

Effects of dose and timing of prenatal alcohol exposure



Take Home Messages

- Heavy and binge alcohol exposure during pregnancy can be associated lower scores on children's tests of development
- Light or moderate exposure does not reliably predict negative outcomes
- Timing and dose of prenatal alcohol exposure are uncertain benchmarks for allocating child development services

Overview

Background

Infant and Child Development Services (ICDS) specialises in assessment and referral services for families of children (0-5 years old) at risk of developmental delays and impairments. ICDS is dedicated to providing family-centered, research-based, and cost effective services. The development of evidence-based service pathways is a priority for ICDS's individualised and cost-effective support services.

Knowledge Impact Strategies Consulting Ltd creates systematic scoping reviews of research evidence for social service organizations. Systematic scoping reviews gather and summarise findings using scientific methods that are transparent, exhaustive, and dispassionate. Decisions regarding the focus and scope of a systematic review are made in collaboration with clients. The scientific method of systematic reviewing permits the client to be confident that the information provided is trustworthy and complete. Knowledge Impact Strategies created this systematic scoping review for ICDS.

Purpose of the research review

Prenatal alcohol exposure is said to cause long-term physical, cognitive, social and emotional impairments in early childhood. ICDS embarked on the development of a service pathway for children exposed prenatally to alcohol. The ICDS Prenatal Alcohol Exposure Pathways team wanted to know the results of recent scholarly research on the effects of timing and dose of alcohol exposure during pregnancy. ICDS's primary research interest concerns children from 0-5 years of age. However they also had interest in research outcomes for children between 6 and 12 years where prenatal alcohol exposure could have latent effects.

Knowing whether there is a safe level of alcohol consumption and how the timing of prenatal alcohol exposure relates to risk allows ICDS to make judicious allocations of resources for assessment, treatment, and social support.

Research review question

Does the dose and timing of prenatal alcohol exposure affect children's development?

Issues to keep in mind

It is difficult to unequivocally isolate prenatal alcohol exposure as the cause of developmental delays or disorders in childhood. Some of the reasons for this difficulty are as follows:

Measures of alcohol consumption

All articles in this review that were empirical studies analysed mothers' self-reports of their alcohol consumption during pregnancy. Bear in mind that these reports may reflect personal and cultural biases. For example, in countries where there is a higher degree of stigma against drinking during pregnancy, mothers may be less likely to report or may underreport incidence of drinking compared with mothers in countries where there is less stigma.

SES

Past studies found that amount of alcohol consumption may be related to SES with higher SES related to low-moderate drinking. However, lower SES is thought to be related to lower or to higher consumption. Studies that find an association between alcohol consumption during pregnancy and child outcomes may in fact be identifying an association between SES and child outcomes. Even when studies statistically control for SES, there may be unidentified correlative factors related to SES that could explain hypothesised associations between prenatal alcohol exposure and child outcomes.

Differences in alcohol metabolism

There are individual differences in the rate of alcohol metabolism. This means that the same quantity of alcohol consumption can result in different concentrations of alcohol in the bloodstream for any two people. Individual differences in the metabolism of alcohol can be due

to genetic or even to lifestyle factors. Therefore, due to differences in metabolism, the association between the amount of alcohol intake and the effect on children can be significantly clouded. In other words, children's development might not be associated with whether alcohol was consumed prenatally but with who was consuming it.

Epigenetics

It is possible that alcohol consumption has only an indirect impact on children through epigenetics. Epigenetics refers to changes in gene expression. These changes can be caused by environmental factors, including alcohol consumption. Epigenetic changes in genetic material (genomic imprinting) can occur prior to conception, and these changes may affect children conceived some time later. This means that alcohol consumption before pregnancy by either parent could lead to adverse outcomes for future children, whether pregnant mothers do or do not consume alcohol during pregnancy.

Alcohol consumption beyond early pregnancy

It is difficult to assess the effects on children's development of timing of alcohol consumption, that is, in middle or late-pregnancy versus early pregnancy. It is probably uncommon to find mothers who only drank alcohol during middle or late pregnancy. Moreover, information about alcohol consumption during pregnancy is typically gathered only at the first prenatal health assessment. For this reason, research on the effect of timing of alcohol consumption on children's development is largely uninterpretable.

Latent effects

Many studies find no evidence that prenatal alcohol consumption had negative effects on children's development. It is possible however that negative effects might not appear until later in childhood when the children are no longer being assessed. On the other hand, it is methodologically difficult if not impossible to separate possible latent effects of prenatal alcohol from other causes, physical, psychological, social, or cultural. Some commentaries on this problem are cited in this review (e.g., Parker & Brennan 2012; Jacobson & Jacobson, 2013).

These issues significantly caution against simple interpretations of research findings on the relationship between prenatal alcohol consumption and children's development.

Review Methods

A literature search was conducted at the University of Waterloo using the Scopus research database. Scopus is said to be the largest library database, compiling and indexing articles from over 20,000 journals with as many as 50 million articles.

Prior to final selection of keywords and implementation of a database search, ICDS confirmed that the keyword search strategy returned articles that pinpointed their research interests. Confirmation was achieved through ICDS's review of and feedback on two "exemplar" articles that resulted from what the reviewer believed to be the best search strategy for the review

question. With the keyword strategy confirmed, the database search for articles was conducted on September 6, 2014.

The search was restricted to recent articles published in English between 2011 and 2014. The Scopus keyword search statement was:

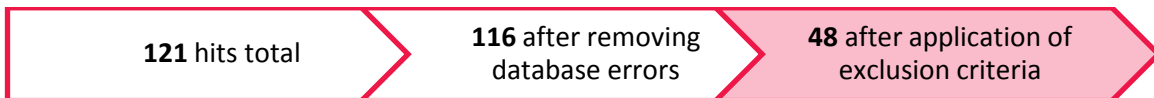
TITLE-ABS-KEY(prenatal OR pregnan*) AND TITLE-ABS-KEY(alcohol) AND TITLE-ABS-KEY(timing OR trimester OR pattern OR early OR late) AND TITLE-ABS-KEY(dose OR binge OR intensity OR amount OR light OR moderate OR heavy) AND TITLE-ABS-KEY(malform* OR defect OR cogniti* OR behavior* OR motor OR intell* OR attention OR language) AND NOT TITLE-ABS-KEY(animal) AND NOT TITLE-ABS-KEY("rats") AND PUBYEAR > 2011

Additionally, the delimiters were set in the software for language (English only) and publication dates (2011 to present).

The search returned 121 articles. Database searching is not an exact science. Despite its restrictions, the search returned 4 articles not published in English and 1 duplicate article. To ensure the relevance of 116 remaining articles, each article was scrutinized to determine if it met any of the following exclusion criteria.

