Summary of significant research on prenatal alcohol use and children's executive functioning and behaviors

Sood et al. (2008). Prenatal alcohol exposure and child behavior at age 6 to 7 years: Dose response effect. ***Pediatrics 108*****(2):e34. (pediatrics.aappublications.org/content/108/2/e34)**

Methods	Conclusions	Summary
• Aim: evaluate the dose-response effect of prenatal alcohol exposure for adverse child behavior outcomes at 6-7 years of age • 506 parent-child combinations • Urban, university-based maternity clinic • Data collected beginning 1986 • Mother-reported alcohol use averaged as absolute alcohol per day throughout pregnancy: no, low (>0 but <0.3 fl oz. absolute alcohol per day); moderate/heavy (>=0.3 fl oz absolute alcohol per day, i.e. 10g) • Children were divided into 3 groups: no, low, and moderate/heavy alcohol exposure. • Variables: Achenbach Child Behavior Checklist (CBCL)*; normative data drawn from a national sample • Controlled for age, education, maternal psychopathology, continuing alcohol and drug use	• Adverse behavioral effects could be observed in children at age 6 with low-level prenatal alcohol exposure (levels as low as 1 drink per week) • Moderate/high exposure increased the adverse behavioral effects observed particularly for delinquent and total problem behaviors • Children with any prenatal exposure were predicted to be 3.2 times as likely to exhibit delinquent (rule-breaking) behavior • Limitations: relationship between PAE and adverse childhood behavior may be affected by other factors; alcohol exposure averaged across entire pregnancy rather than looking at specific timing; sample may not have been representative; conflation of moderate & heavy use into one group for analysis.	• Low-level PAE associated with behavioral effects at 6 years old. • **Increased dose associated with increased behavioral effects.** • Children with PAE 3 times as likely to exhibit delinquent or rule-breaking behaviors according to the CBCL. • **While some mothers used cocaine as well; research has consistently shown that alcohol has most significant long-term teratogenic effects.** • Limitation: Sample may not be representative of wider population. *CBCL scoring based on groupings of sets of behaviors that typically occur together. Similar questions are grouped into syndrome scale scores; scores are summed to produce a raw score for that syndrome. The syndrome scales are: Aggressive Behavior; Anxious/Depressed; Attention Problems; Rule-Breaking Behavior; Somatic Complaints; Social Problems; Thought Problems; Withdrawn/Depressed. There are two "broad band" scales that combine several of the syndrome scales: Internalizing sums the Anxious/Depressed, Withdrawn/Depressed, and Somatic Complaints scores; Externalizing combines Rule-breaking and Aggressive Behavior. There also is a Total problems score, which is the sum of the scores of all the problem items.

O'Callaghan et al. (2007). Prenatal alcohol exposure and attention, learning, and intellectual ability at 14 years: A prospective longitudinal study. ***Early Human Development 83*****(2):115-123. (doi.org/10.1016/j.earlhumdev.2006.05.011)**

Methods	Conclusions	Summary
• Aim: examine whether timing or quantity of alcohol consumption during pregnancy is associated with problems of attention, learning, cognition in adolescence • Ongoing birth cohort study: 5139 mothers and adolescents pairs at 14-year mark	• Consumption of <1 drink/day in early or late pregnancy not associated with adverse attention, learning, cognition • Relationship between consumption >=1 drink per day & adverse attention, learning, cognition had strongest estimates of effect; findings	• Limitation: Binge drinking frequency and timing not reliably assessed – binge drinking in animal models has been shown to be particularly impactful, especially in early pregnancy. • Limitation: Focus on attention, learning, and intellectual ability misses many of the areas of functioning that adolescents and young adults

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• Mothers completed interviews at various time points, latest at 14 years (this study) • Mothers completed the Child Behavior Checklist (CBCL) • Other variables: age, education, marital status, total family incomes, pre-pregnant maternal BMI, and level of maternal smoking in early and late pregnancy • The adolescent completed the Youth Self Report and the Wide Range Achievement Test – Revised (WRAT-R) • Adolescent cognitive ability assessed by the Raven's Standard Progressive Matrices Test	consistent with literature on adverse effects of heavy alcohol consumption in pregnancy • Binge drinking associated with higher prevalence Raven's score <85 • Exposure to >1.5 drinks/occasion in early pregnancy associated with lower average scores on "word attack" and arithmetic measures and decreased sustained attention and spatial memory • Limitations: potential for under-reporting of consumption; low prevalence of heavy drinkers in sample and loss of heavy drinkers during follow-up limited conclusions regarding the effects of heavy drinking and adolescent outcomes; binge drinking measure could not provide an accurate frequency –didn't indicate a specific time during pregnancy; test used to examine cognitive ability (Raven's Test) has significant limitations & attention scales not sufficient to diagnose ADHD	with an FASD struggle with, e.g.., executive functioning. • Limitation: Tests used to assess attention, learning, and intellectual ability have significant limitations in the areas where we see individuals with an FASD struggle. • **Results consistent with other studies re: impact of higher levels of exposure and binge drinking – attention and spatial memory, as well as language and arithmetic skills affected**. *Word attack tests assess a student's decoding skills and strategies.

