years (<i>n</i> = 316)	Exposed (confirmed- unquantifiable) = NR	Maternal age, current cocaine use, current alcohol use, current marijuana use, gestational marijuana use, gestational tobacco, gestational cocaine, concurrent verbal IQ.	Executive function (tapping inhibition)	Children with PAE had worse inhibition and this effect persisted following control of confounding environmental, other prenatal drugs and verbal intelligence were controlled for.
Robertson et al 2016 South Africa Structural Neuro	Cape coloured pregnant women with children assessed at 10.5-11yrs (n = 78)	Diagnosed study (IOM 2005). Continuous measure of average ounces of alcohol per day during pregnancy	Maternal education, socioeconomic status, and cigarettes/day.	Cortical thickness in occipitotemporal, parietal and occipital regions.	After controlling for confounding variables significant association between PAE and cortical thickness in all areas assessed.
	n = 99 across 3 sites 8-16yrs Los Angeles	FASD vs Control	Site, age, intracranial volume.	Regional brain volumes	After controlling for covariates significant differences between FASD

U.S	10-14yrs San Diego 13-15yrs Cape Town				and control in total grey matter left and right hemispheres, putamen, pallidum.
CIFASD					panidum.
Structural Neuro					
		Low (moderate PAE) = 29.4g/w; Moderate/Heavy (moderate PAE) = 98.84g/w	, , , , , ,	CBCL (parent questionnaire - assessed externalising behaviour,	PAE remained a significant predictor of behaviour after adjusting for covariates.
	(n = 501)	, , , , , , , , , , , , , , , , , , , ,	cigarettes, HOME inventory, maternal education.	aggressive behaviour, delinquent behaviour, internalizing behaviour, withdrawn behaviour, attention problems, total behaviour score)	
1980		Continuous measure of average ounces of alcohol per day during pregnancy	gestational age, maternal parity, maternal education.	Bayley Scales of Infant Mental (Mental Development Index; MDI) and Motor	Following adjustment significant association between PAE and MDI and PDI.
Functional Neuro				Development (Psycho Motor Development Index; PSI).	
1984		Continuous measure of average ounces of alcohol per day during pregnancy	Maternal caffeine intake, maternal nutrition, maternal education, birth order, rates of errors commission.	Vigilance task	After control for covariates PAE associated with attention challenges (increased errors of omission and
U.S Functional Neuro	452)				commission) and longer reaction times.
		Heavy drinkers (very heavy PAE) = 329.28g/w	Age, sex, maternal cigarette smoking, maternal age at delivery.	White matter	After controlling for covariates PAE was associated with lower axial
U.S Structural Neuro					diffusivity in all networks.
Verkerk et al 1993	Pregnant women with children assessed at birth (n = 3447)	Abstainer = 0g/week; 1- 50g/week = 25.5g/week (moderate); 51-120g/week = 85.5g/week (moderate);	Maternal smoking, paternal smoking, education, employment, maternal age, marital status.	Birth weight	No significant association with birth weight.

Physical Size		>120g/week =		1	1
ir Hysicai Size		o .			
		171.75g/week (heavy)			
Virji et al 1991	Pregnant women	Light (light PAE) = 8.5g/w;	Maternal age, maternal education,	Birth weight	Significant differences between heavy
	with children	Moderate = (heavy PAE) =	gestational age, parity, weight gain,		exposure and no exposure remained
U.S	assessed at birth (n =	119g/w; Heavy (very heavy	smoking		after controlling for confounding
	5,400)	PAE) = 391g/w			variables.
Physical size					
Walthall et al	Children assessed at	Diagnosed study (4-digit	Child ethnicity, child age, child full	National Institute for	After controlling for covariates PAE
2008	6-12yrs (n = 130)	code). Continuous measure	scale IQ, socialization standard score,	Mental Health	was associated with anxiety
		of average ounces of	caregiver marital status, education,	computerized Diagnostic	(separation and GAD), ADHD, ODD,
U.S		alcohol per day during	home placement.	Interview Schedule for	Conduct, MDD, mania, hypomania,
		pregnancy	'	Children (NIMH C-DISC-	
Functional Neuro				IV)	
Willford et al	Pregnant women	Continuous measure of	Maternal intellectual ability, birth	Stanford-Binet	After controlling for covariates there
2006	with offspring	average ounces of alcohol	weight, child injuries/illnesses, current	Intelligence Scale	was a significant association between
	assessed at 10yrs (n =	per day during pregnancy	maternal depression, current maternal	(IQ/cognitive ability)	PAE and IQ for African American
U.S	636)		alcohol use, child depression, tobacco		children but not for Caucasian
			use during relevant trimester, current		children.
Functional Neuro			maternal substance use (cocaine,		
			marijuana), home environment, life		
			events, parity.		