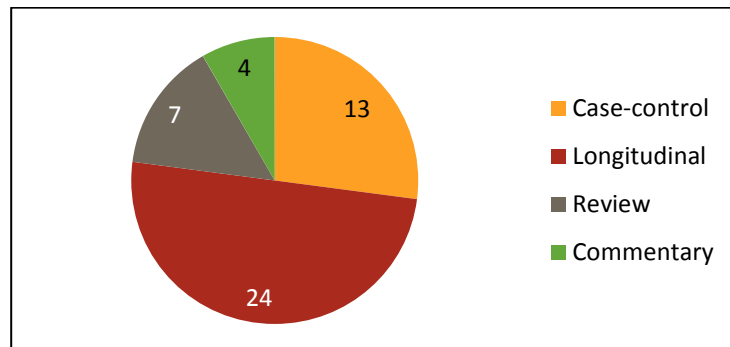
- No mention of prenatal alcohol or drug exposure
- No mention of human children's development
- All children studied were 13 years of age or older
- The outcomes were not studied with respect to prenatal alcohol exposure

As a result of meeting the above criteria, 68 articles had to be excluded.



Characteristics of the Articles

Research strategies



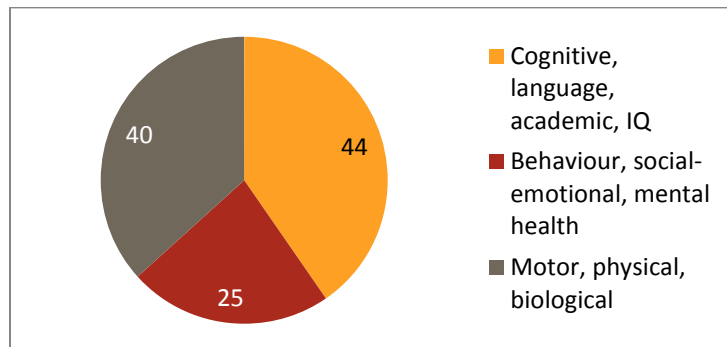
Half of the 48 articles were reports of studies that followed a sample of children longitudinally. As a group, the children varied in time and dose of prenatal alcohol exposure. Approximately one-quarter of the studies were reports of case-control comparisons. Four reports were commentaries about prenatal alcohol exposure and contained no original data or observations of children.

There were seven reviews of the literature. Two were systematic reviews with meta-analyses, and the remaining were brief overviews. One systematic review studied the association between amount of alcohol consumption during pregnancy and psychological and behavioural outcomes, while the other review studied only the association between amount and timing of alcohol consumption and children’s orofacial clefts.

The majority of studies were conducted in the United States, Denmark, and the United Kingdom. A few studies were conducted in Europe, Australia, and Africa.

Outcome measures

The effects of prenatal alcohol were typically assessed in the domains of physical, cognitive, and/or behavioural development. Many articles assessed more than one domain. The figures below reflect the number of tests of domains across articles.



Specification of timing and dose variables

Forty three of the 48 articles were concerned with the amount of alcohol that was reported to be consumed by participants in the study. Twenty-six of the 48 articles studied factors relating to the time during pregnancy at which alcohol was consumed.

	# of studies
Dose specified	43
Timing specified	26

Highlights of Research Results

Amount of alcohol consumption

The terms used to quantify the amount of alcohol consumption varied amongst studies, but in general expressed the concepts of low, moderate, heavy, and binge. The amounts that defined the concepts across studies were typically:

- Low: up to 2 drinks per week
- Moderate: 3 to 7 drinks per week
- Heavy: More than 7 drinks per week
- Binge: more than 5 drinks in one occasion

Most studies compared some level of prenatal alcohol exposure with abstinence during pregnancy. One study might compare low, moderate, and heavy drinking while another study might compare heavy drinking with binge drinking. “Number of tests” refers to the number of times, across all studies, the children’s development was assessed with respect to a particular dosage.

	Number of tests	Negative effect	No effect	Positive effect
Low	41	8 (20%)	28 (68%)	5 (12%)
Moderate	35	8 (23%)	24 (69%)	3 (9%)
Heavy	51	30 (59%)	19 (37%)	2 (4%)
Binge	36	19 (53%)	16 (44%)	1 (3%)

Summary: Research on low and moderate prenatal alcohol exposure most often found no negative effects on children’s development. Research on heavy and binge exposure reported more negative effects than null effects.

Threshold amount of drinking

Of the studies 48 studies that compared more than one dose, four found a dose-response relationship across levels of consumption (Meintjes et al., 2014; Ortega-Garcia et al., 2012; Roussotte et al., 2012; Sawada-Feldman et al., 2012). Higher reported prenatal alcohol consumption was correlated with lower children’s development scores.

Timing of alcohol consumption

The terms used to define the timing of alcohol consumption varied across studies but were generally reflected as:

- Early: first trimester
- Middle: second trimester
- Late: third trimester

The effects of alcohol exposure *early* in pregnancy have been studied most frequently. Of the 63 tests that specified the timing of prenatal alcohol consumption, 41 were related to early exposure. Tests of effects on children’s development of early prenatal exposure have mixed results. Forty-four percent found negative effects but another 44% found no effects. Similar ambivalent results were found for middle and late prenatal exposure.

	Number of tests	Negative effect	No effect	Positive effect
Early	41	18 (44%)	18 (44%)	5 (12%)
Middle	10	4 (40%)	4 (40%)	2 (20%)
Late	12	4 (33%)	6 (50%)	2 (17%)
Unspecified	35	22 (63%)	11 (31%)	2 (6%)

Summary: At any stage of pregnancy, the likelihood of results showing negative impact on children’s development was no greater than the likelihood of results showing no impact.

Type of outcome measured and the effects of prenatal alcohol consumption

Note: Some articles reported more than one test within the same outcome category (e.g., memory and attention tests are both assessments of cognition), or reported test results in more than one category. Therefore the number of tests does not equal the number of articles that were reviewed (48).

	Number of tests	Negative effect	No effect	Positive effect
Cognitive	15	10 (67%)	5 (33%)	0 (0%)
Behaviour	14	7 (50%)	7 (50%)	0 (0%)
Motor	3	1 (33%)	2 (67%)	0 (0%)
Language	3	2 (67%)	1 (33%)	0 (0%)
Social-emotional	7	3 (43%)	4 (57%)	0 (0%)
Physical	16	10 (63%)	4 (25%)	2 (13%)
Biological	16	8 (50%)	5 (31%)	3 (19%)
Academic	11	5 (45%)	4 (36%)	2 (18%)
Mental health	1	1 (100%)	0 (0%)	0 (0%)
IQ	20	12 (60%)	7 (35%)	1 (5%)

Summary: Amongst the tests of cognitive, behavioural, social-emotional, physical, biological, academic, and IQ, some domains showed some disadvantages for children whose mothers reported prenatal alcohol consumption. Few articles reported tests of children’s motor abilities, language, or mental health.

Conclusions

A sample of 48 recent research studies were reviewed in an attempt to answer the question: *Does the dose and timing of prenatal alcohol exposure affect children's development?* Heavy and binge drinking were more frequently but not always associated with negative consequences on children. When studies tested effects of alcohol consumption in early pregnancy they sometimes found negative effects but not always.

Our conclusions support those of a similar systematic review that was identified by our search strategy: Flak et al., 2014. The authors point to the importance of assessing the methodological quality of studies and socio-economic status before drawing conclusions about the effects of prenatal alcohol exposure.

There is little doubt that once identified as having the physical, behavioural, and cognitive patterns of development and behaviour associated with what is called Fetal Alcohol Spectrum Disorder children need special social services. The question remains as to whether the need for these services can be meaningfully *predicted* in advance by maternal reports of prenatal alcohol consumption.