Robinson et al. (2010). Low-moderate prenatal alcohol exposure and risk to child behavioral development: A prospective cohort study. *BJOG 117*(9):1139-1150. (europepmc.org/abstract/med/20528867)

Methods	Conclusions	Summary
• Aim: Examine association between alcohol exposure during pregnancy and adolescent behavioral development • Prospective study • Participants from the Western Australian Pregnancy Cohort (WAPC) • 2868 live births: 1860 in 14-year follow up • Sample representative of the demographic characteristics of the general Western Australian population • Longitudinal design • Child Behavior Checklist main measurement tool to assess child behavior at every follow-up visit; high scores indicate more disturbed emotions and behaviors	• Low levels of alcohol consumption during early pregnancy did not appear to be harmful to the mental health of the child • High levels of alcohol consumption during pregnancy should be discouraged based on the findings from other studies • Limitations: Consumption of drinks per week was averaged, not reliably reflect binge drinking patterns; small number of heavy drinkers in cohort; lower SES participants less likely remain in study at 14 years; unable to adjust specifically for maternal psychopathology (may increase likelihood of drinking); development of behavioral problems is also associated with high maternal stress; alcohol consumption and behavioral consequences for the child may not	• **Alcohol consumption and behavioral consequences for the child may not follow a simple linear dose-response pattern** – there appears to be a subtle interaction between variables that mean there are individual impacts to each mother-child pair. • Limitation: Binge drinking patterns not reliably assessed. • **We cannot predict which mother-child pair may be most significantly impacted by "moderate" alcohol consumption during pregnancy.** • Authors still recommend discouraging alcohol consumption during pregnancy.

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• Alcohol consumption during pregnancy was based on self-reports and converted to total number of standard drinks per week: no or occasional drinking (up to 1 standard drink/week; light (2-6 standard drinks/week); moderate (7-10 standard drinks/week); heavy (11+ standard drinks/week) • Standard drink = 10g pure alcohol, i.e. 0.3 fl oz	follow a simple linear dose-response pattern; participants asked to indicate number of "glasses" of wine, "nips" of spirits	

Skogerbø 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. *BJOG 119*(10):1201-1210. (doi.org/10.1111/j.1471-0528.2012.03397.x)

Methods	Conclusions	Summary
• Aim: Examine the effects of low to moderate maternal alcohol consumption and binge drinking in early pregnancy on children's executive functions at age 5 years • Danish National Birth Cohort (DNBC): 1628 mothers and their children (single births only) • Women interviewed about their alcohol consumption between 14 and 20 weeks gestation • Behavioral Rating Inventory of Executive Function (BRIEF) used to evaluate a child's executive function with minor adjustments. Administered to parents and preschool teachers • Mothers were given an adult IQ test • Comprehensive neuropsychological battery of tests given to children • Multiple imputation of the variables collected; covariates used to predict any missing values	• Results considered inconclusive: authors still recommend abstinence during pregnancy • No consistent effect of low to moderate level of prenatal alcohol exposure on executive functioning at the age of 5 years and insignificant associations found for binge drinking • Limitations: age of child at assessment – a child's executive functioning capability is not fully mature until adolescence; biased parent and teacher rates indicated by low index scores; results skewed by the mothers who chose to participate; relatively middle-class homogenous population; lack of sufficient statistical power, particularly with the groups with moderate consumption (5-8 and ≥ 9 drink/week); limitations in assessing exposure due to biological factors and timing of consumption; lack of statistically significant findings suggests the effects of low to moderate consumption and binge drinking on executive function may be subtle and difficult to detect with the current measures for neurodevelopment	• Limitation: The executive functioning capabilities of five year olds are different from those of teenagers and young adults. Many individuals with an FASD don't start having significant difficulties until early adolescence as expectations change. • Limitation: Timing of consumption during not adequately addressed. • **Effects of low to moderate consumption and binge drinking on executive function may be subtle and difficult to detect with the current measures for neurodevelopment – but this does not mean that an individual does not have significant challenges in their daily lives.** • **Authors still recommend that women abstain from alcohol consumption during pregnancy as they did not consider their results to be conclusive or indicative of safety to neurodevelopment.**

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Burd et al. (2012). Prenatal alcohol exposure, blood alcohol concentrations and alcohol elimination rates for the mother, fetus, and newborn. *Journal of Perinatology 32*:652-659. (doi.10.1038/jp.2012.57)

Methods	Conclusions	Summary
• Aim: Review existing research articles reporting on perinatal alcohol exposure, neonatal alcohol elimination rates (AER), and blood alcohol concentrations (BAC) • Search terms: alcoholism, blood, blood alcohol, blood concentration, blood level, ethanol, fetal, FAS, fetus, foetal, gestational age, maternal-fetal exchange, neonate, newborn, pregnancy, prenatal exposure delayed effects • Only human studies, no date limits, no language limits	• Fetal elimination relies on mother's capacity. After rise in maternal BAC, ethanol can be detected in fetus within 1 minute; fetal BAC equilibrizes with maternal BAC • Maternal and fetal pathways for metabolization of ethanol are the same, but in fetus there is much reduced capacity • ADH pathway accounts for 90-95% of metabolism by liver. ADH detectable in fetus at 2 months gestation but metabolic capacity is 5-10% of adult activity • Ethanol excreted by fetus through renal and pulmonary pathways can be reabsorbed from amniotic fluid, increasing duration of exposure • Smoking is often comorbid with alcohol use – is a vasoconstrictor that may modify elimination in fetus. Alcohol is also a vasoconstrictor. Combination may increase exposure time. • Limitations: No available data on effects of chronic exposure on development of tolerance, metabolic rates of fetus/newborn; accuracy & comparability of methods used to determine BAC values unknown; studies did not differentiate between umbilical vein and umbilical artery	• **Fetal elimination relies primarily on mother's metabolism. Fetus has very limited capacity to eliminate alcohol and may reabsorb some eliminated into amniotic fluid increasing length of exposure.** • Ethanol elimination in the newborn has a mean of 83.5% capacity of an adult. • Capacity of placenta to metabolize alcohol is very limited; alcohol easily crosses the placenta. • Comorbid smoking may increase duration of alcohol exposure by fetus.

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