An investigation of the link between prenatal alcohol exposure and sleep problems across childhood

5 authors, including:

Ned Chandler-Mather
Griffith University
7 PUBLICATIONS **20** CITATIONS

SEE PROFILE

Stefano Occhipinti
The Hong Kong Polytechnic University
100 PUBLICATIONS **4,024** CITATIONS

SEE PROFILE

Doug Shelton
Gold Coast University Hospital
27 PUBLICATIONS **559** CITATIONS

SEE PROFILE

Sharon Dawe
Griffith University
163 PUBLICATIONS **6,719** CITATIONS

SEE PROFILE

Some of the authors of this publication are also working on these related projects:

Project   Honours Thesis View project

Project   Improving executive functions and self regulation in vulnerable children View project

An investigation of the link between prenatal alcohol exposure and sleep problems across childhood

Ned Chandler-Mather[a], BPsySc(Hons), Stefano Occhipinti[a,b], PhD, Caroline Donovan[a], PhD, Doug Shelton[c], MBBS, Dip Paed, FRACP, Sharon Dawe[a,d], BA, MA(Hons), PhD

[a]School of Applied Psychology, Griffith University, Brisbane, Australia

[b]EPIC Health Systems, Menzies Health Institute Queensland

[c]Gold Coast University Hospital, Southport, Australia

[d]The Hopkins Centre, Griffith University

Correspondence:

Ned Chandler-Mather

School of Applied Psychology, Griffith University, Messines Ridge Road, Brisbane, QLD, 4122, Australia.

ned.chandler-mather@griffithuni.edu.au

Abstract

Objective

To investigate the association between dose and frequency of prenatal alcohol exposure (PAE) and sleep problems in children, after controlling for established risk factors for sleep problems.

Methods

Data from the birth cohort of the Longitudinal Study of Australian Children (LSAC) was used. Mothers of 3447 children provided information on alcohol consumption during pregnancy, children's sleep problems from 2- to 9-years, and potential confounders associated with sleep problems. Children were classified into PAE groups based on distinct patterns of maternal drinking during pregnancy: abstinent, occasional, low, moderate, and heavy. The effect of PAE on the number and persistence of sleep problems across childhood (2−9 years) was examined.

Results

After controlling for multiple covariates that impact sleep, children with heavy PAE had 1.13 more sleep problems across childhood (2−9 years) relative to children whose mothers were abstainers, in particular 0.37 more at 2- to 3-years (0.504, 95 % CI 0.053, 0.956), and 0.34 more at 6- to 7-years (0.847, 95 % CI 0.299, 1.396). Compared to children of abstainers, heavy PAE increases the probability of having persistent sleep problems from 2- to 9-years by 22.57 %. No negative associations between moderate or low PAE and sleep were observed. Parenting, family, economic, and child health factors also significantly affected child sleep.

Conclusion

Heavy PAE was associated with significantly more sleep problems across childhood and a

higher probability of reporting persistent sleep problems, relative to children with no PAE.

Implications for the understanding and management of sleep in young children with PAE and

FASD are discussed.

Keywords

Prenatal alcohol exposure (PAE); Alcohol; Fetal alcohol spectrum disorder (FASD), Sleep;

Pregnancy; Child development

An investigation of the link between prenatal alcohol exposure and sleep problems across

childhood

1. Introduction

There is a clear association between prenatal alcohol exposure (PAE) and damage to

the underlying mechanisms that regulate sleep (Inkelis & Thomas, 2018). Preclinical studies

indicate that PAE can lead to the dysregulation of GABAergic neurons throughout the cortex

(Smiley et al., 2015), which are part of inhibitory circuits that support sleep regulation (Luppi

& Fort, 2018). In humans, the neural circuitry involved in arousal and stress control, both

crucial for initiating and maintaining sleep (Dahl, 1996), are potentially affected by PAE

(Fryer et al., 2007; Haley, Handmaker, & Lowe, 2006; Kable & Coles, 2004) leading to over-

activity at bedtime (Keiver, Bertram, Orr, & Clarren, 2015; McLachlan et al., 2016). There is

also emerging evidence that children and adolescents with PAE who meet criteria for Fetal

Alcohol Spectrum Disorder (FASD) have dysfunctional circadian systems, with 79% of

children and adolescents showing abnormal melatonin release across the evening (Goril,

Zalai, Scott, & Shapiro, 2016). In addition, positive genetic correlations between alcohol use

problems and insomnia may provide a separate link between heavy maternal drinking during

pregnancy and sleep problems in their children (Kranzler et al., 2019).

Clinical studies have documented that children with FASD have significantly disrupted sleep

behaviour (Hanlon-Dearman, Chen, & Olson, 2017). Young children with FASD have been

reported to take longer to fall asleep and have higher rates of parent-reported sleep problems,

such as bedtime resistance, short sleep duration, sleep anxiety, night awakenings, and

parasomnias compared to typically developing children (Chen, Olson, Picciano, Starr, &

Owens, 2012; Wengel, Hanlon-Dearman, & Fjeldsted, 2011). In qualitative studies, parents

and caregivers have reported that their child with FASD has significant sleep disturbances

(Spruyt, Ipsiroglu, Stockler, & Reynolds, 2018) and that these problems are often missed by clinicians (Ipsiroglu, McKellin, Carey, & Loock, 2013).