Spreadsheet Legend

Method

- Case-control: two or more groups that differ on known outcomes (e.g., children's development) are assessed after the fact on current or past characteristics
- Longitudinal: participants are followed and data are collected from at least two time points (may or may not be case-control groups)
- Reviews: report of aggregated findings of one or more existing studies
- Commentaries: published viewpoints on a journal article

Outcomes

- Cognitive: intellectual ability and executive functioning (including attention, memory, sensory processing, problem solving and decision making) not including standardised tests of general intelligence
- Behavioural: internalizing and externalizing behaviour towards self and others, positive and negative behaviours
- Motor: fine and gross motor muscle movements, visual-motor coordination
- Language: articulation, comprehension and overall development
- Social-emotional: interactions with family and peers, ability to form attachments, general affect
- Physical: external appearances and characteristics, including facial features
- Biological: medical conditions (brain, birth complications, mortality)
- Academic: academic achievement in school, school test scores
- Mental health: Mental disorders classified in the DSM, such as attention-deficit hyperactivity disorder, conduct disorder, and oppositional defiant disorder

- IQ: general Intelligence on a standardised test (e.g., Wechsler Preschool and Primary Scale of Intelligence, British Ability Scales).

Abbreviations

- ADHD – Attention Deficit Hyperactivity Disorder
- EF – Executive Functioning
- FASD – Foetal Alcohol Spectrum Disorder
- PAE – Prenatal Alcohol Exposure
- SDQ – Strengths and Difficulties Questionnaire

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes							
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic
Alati, R., Davey Smith, G., Lewis, S. J., Sayal, K., Draper, E. S., Golding, J., et al. (2013). Effect of prenatal alcohol exposure on childhood academic outcomes: Contrasting maternal and paternal associations in the ALSPAC study. <i>Plos One</i> , 8(10)	<ul style="list-style-type: none"> Association between low-moderate everyday consumption of alcohol and binge drinking during first trimester, and school test scores (English, Math, Science) at age 11 	<ul style="list-style-type: none"> Binge drinking associated with poorer test scores Low-moderate everyday alcohol consumption was not associated with test scores 	UK	11 yrs		•			•	•							•	
Alvik, A., Aalen, O. O., & Lindemann, R. (2013). Early fetal binge alcohol exposure predicts high behavioral symptom scores in 5.5-year-old children. <i>Alcoholism: Clinical and Experimental Research</i> , 37(11), 1954-1962.	<ul style="list-style-type: none"> Association between binge drinking during 0-6 weeks of pregnancy and child's behavioural and social outcomes as measured on the SDQ at age 5.5 	<ul style="list-style-type: none"> Exposure to early pregnancy binge drinking predicted higher SDQ Total, Emotional problems, Conduct problems, and Hyperactivity/inattention scores Exposure to binge drinking less than once a week predicted SDQ Total and Hyperactivity/inattention scores in the Abnormal and Borderline range Exposure to binge drinking more than once a week predicted SDQ Total, Emotional, and Conduct problems scores in the Abnormal and Borderline range, and Total, Conduct problems and Hyperactivity/inattention scores in the Abnormal range 	Norway	5.5 yrs		•			•	•		•						
Bell, J. C., Raynes-Greenow, C., Turner, R. M., Bower, C., Nassar, N., & O'Leary, C. M. (2014). Maternal alcohol consumption during pregnancy and the risk of orofacial clefts in infants: A systematic review and meta-analysis. <i>Paediatric and Perinatal Epidemiology</i> , 28(4), 322-332.	<ul style="list-style-type: none"> Systematic review and meta-analysis of the association between alcohol consumption during pregnancy and orofacial clefts (cleft lip and palate). Articles studied alcohol consumption in the first trimester of pregnancy, throughout pregnancy, binge drinking and more regular drinking patterns 	<ul style="list-style-type: none"> No association found between maternal alcohol consumption and orofacial clefts Authors warn that even though no association was found, a true association may have been obscured by other factors 	Multiple	Multiple			•		•	•				•				
Benedum, C. M., Yazdy, M. M., Mitchell, A. A., & Werler, M. M. (2013). Risk of spina bifida and maternal cigarette, alcohol, and coffee use during the first month of pregnancy. <i>International Journal of Environmental Research and Public Health</i> , 10(8), 3263-3281.	<ul style="list-style-type: none"> Association between alcohol consumption during first month of pregnancy and spina bifida in the child 	<ul style="list-style-type: none"> Alcohol exposure at any frequency or dose in early pregnancy not related to increased spina bifida risk in child Modest evidence of increased spina bifida risk for mothers who were heavy smokers as well as heavy drinkers 	US, Canada	Birth	•				•	•							•	
Caspers Conway, K. M., Romitti, P. A., Holmes, L., Olney, R. S., & Richardson, S. D. (2014). Maternal periconceptional alcohol consumption and congenital limb deficiencies. <i>Birth Defects Research Part A - Clinical and Molecular Teratology</i> , 100(11), 863-876.	<ul style="list-style-type: none"> Association between specific congenital limb deficiencies and alcohol consumption during early pregnancy 	<ul style="list-style-type: none"> Maternal alcohol consumption related to lower chance of having a limb deficiency The strength of association differed depending on type of alcoholic beverage consumed and type of limb deficiency examined 	US	Birth	•				•	•				•				

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
Chen, J.-H. (2012). Maternal alcohol use during pregnancy, birth weight and early behavioral outcomes. <i>Alcohol and Alcoholism</i> , 47(6), 649-656.	<ul style="list-style-type: none"> Relationship between alcohol consumption during pregnancy (light-moderate and heavy drinking), and behaviour of children under 23 mos (positive mood, fearfulness, and difficulty) and birth weight 	<ul style="list-style-type: none"> Any level of drinking during pregnancy related to more difficult behaviour (fussy, difficult to calm). Heavy drinking related to worse scores, evidence of dose-response relationship Heavy drinking (but not mild-moderate drinking) is a risk factor for low birth weight No relationship between PAE and other behaviour outcomes measured after adjusting for confounds Infant behavioural difficulty is more susceptible to alcohol exposure than physical growth 	US	23 mos - 4 yrs		•														
Chiodo, L. M., Bailey, B. A., Sokol, R. J., Janisse, J., Delaney-Black, V., & Hannigan, J. H. (2012). Recognized spontaneous abortion in mid-pregnancy and patterns of pregnancy alcohol use. <i>Alcohol</i> , 46(3), 261-267.	<ul style="list-style-type: none"> Relationship between spontaneous abortion (miscarriage) before completing 20 wks gestation and pattern of alcohol use during pregnancy and in the periconceptual period (e.g., frequency of drinking, amount of alcohol consumed per drinking day, amount of alcohol consumed on average) 	<ul style="list-style-type: none"> Higher frequency and average dose of alcohol consumption during pregnancy and around conception associated with higher risk of spontaneous abortion Frequency-dependent relationship between drinking and spontaneous abortion Bingeing and average amount of alcohol consumed per drinking day during pregnancy or around conception not related to spontaneous abortion 	US	Prenatal		•		•	•											

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes													
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ				
Colin Carter, R., Jacobson, J. L., Molteno, C. D., Jiang, H., Meintjes, E. M., Jacobson, S. W., et al. (2012). Effects of heavy prenatal alcohol exposure and iron deficiency anemia on child growth and body composition through age 9 years. <i>Alcoholism: Clinical and Experimental Research</i> , 36(11), 1973-1982.	<ul style="list-style-type: none"> Association between heavy alcohol consumption during pregnancy, and child growth (weight, height, head circumference) up to 9 yrs Whether the effects of PAE on child growth are constant or change over time Whether effects of PAE are larger for children who were iron deficient during infancy Association between PAE and body composition at 9 yrs 	<ul style="list-style-type: none"> At birth, children of heavy drinkers had lower weight (and more likely to be classified to be at a low birth weight), height and head circumference compared to controls with minimal PAE The same was found when the children were 5 years old, but these effects were much smaller than those found at birth after controlling for birth weight and gestational age. This means that the effect of PAE is largely determined at birth At birth and at 5 yrs, children of heavy drinkers more likely to have iron deficiency anaemia, compared to controls with minimal PAE At 5 and 9 yrs, similar weight-for-length and BMI for heavily exposed and minimally exposed children. At 9 yrs, similar body composition between groups. Children of heavy drinkers were delayed in postnatal weight and height gain but the rate of gain catches up to controls by age 5 Growth of head circumference similar between heavily and minimally exposed children for all ages except from age 5 to 9 (less head growth for heavily exposed children) Iron deficiency anaemia worsens the effect of PAE on weight and height for age Low food security did not interact with the effect of PAE on child growth 	South Africa	0 - 9 yrs		•									•	•								
Comasco, E., Hallberg, G., Helander, A., Orelund, L., & Sundelin-Wahlsten, V. (2012). Alcohol consumption among pregnant women in a Swedish sample and its effects on the newborn outcomes. <i>Alcoholism: Clinical and Experimental Research</i> , 36(10), 1779-1786.	<ul style="list-style-type: none"> Association between alcohol consumption and birth outcomes (birth weight, gestational age, method of labour, route of delivery, sex and length of newborn, Apgar scores) 	<ul style="list-style-type: none"> Birth weight of newborn females higher in women who drank during pregnancy compared to those who did not. No other significant associations found. 	Sweden	Birth		•										•	•							

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
Crocker, N., Riley, E. P., & Mattson, S. N. (2014). Visual-spatial abilities relate to mathematics achievement in children with heavy prenatal alcohol exposure. <i>Neuropsychology</i> , 29(1), 108-116.	<ul style="list-style-type: none"> Relationship between math ability and the general cognitive abilities of attention, working memory, visual memory and spatial processing in children with heavy PAE 	<ul style="list-style-type: none"> Exposed group had poorer outcomes than non-exposed group on almost all of the measures of general cognitive ability, meaning that differences in general cognitive ability play a role in math deficits in the exposed group Spatial processing (including spatial attention and memory) was the strongest predictor of mathematic ability for both exposed and non-exposed groups Global IQ also predicts math ability (note that the IQ test used includes measures of spatial processing) Differences in math ability between exposed and non-exposed group is not completely explained by differences in the general cognitive abilities measured, which suggests that skills specific to math are also impaired in the exposed group 	US	7 - 12 yrs						•									•	
Falgreen Eriksen, H.-L., Mortensen, E. L., Kilburn, T., Underbjerg, M., Bertrand, J., Støvring, H., et al. (2012). The effects of low to moderate prenatal alcohol exposure in early pregnancy on IQ in 5-year-old children. <i>BJOG: An International Journal of Obstetrics and Gynaecology</i> , 119(10), 1191-1200.	<ul style="list-style-type: none"> Association between low-moderate alcohol consumption during pregnancy and child IQ test scores at 5 yrs 	<ul style="list-style-type: none"> No difference in IQ test scores between women who drank low-moderate levels of alcohol and those who did not drink Higher risk of having low full-scale IQ and verbal IQ scores for children exposed to high levels of alcohol, but performance IQ scores were not impaired 	Denmark	5 yrs															•	
Flak, A. L., Su, S., Bertrand, J., Denny, C. H., Kesmodel, U. S., & Cogswell, M. E. (2014). The association of mild, moderate, and binge prenatal alcohol exposure and child neuropsychological outcomes: A meta-analysis. <i>Alcoholism: Clinical and Experimental Research</i> , 38(1), 214-226.	<ul style="list-style-type: none"> Systematic review and meta-analysis of the association between amount of alcohol consumption during pregnancy and child's neuropsychological outcomes (academic, attention, behavior, cognition, language, memory, visual and motor, and executive function) 	<ul style="list-style-type: none"> When studies of any quality were included binge drinking associated with poorer child cognition and IQ. No other associations found when all studies included. When only high quality studies included, moderate drinking associated with poorer behaviour outcomes When only high quality studies included, mild-moderate drinking associated with slightly better cognitive outcomes, but the effect was no longer significant when only studies that controlled for SES were included 	Multiple	6 mos - 15 yrs							•								•	

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes										
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ	
Fryer, S. L., Mattson, S. N., Jernigan, T. L., Archibald, S. L., Jones, K. L., & Riley, E. P. (2012). Caudate volume predicts neurocognitive performance in youth with heavy prenatal alcohol exposure. <i>Alcoholism: Clinical and Experimental Research</i> , 36(11), 1932-1941.	<ul style="list-style-type: none"> • Association between regional brain volume (frontal, parietal, and temporal lobes, cerebellum, caudate nucleus and hippocampus), and cognitive and language performance (tasks measured cognitive control, verbal learning and verbal recall) in older children and youth with heavy PAE 	<ul style="list-style-type: none"> • Caudate nucleus volume was the strongest predictor of cognitive control, verbal learning and recall • Frontal lobe volume associated with verbal learning • Cerebellar volume associated with cognitive control • The relationships between regional brain volume and developmental outcomes are specific (the ability for brain volume to predict outcomes depends on the brain region studied and the outcome of interest). • No other significant association between regional brain volume and measured outcomes or potential confounders 	US	9 - 21 yrs					•	•											
Glass, L., Ware, A. L., Crocker, N., Deweese, B. N., Coles, C. D., Kable, J. A., . . . Collaborative Initiative on Fetal Alcohol Spectrum Disorders. (2013). Neuropsychological deficits associated with heavy prenatal alcohol exposure are not exacerbated by ADHD. <i>Neuropsychology</i> , 27(6), 713-724.	<ul style="list-style-type: none"> • Compared cognitive functioning and IQ of children with and without PAE and ADHD • Four groups of children were studied: alcohol-exposed children with ADHD, alcohol-exposed children without ADHD, non-exposed children with ADHD, non-exposed children without ADHD 	<ul style="list-style-type: none"> • Alcohol-exposed children had more deficits in cognition and IQ, regardless of whether they had ADHD or not • ADHD diagnosis in alcohol-exposed children did not result in more severe deficits in functioning compared to alcohol-exposed children without ADHD 	US	8 - 16 yrs	•						•								•	•	