Sleep problems during childhood can be disruptive for the child and their parents. They can lead to greater parental stress and mental health issues (Lam, Hiscock, & Wake, 2003; Quach, Hiscock, & Wake, 2012) and can have a negative impact on the child's cognitive development (Astill, Van der Heijden, Van IJzendoorn, & Van Someren, 2012; Bernier, Beauchamp, Bouvette-Turcot, Carlson, & Carrier, 2013; Turnbull, Reid, & Morton, 2013) and their regulation of their behaviour (Quach, Nguyen, Williams, & Sciberras, 2018) and emotions (Williams, Berthelsen, Walker, & Nicholson, 2017). A separate line of research is investigating how the sleep problems in children with FASD contribute to both cognitive (Wilson et al., 2016), and emotional difficulties (Mughal, Joyce, Hill, & Dimitriou, 2020).

What remains unclear, is whether PAE has a significant effect on child sleep problems after potential confounders are controlled for (May et al., 2013). Notably, many children with PAE are also exposed to a range of other prenatal exposures and postnatal environmental stressors that, independent of alcohol exposure, have also been associated with sleep problems. These include a lack of family routines and structure (Whitesell, Crosby, Anders, & Teti, 2018), lower socioeconomic status and single parent households (El-Sheikh et al., 2013), and compromised parent-child relationships (Bell & Belsky, 2008; Giallo, Rose, & Vittorino, 2011; Kiel, Hummel, & Luebbe, 2015). Early adversity may also include neglect, parental separation or divorce, placement in residential or foster care, and physical abuse (Kambeitz, Klug, Greenmyer, Popova, & Burd, 2019; Streissguth et al., 2004). There is some evidence of insecure attachment relationships in children of mothers from low socioeconomic backgrounds who drank during pregnancy (O'Connor, Kogan, & Findlay, 2002). Finally, in utero exposure to nicotine is common, as many pregnant women who drink also smoke (McCormack et al., 2018), and parental smoking is associated with sleep difficulties in young

children, primarily through nicotine's effects on respiratory and arousal systems (Stéphan-Blanchard et al., 2008; Stone et al., 2010). Thus, confounding factors could equally explain higher rates of sleep problems in children with FASD/PAE.

Previous studies investigating the association between PAE and child sleep problems have led to inconsistent findings. Some studies have found no association (Stone et al., 2010), others have found an association with fragmented and shorter sleep (Pesonen et al., 2009), and an increase in night-time parasomnias (Shang, Gau, & Soong, 2006) in children. However, study limitations include lack of control for the effects of family stress and parenting (Pesonen et al., 2009) and a failure to examine dose and frequency of PAE (Pesonen et al., 2009; Shang et al., 2006). Animal model studies demonstrating a detrimental effect of alcohol exposure early in development on sleep behaviour in mice often administer doses of ethanol that would result in approximate mean blood alcohol concentrations of between 300 mg/dL and 500 mg/dL (Ipsiroglu et al., 2019; Stone et al., 1996; Volgin & Kubin, 2012; Wilson et al., 2016), which would correspond to a heavy dose in humans (Patten, Fontaine, & Christie, 2014), leaving the effect of lower doses unexplored.

Further, it is not clear whether there are age effects or whether sleep problems are consistent across childhood. Studies to date have focused on the relationship between PAE and sleep problems at a single time point, e.g., 8 years (Pesonen et al., 2009), or have averaged parent-reported sleep problems across birth to early adolescence (Stone et al., 2010). One study that tracked separate cohorts of children with FASD from age 5.6 years to 9.7 years, 5.7 years to 14.2, and 10.2 years to 13.2 years found that many children had sleep problems that did not remit (Steinhausen & Spohr, 1998). Persistent sleep problems might reflect lasting damage to neurobiological structures that underpin the regulation of sleep-wake states as a result of alcohol exposure in utero (Inkelis & Thomas, 2018; Wilson et al., 2016). However, the study

by Steinhausen & Spohr (1998) did not control for the potential effects of adversity and environmental stressors on sleep problems.

The present study examined the relationship between PAE and the number of sleep problems in a nationally representative cohort of children across childhood (2-9 years), controlling for prenatal and postnatal factors that might also impact child sleep. Further, the relationship between prenatal alcohol exposure and the persistence of sleep problems was investigated. Given the existing evidence for the detrimental effects of heavy PAE on sleep (e.g., Wilson et al., 2016), we predicted that heavy PAE would predict significantly more sleep problems across childhood and a higher probability of developing persistent sleep problems relative to children with no PAE. Since there is a lack of evidence regarding lower levels of PAE, our analyses at these levels were exploratory.