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
Jacobson, J. L., & Jacobson, S. W. (2013). Low-level alcohol consumption in early pregnancy may not affect child intelligence, attention or executive function at 5 years of age. Evidence-Based Mental Health, 16(1), 4.	<ul style="list-style-type: none"> • Commentary on a study that found no association between low-moderate alcohol consumption or binge drinking during early-mid pregnancy, and attention, EF and IQ at 5 yrs 	<ul style="list-style-type: none"> • There is consistent evidence that moderate drinking results in poorer growth and cognition • Effect of PAE on cognition may not appear until children reach school age (6 years old in Denmark where the original study was conducted) • The study did not account for possible moderators, especially maternal age and maternal alcohol abuse, which increase the risk of negative outcomes resulting from moderate PAE in the child 	NA	5 yrs				•	•	•	•								•	
Jacobson, S. W., & Jacobson, J. L. (2014). The risk of low-to-moderate prenatal alcohol exposure on child academic underachievement and behaviour may be difficult to measure and should not be underestimated. Evidence-Based Medicine, 19(2), e7.	<ul style="list-style-type: none"> • Commentary on two studies that found no detrimental effect of low-moderate maternal drinking during pregnancy on child academic and EF outcomes 	<ul style="list-style-type: none"> • The null findings are inconsistent with prior longitudinal research showing negative effects of moderate PAE on behaviour, cognition and growth • Limitations in methodology and statistical analyses used may have been the reason no negative effect of low-moderate PAE was found 	NA	5 yrs, 8-9 yrs				•	•	•	•								•	
Kelly, Y. J., Sacker, A., Gray, R., Kelly, J., Wolke, D., Head, J., et al. (2012). Light drinking during pregnancy: Still no increased risk for socioemotional difficulties or cognitive deficits at 5 years of age? Journal of Epidemiology and Community Health, 66(1), 41-48.	<ul style="list-style-type: none"> • Association between light drinking during pregnancy and socio-emotional and behavioural outcomes (measured using the SDQ), and cognitive outcomes at 5 yrs 	<ul style="list-style-type: none"> • Boys of mothers who drank lightly during pregnancy scored better in the naming vocabulary and picture similarities tasks after adjusting for all potential confounders, compared to children of mothers who did not drink • Other associations between light drinking and child outcomes were non-significant after adjusting for potential confounders 	UK	5 yrs		•				•	•			•					•	
Kesmodel, U. S., & Mortensen, E. L. (2013). Light drinking in pregnancy is not associated with poor child mental health and learning outcomes at age 11. Evidence-Based Medicine, 18(6), 231-232.	<ul style="list-style-type: none"> • Commentary on a study that found no association between light drinking during pregnancy and child social-emotional and behavioural outcomes, and academic achievement at 11 yrs 	<ul style="list-style-type: none"> • Original study lacked adjustment for possible confounding variables (e.g., parent intelligence) • Must note however that a strong association was not found between light drinking and outcomes measured 	NA	11 yrs				•	•	•			•						•	
Kesmodel, U. S., Bay, B., Wimberley, T., Eriksen, H.-L. F., & Mortensen, E. L. (2013). Does binge drinking during early pregnancy increase the risk of psychomotor deficits? Alcoholism: Clinical and Experimental Research, 37(7), 1204-1212.	<ul style="list-style-type: none"> • Effect of binge alcohol consumption during pregnancy on child motor function 	<ul style="list-style-type: none"> • Binge drinking at any frequency or timing during pregnancy not related to child motor function 	Denmark	5 yrs		•			•	•										

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
Kesmodel, U. S., Bertrand, J., Støvring, H., Skarpness, B., Denny, C., & Mortensen, E. L. (2012). The effect of different alcohol drinking patterns in early to mid pregnancy on the child's intelligence, attention, and executive function. <i>BJOG: An International Journal of Obstetrics and Gynaecology</i> , 119(10), 1180-1190.	<ul style="list-style-type: none"> Association between amount and pattern of drinking during early-mid pregnancy, and child's IQ, attention and EF test scores at age 5 	<ul style="list-style-type: none"> Average alcohol consumption and binge drinking during early-mid pregnancy were not associated with measured child outcomes 	Denmark	5 yrs		•			•	•	•									•
Kesmodel, U. S., Eriksen, H.-L. F., Underbjerg, M., Kilburn, T. R., Støvring, H., Wimberley, T., et al. (2012). The effect of alcohol binge drinking in early pregnancy on general intelligence in children. <i>BJOG: An International Journal of Obstetrics and Gynaecology</i> , 119(10), 1222-1231.	<ul style="list-style-type: none"> Association between binge drinking during early pregnancy and child's IQ scores at age 5 	<ul style="list-style-type: none"> Overall no association between binge drinking and child IQ. However, binge drinking of any frequency during the first 2 weeks of gestation lowered the risk of child having a low full-scale IQ Boys had higher performance IQ if exposed to binge drinking in early pregnancy 	Denmark	5 yrs		•			•	•										•
Kuehn, D., Aros, S., Cassorla, F., Avaria, M., Unanue, N., Henriquez, C., et al. (2012). A prospective cohort study of the prevalence of growth, facial, and central nervous system abnormalities in children with heavy prenatal alcohol exposure. <i>Alcoholism: Clinical and Experimental Research</i> , 36(10), 1811-1819.	<ul style="list-style-type: none"> Prevalence of growth and facial abnormalities, low IQ, motor deficits, language delay and attention/hyperactivity problems in children with heavy PAE 	<ul style="list-style-type: none"> Heavily exposed children more likely to have an abnormality compared to non-exposed children Heavily exposed children more likely to have growth restriction, facial abnormalities (related to PAE), smaller head circumference, poorer IQ test scores, poorer motor and mental development, be suspected to have language delay and be suspected to have hyperactivity problems. No difference in likelihood of being suspected to have inattention problems. Binge drinking and total number of drinks per week independently predict adverse child outcomes No abnormalities found in 20% of exposed children 	Chile	0 to 8.5 yrs		•			•		•	•		•				•	•	

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes							
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic
Lebel, C., Mattson, S. N., Riley, E. P., Jones, K. L., Adnams, C. M., May, P. A., et al. (2012). A longitudinal study of the long-term consequences of drinking during pregnancy: Heavy in utero alcohol exposure disrupts the normal processes of brain development. <i>Journal of Neuroscience</i> , 32(44), 15243-15251.	<ul style="list-style-type: none"> Association between heavy PAE, and brain maturation and plasticity, facial dysmorphology and IQ scores in children and youth 	<ul style="list-style-type: none"> Exposed group had greater facial dysmorphology and lower IQ scores than control Exposed group demonstrated less brain plasticity, with less change in brain volume (while control group showed greater increases followed by greater decreases) Higher IQ and more normal facial morphology associated with larger changes in brain volume, but the brain regions for which this correlation was found differed between the exposed and control groups For the exposed group, amount of maternal alcohol consumption was associated with changes in regional brain volume 	US, South Africa	5-7 yrs and up		•				•					•	•		•
Mateja, W. A., Nelson, D. B., Kroelinger, C. D., Ruzek, S., & Segal, J. (2012). The association between maternal alcohol use and smoking in early pregnancy and congenital cardiac defects. <i>Journal of Women's Health</i> , 21(1), 26-34.	<ul style="list-style-type: none"> Association between maternal alcohol consumption and smoking in the 3 months before pregnancy (which is used as a proxy measure of alcohol consumption and smoking during early pregnancy), and congenital cardiac defects in the child 	<ul style="list-style-type: none"> More than one episode of binge drinking in the 3 months before pregnancy associated with a higher risk of congenital cardiac defect. A single episode of binge drinking was not found to be a risk factor Binge drinking (1 or more episodes) and smoking concurrently in the 3 months before pregnancy were associated with a higher risk of congenital cardiac defect. Smoking was not independently associated with congenital cardiac defects. 	US	Birth	•			•	•							•		
May, P. A., Blankenship, J., Marais, A.-S., Gossage, J. P., Kalberg, W. O., Joubert, B., et al. (2013). Maternal alcohol consumption producing fetal alcohol spectrum disorders (FASD): Quantity, frequency, and timing of drinking. <i>Drug and Alcohol Dependence</i> , 133(2), 502-512.	<ul style="list-style-type: none"> Relationship between quantity, frequency and timing of drinking during pregnancy, and specific diagnoses on the FASD spectrum, physical, behavioural and cognitive outcomes, IQ (non-verbal and verbal IQ), and working memory in Grade 1 children 	<ul style="list-style-type: none"> Larger amount and more frequent alcohol consumption were related to more severe FASD diagnosis Binge drinking and amount of average drinking related to physical indicators of FASD (facial dysmorphology, head circumference, vermillion border, palpebral fissure length). This pattern emerged when examining alcohol consumption throughout pregnancy as well as looking at each trimester separately. Average drinking in the second or third trimesters not associated with physical outcomes when controlling for first trimester drinking Binge drinking related to behaviour problems and poorer working memory 	South Africa	6 - 7 yrs	•			•	•	•	•				•			•

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
McDonnell-Naughton, M., McGarvey, C., O'Regan, M., & Matthews, T. (2012). Maternal smoking and alcohol consumption during pregnancy as risk factors for sudden infant death. Irish Medical Journal, 105(4), 105-108.	<ul style="list-style-type: none"> Association between alcohol consumption during pregnancy (amount of alcohol consumed per week, how long across the pregnancy drinking occurred) and risk of Sudden Infant Death Syndrome (SIDS) 	<ul style="list-style-type: none"> Alcohol consumption throughout all three trimesters (but not one or two trimesters) associated with increased risks of SIDS No significant association found between amount of alcohol consumed during pregnancy and SIDS 	Ireland	Mean 18 wks																
Meintjes, E. M., Narr, K. L., Van Der Kouwe, A. J. W., Molteno, C. D., Pirnia, T., Gutman, B., et al. (2014). A tensor-based morphometry analysis of regional differences in brain volume in relation to prenatal alcohol exposure. NeuroImage: Clinical, 5, 152-160.	<ul style="list-style-type: none"> Association between alcohol consumption during pregnancy, and child's regional brain volume and IQ 2 groups of children were recruited: children of mothers who were heavy or binge drinkers (exposed group), and children of mothers who did not consume alcohol during pregnancy (non-exposed group) 	<ul style="list-style-type: none"> Dose-response relationship between amount of alcohol consumed and IQ. Exposed group had lower IQ than non-exposed group Dose-response relationship between amount of alcohol consumed during pregnancy and reductions in child's regional brain volume of several midline regions (parts of the thalamus, cerebellum, occipital lobe, and parietal lobe) 	South Africa	9-11 yrs																
Memo, L., Gnoato, E., Caminiti, S., Pichini, S., & Tarani, L. (2013). Fetal alcohol spectrum disorders and fetal alcohol syndrome: The state of the art and new diagnostic tools. Early Human Development, 89(Supp.1), S40-S43.	<ul style="list-style-type: none"> Brief summary of characteristics of alcohol-exposed children 	<ul style="list-style-type: none"> PAE can lead to dysmorphic facial features, neurocognitive deficits, failure to thrive and growth retardation Neuroimaging shows reduced brain volume, regional differences in cortical thickness, white matter degeneration and differences in cerebral blood flow 	NR	NR																
Milne, E., Greenop, K. R., Scott, R. J., De Klerk, N. H., Bower, C., Ashton, L. J., . . . Armstrong, B. K. (2013). Parental alcohol consumption and risk of childhood acute lymphoblastic leukemia and brain tumors. Cancer Causes and Control, 24(2), 391-402.	<ul style="list-style-type: none"> Whether alcohol consumption during pregnancy increases the child's risk of developing acute lymphoblastic leukemia (ALL) or other childhood malignancy and brain tumours (CBT) 	<ul style="list-style-type: none"> Maternal alcohol use during pregnancy did not increase risk of ALL or CBT Evidence that alcohol consumption during pregnancy reduces risk of ALL, less so for CBT Associations stayed the same when taking into account the trimester in which alcohol consumption took place 	Australia	0 - 14 yrs																
Murphy, D. J., Mullally, A., Cleary, B. J., Fahey, T., & Barry, J. (2013). Behavioural change in relation to alcohol exposure in early pregnancy and impact on perinatal outcomes - a prospective cohort study. BMC Pregnancy and Childbirth, 13, 8	<ul style="list-style-type: none"> Whether reducing alcohol consumption early on in pregnancy leads to improved perinatal outcomes (gestational age at birth, birth weight, Apgar scores, admission to neonatal unit, live birth or stillbirth, suspected congenital abnormalities, and neonatal death), compared to children whose mothers were still drinking during early pregnancy 	<ul style="list-style-type: none"> Current heavy alcohol consumption or binge drinking increased risk of intrauterine growth restriction and low Apgar scores Current, light drinkers had similar or better outcomes than non-drinkers Except for increased risk of congenital abnormality, ex-drinkers had similar perinatal outcomes as non-drinkers Highest risk of intrauterine growth restriction for mothers who continued to drink and smoke 	Ireland	Perinatal																

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
Niclasen, J., Andersen, A.-M. N., Strandberg-Larsen, K., & Teasdale, T. W. (2014). Is alcohol binge drinking in early and late pregnancy associated with behavioural and emotional development at age 7 years? <i>European Child and Adolescent Psychiatry</i> , 23(12), 1175-1180.	<ul style="list-style-type: none"> Association between binge drinking during early and late pregnancy, and child's behavioural and social outcomes as measured on the SDQ at age 7 	<ul style="list-style-type: none"> Both early and late binge drinking associated with externalising behaviours (Hyperactivity/inattention and Conduct problems scales). Late binge drinking is more strongly associated than early binge drinking Both early and late binge drinking are not associated with clinical levels of behavioural and social problems in the child No other significant associations between PAE and SDQ scores were found 	Denmark	7 yrs		•			•	•		•								
O'Brien, J. W., Norman, A. L., Fryer, S. L., Tapert, S. F., Paulus, M. P., Jones, K. L., . . . Mattson, S. N. (2013). Effect of predictive cuing on response inhibition in children with heavy prenatal alcohol exposure. <i>Alcoholism: Clinical and Experimental Research</i> , 37(4), 644-654.	<ul style="list-style-type: none"> Performance and brain activation of children and adolescents with heavy PAE on a response inhibition task with a predictive cue 	<ul style="list-style-type: none"> Exposed group had less cognitive resources for response inhibition Exposed group benefited less from the predictive cue, suggesting deficits in nonverbal learning Differences in brain activation between exposed and control group 	US	8 - 18 yrs	•				•					•						
O'Leary, C. M., Taylor, C., Zubrick, S. R., Kurinczuk, J. J., & Bower, C. (2013). Prenatal alcohol exposure and educational achievement in children aged 8-9 years. <i>Pediatrics</i> , 132(2), e468-e475.	<ul style="list-style-type: none"> Association between dose, timing and pattern of PAE and academic outcomes (reading, writing, spelling and numeracy) at 8 and 9 yrs Control group were mothers who were previous drinkers but abstained during pregnancy 	<ul style="list-style-type: none"> Children more likely to not achieve benchmark reading, writing and spelling if heavily exposed to alcohol during first trimester Children more likely to not achieve benchmark spelling and writing if occasionally exposed to binge alcohol throughout pregnancy Children exposed to occasional binge drinking during late pregnancy more likely to be below benchmark for writing More children who were exposed to low-moderate amounts of alcohol passed the benchmark in the four outcome areas compared to children whose mothers stopped drinking during pregnancy 	Australia	8 - 9 yrs		•			•	•						•				

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
Ortega-García, J. A., Gutierrez-Churango, J. E., Sánchez-Saucó, M. F., Martínez-Aroca, M., Delgado-Marín, J. L., Sánchez-Solis, M., et al. (2012). Head circumference at birth and exposure to tobacco, alcohol and illegal drugs during early pregnancy. <i>Child's Nervous System</i> , 28(3), 433-439.	<ul style="list-style-type: none"> • Association between timing and amount of alcohol consumption during pregnancy, and head circumference at birth of healthy infants • Head circumference was studied because it is associated with IQ and is one of the criteria examined when diagnosing FASD 	<ul style="list-style-type: none"> • Mild-moderate alcohol consumption during weeks 8-10 (but not weeks 3-7) of pregnancy predicted smaller head circumference of child at birth • No safe threshold level of alcohol consumption was found 	Spain	Birth		•			•	•						•				
Parker, M. O., & Brennan, C. H. (2012). Low and moderate alcohol consumption during pregnancy: Effects on social behaviour and propensity to develop substance abuse in later life. <i>BJOG: An International Journal of Obstetrics and Gynaecology</i> , 119(13), 1671-1672.	<ul style="list-style-type: none"> • Commentary on an article that found no association between mild-moderate PAE and cognitive outcomes (IQ, EF and sustained attention) at 5 yrs 	<ul style="list-style-type: none"> • The effect of mild-moderate PAE on cognition may only become evident in adolescence. Because PAE has been shown to affect social behaviour in humans, perhaps only later in life when there are more complex interactions between executive functioning and the social environment will deficits in executive functioning become problematic 	NA	5 yrs																•
Pruett, D., Waterman, E. H., & Caughey, A. B. (2013). Fetal alcohol exposure: Consequences, diagnosis, and treatment. <i>Obstetrical and Gynecological Survey</i> , 68(1), 62-69.	<ul style="list-style-type: none"> • Outcomes of prenatal alcohol exposure • Characteristics for diagnosis of FASD • Mechanism of how PAE affects the child, how that relates to the role of dose and timing of consumption on child outcomes, and variable susceptibility 	<ul style="list-style-type: none"> • PAE leads to a range of adverse outcomes from pregnancy outcomes into adulthood • Diagnosis of FAS requires presence of maternal alcohol consumption during pregnancy, characteristic facial dysmorphology, neurodevelopment abnormalities and growth retardation • Neurological effects persist into early adulthood • Dose-response relationship between maternal alcohol consumption and child outcome differs depending on outcome measured. Effect of binge drinking on child outcomes unclear • Difficult to isolate how the timing of maternal alcohol consumption in pregnancy is related to child outcomes. Suggests that drinking during any period could lead to harmful effects on the foetus • Genetic differences in the child's susceptibility to the effects of PAE 	NR	NR																•

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
Radosavljević, T., & Vučević, D. (2013). Binge drinking: Pathophysiological and psychological aspects. In S. B. Harris (Ed.), Binge eating and binge drinking (pp. 201-216). New York: Nova Science Publishers, Inc.	<ul style="list-style-type: none"> • Overview of effects of binge drinking on the developing foetus 	<ul style="list-style-type: none"> • Binge drinking is harmful to the foetus especially during the early stages of pregnancy • Binge drinking can lead to FAS, resulting in one or more of the following deficits in the child: low birth weight and size, mental retardation, birth defects (facial and cardiac defects most common), delayed postnatal growth and behaviour development • Foetus is very quiet in utero, more likely to present in breech position • Risk of harmful effects on child is higher the more a mother drinks per day • Can lead to permanent neurological changes in the foetus brain by interfering with normal processes of brain 	NR	NR			•	•	•				•	•				•		
Roussotte, F. F., Sulik, K. K., Mattson, S. N., Riley, E. P., Jones, K. L., Adnams, C. M., . . . Sowell, E. R. (2012). Regional brain volume reductions relate to facial dysmorphism and neurocognitive function in fetal alcohol spectrum disorders. Human Brain Mapping, 33(4), 920-937.	<ul style="list-style-type: none"> • Relationship between alcohol consumption during first trimester of pregnancy, and brain structure, IQ and facial morphology (palpebral fissure length and appearance of philtrum) • In the South Africa test site, information on dose of maternal alcohol drinking was available and used to examine if there were any associations between dose and any other measured outcomes 	<ul style="list-style-type: none"> • Exposed group had overall lower brain volume than unexposed group • When controlling for overall brain volume, exposed group had lower volume of regions in the basal ganglia and diencephalon • In the exposed group, higher facial dysmorphism associated with lower volume of some brain regions. Lower IQ scores were associated with lower volume of some brain regions and higher facial dysmorphism • For the unexposed group, no association found between facial morphology or IQ and regional brain volume • For the exposed group in South Africa, dose-response relationship between maternal drinking in the first trimester and child's overall brain volume (higher amount of maternal drinking associated with lower overall brain volume). This association was not found for drinking in other trimesters or drinking throughout all trimesters. No association found between regional brain volume and dose of maternal alcohol 	US, South Africa	8-16 yrs	•	•	•						•	•			•			

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
Sawada Feldman, H., Lyons Jones, K., Lindsay, S., Slymen, D., Klonoff-Cohen, H., Kao, K., . . . Chambers, C. (2012). Prenatal alcohol exposure patterns and alcohol-related birth defects and growth deficiencies: A prospective study. <i>Alcoholism: Clinical and Experimental Research</i> , 36(4), 670-676.	<ul style="list-style-type: none"> Association between quantity, timing and pattern of alcohol consumption during pregnancy and child physical growth characteristics (weight, length and head circumference) and facial morphology (palpebral fissure length, philtrum characteristics, vermilion border width) Age range of participants not specified. Majority of children had measurements completed before age 3 years. 	<ul style="list-style-type: none"> Any pattern of drinking during the latter half of the 1st trimester (6-12 weeks after conception) was associated with most of the outcomes measured and also most strongly associated with the incidence of those outcomes (smooth philtrum, thin vermilion, microcephaly, reduced birth weight and length). The associations found were dose-response relationships with no safe threshold of alcohol consumption. In the 2nd trimester, only some alcohol consumption patterns associated (in particular number of binge drinking episodes) with having a smooth philtrum, reduced birth weight and length In the 3rd trimester, only some drinking patterns were associated with birth length 	US	NR		•			•	•						•				
Sayal, K., Draper, E. S., Fraser, R., Barrow, M., Smith, G. D., & Gray, R. (2013). Light drinking in pregnancy and mid-childhood mental health and learning outcomes. <i>Archives of Disease in Childhood</i> , 98(2), 107-111.	<ul style="list-style-type: none"> Whether first trimester light drinking is associated with behavioural, social-emotional or school test scores at age 11 yrs Behavioural and social-emotional functioning measured using the SDQ as reported by parents and teachers 	<ul style="list-style-type: none"> Overall, no evidence that alcohol exposure is related to adverse social, behavioural or academic outcomes Girls whose mothers drank less than once a week had slightly worse overall ratings on the parent SDQ compared to non-exposed girls Children whose mothers drank one or more days per week had slightly worse overall ratings on the teacher SDQ compared to non-exposed children 	UK	11 yrs		•			•	•		•						•		

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes											
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ		
Sithisarn, T., Granger, D. T., & Bada, H. S. (2012). Consequences of prenatal substance use. <i>International Journal of Adolescent Medicine and Health</i> , 24(2), 105-112.	<ul style="list-style-type: none"> Outcomes of PAE in childhood and adolescence 	<ul style="list-style-type: none"> PAE can lead to FASD, which can result in growth deficiency, brain malformations (which cause behavioural/cognitive problems), and dysmorphic features Neonatal effects: lower birth weight, shorter birth length, smaller head circumference and dysmorphic features. Neurobehavioural changes include irritability, tremors, abnormal reflexes, seizures, autonomic dysregulation, and stress abstinence. These can affect the child-caregiver interaction influencing later development Higher risk of mental difficulties and disorders: depression, anxiety disorder, obsessive compulsive disorder, conduct disorder, maladaptive social functioning, ADHD, suicide threats or attempts, passive aggressive disorder and antisocial personality disorder There appears to be a dose-effect relationship between PAE and childhood behavioural outcomes. Even low alcohol consumption is associated with adverse outcomes like mental health problems at school age Gender differences in risk of developing different mental health outcomes 	NR	NR																		
Skogerbø, Å., Kesmodel, U. S., Denny, C. H., Kjaersgaard, M. I. S., Wimberley, T., Landrø, N. I., Mortensen, E. L. (2013). The effects of low to moderate alcohol consumption and binge drinking in early pregnancy on behaviour in 5-year-old children: A prospective cohort study on 1628 children. <i>BJOG: An International Journal of Obstetrics and Gynaecology</i> , 120(9), 1042-1050.	<ul style="list-style-type: none"> Relationship between low-moderate alcohol consumption and binge drinking during pregnancy, and child behaviour and social-emotional outcomes at age 5 yrs Behaviour and social-emotional functioning measured using SDQ completed by parents and teachers 	<ul style="list-style-type: none"> Both low-moderate and binge alcohol consumption not related to lower ratings on the SDQ 	Denmark	5 yrs																		

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
Skogerbø, Å., Kesmodel, U. S., Wimberley, T., Støvring, H., Bertrand, J., Landrø, N. I., et al. (2012). The effects of low to moderate alcohol consumption and binge drinking in early pregnancy on executive function in 5-year-old children. <i>BJOG: An International Journal of Obstetrics and Gynaecology</i> , 119(10), 1201-1210.	<ul style="list-style-type: none"> Association between pattern of alcohol consumption (average daily dose, frequency and timing of binge episodes) in early pregnancy and child's EF at 5 yrs EF measured using the Behavior Rating Inventory of Executive Function completed by parents and teachers. Three scores are obtained: overall score, BRI (reflects inhibition, shifting and emotional control abilities) and MI (reflects working memory, planning, organising, initiating tasks independently and self-monitoring) 	<ul style="list-style-type: none"> Low-moderate drinking not related to overall EF Moderate-heavy drinking related to poorer parent-reported MI Binge drinking from week 9 of gestation onward was related to worse parent-reported BRI, and a higher risk of scoring at a clinically-significant range on the teacher-reported MI Inconsistency between parent-report and teacher-report scores for both BRI and MI scores All other associations between alcohol consumption and EF scores were non-significant when adjusted for possible confounding variables 	Denmark	5 yrs		•			•	•	•									
Underbjerg, M., Kesmodel, U. S., Landrø, N. I., Bakketeig, L., Grove, J., Wimberley, T., . . . Mortensen, E. L. (2012). The effects of low to moderate alcohol consumption and binge drinking in early pregnancy on selective and sustained attention in 5-year-old children. <i>BJOG: An International Journal of Obstetrics and Gynaecology</i> , 119(10), 1211-1221.	<ul style="list-style-type: none"> Association between pattern of alcohol consumption (average daily dose, frequency and timing of binge episodes) in early pregnancy and child's selective and sustained attention at 5 yrs 	<ul style="list-style-type: none"> Heavy alcohol consumption was related to poorer overall attention scores as well as selective and sustained attention scores alone. Maternal smoking combined with moderate-heavy alcohol consumption could further worsen attention outcomes Low-moderate consumption and binge drinking not associated with any scores 	Denmark	5 yrs		•			•	•	•									
Ware, A. L., Crocker, N., O'Brien, J. W., Dewese, B. N., Roesch, S. C., Coles, C. D., et al. (2012). Executive function predicts adaptive behavior in children with histories of heavy prenatal alcohol exposure and attention-Deficit/Hyperactivity disorder. <i>Alcoholism: Clinical and Experimental Research</i> , 36(8), 1431-1441.	<ul style="list-style-type: none"> Whether EF is related to adaptive behaviour in children with heavy PAE (some with ADHD), children with ADHD but no history of PAE, and controls without ADHD or history of PAE Children completed executive functioning tasks and caregivers rated them on scales of adaptive behaviour 	<ul style="list-style-type: none"> For the alcohol-exposed group, non-verbal measures of executive functioning were related to level of adaptive functioning. Verbal measures were not related to adaptive functioning. Alcohol-exposed children with ADHD had lower adaptive functioning than exposed children without ADHD 	US	8 - 18 yrs	•				•	•	•								•	

Citation	What Was Studied?	What Was Found?	Country	Age	Method				Exposure factors		Outcomes									
					Case-control	Longitudinal	Reviews	Commentaries	Timing	Dose	Cognitive	Behaviour	Motor	Language	Social-emotional	Physical	Biological	Academic	Mental health	IQ
Zuccolo, L., Lewis, S. J., Smith, G. D., Saya, K., Draper, E. S., Fraser, R., et al. (2013). Prenatal alcohol exposure and offspring cognition and school performance. A Mendelian randomization natural experiment. <i>International Journal of Epidemiology</i> , 42(5), 1358-1370.	<ul style="list-style-type: none"> Relationship between maternal alcohol consumption during first trimester and maternal genetic predisposition to drink alcohol, and child IQ scores at age 8 yrs and academic outcomes (KS2 scores) at age 11 yrs 	<ul style="list-style-type: none"> Children of mothers carrying an allele that predisposes lower alcohol consumption had higher KS2 scores, but not higher IQ scores Light and moderate alcohol consumption related to better IQ scores and academic achievement. Heavy drinking related to slightly worse IQ scores Amount of alcohol consumption related to social class. Authors warn that the positive effect of alcohol consumption may be due to residual confounding between child outcomes and family social class 	UK	8 and 11 yrs		•			•	•								•	•	

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