2. Material and methods

Data were drawn from the birth cohort of the Longitudinal Study of Australian Children (LSAC), which includes children born between March 2003 and February 2004 (n = 5107). Parents were interviewed face-to-face and completed questionnaires every two years that assessed factors with the potential to influence child development. A more detailed description of the LSAC methodology can be found elsewhere (Soloff, Lawrence, & Johnstone, 2005). The LSAC was approved by the Australian Institute of Family Studies Ethics Committee, which is a Human Research Ethics Committee registered with the National Health and Medical Research Council (NHMRC). Permission to use the data for research purposes was obtained by Ned Chandler-Mather from the Australian Data Archive on behalf of the Australian Institute of Family Studies, Department of Social Services, and the Australian Bureau of Statistics. Demographic and drinking data were extracted at Wave 1

(0−1 year). Sleep problem and covariate data were extracted at Waves 2 (2 −3 years), 3 (4−5 years), 4 (6−7 years), and 5 (8−9 years).

2.1 Participants

We extracted a subsample of children from the 2004 birth cohort (N=3447, 67.50 %) who had data from their biological mother on marital status, maternal alcohol and cigarette use during pregnancy, combined family income, highest level of maternal education, child birthweight, number of weeks of gestation, maternal age, and stressful life events at Wave 1 (n = 1345 excluded), who met one of the PAE group criteria below (n = 7), and were missing no more than 50 % of their sleep outcome data (n = 308).

Demographic characteristics collected at Wave 1 are detailed in Table 1. This can be considered to be a representative sample; there were no differences on median maternal age (32 years in LSAC vs 30.8 years in census) or median household income ($1000−$1499 per week in LSAC vs $1027 per week in census) when compared to 2006 Australian census data (Australian Bureau Of Statistics, 2006), although more mothers had completed at least a Bachelor's degree or Diploma in our subsample of the LSAC data set than in the general population (35.5% in LSAC vs 25.6% in census).

2.2 Measures

2.2.1 Maternal alcohol use during pregnancy

Information about alcohol use during pregnancy was collected retrospectively for each trimester at Wave 1. Mothers were asked to record the frequency (occasional, or number of days/week) of alcohol consumption per trimester and the average number of drinks they consumed per drinking occasion over the entire pregnancy (quantity). We used this information to form PAE categories that capture discrete patterns of alcohol consumption during pregnancy.

 We categorised PAE based on a recently developed method that aims to capture different patterns of alcohol use during pregnancy (O'Leary, Bower, et al., 2010). There were some deviations from this composite method owing to the structure of the LSAC survey data that are described below.

We included an occasional PAE group (defined below) because mothers could choose to rate their drinking frequency as "occasional" instead of by the number of occasions per week. Our PAE groups were based on drinking patterns across the entire pregnancy because in the LSAC survey mothers were asked to estimate quantity of alcohol consumed per occasion over the entire pregnancy, rather than per trimester. To compute the average number of drinks per week for the entire pregnancy, we first computed the average number of drinks per week for each trimester by multiplying the frequency of drinking per week for each trimester ("occasional" taken as 0.5 drinks/week) by the quantity of drinks per occasion, which were then averaged to obtain an estimate for the entire pregnancy. Lastly, in addition to O'Leary et al.'s (2010) criteria for heavy drinking, owing to the low numbers of women who reported drinking binge-level amounts during pregnancy, we assigned 2 women who reported drinking 11 drinks or more during pregnancy to the "heavy" group regardless of their average daily intake over the pregnancy as this would constitute a binge event.

Thus, the PAE groups were as follows: (i) abstinent (no alcohol consumption across the entire pregnancy), (ii) occasional (only frequency of alcohol consumption reported was "occasionally" across any of the three trimesters and never more than 1−2 standard drinks per occasion), (iii) low (drank < 7 drinks per week on average across the entire pregnancy and no more than 1−2 drinks per occasion), (iii) moderate (drank ≤ 7 standard drinks/week on average across the entire pregnancy and < 5 drinks per occasion), and (iv) heavy (drank > 7 standard drinks per week on average, or drank ≥ 5 drinks per occasion and drank on > 2

occasions/week during any trimester across the entire pregnancy, or drank 11 or more drinks per occasion regardless of frequency of consumption).

2.2.2 Child sleep problems

Four items that map onto objective measures of sleep (Byars, Yolton, Rausch, Lanphear, & Beebe, 2012; Sadeh, Mindell, & Rivera, 2011; Williamson, Mindell, Hiscock, & Quach, 2019) and that have been used previously to examine the developmental effects of sleep problems (Quach et al., 2018) were extracted from the LSAC dataset to measure the number of child sleep problems at each wave (Waves 2−5). On each item, the primary caregiver (almost always the biological mother) was asked to respond "yes" or "no" to whether certain sleep-related behaviours were a problem "four or more nights per week, that is, more than half the time". These behaviours included "getting off to sleep at night", "not happy to sleep alone", "waking during the night", and "restless sleep". "Don't know" responses were coded as missing. "Yes" responses to each item were summed to create a total count of sleep problems for each child at each Wave after imputing missing data (see Missing Data section). Children were categorised as having persistent sleep problems if their parents reported at least one sleep problem at three of the four Waves (Gregory et al., 2005; Gregory, Caspi, Moffitt, & Poulton, 2009).

2.2.3 Covariate data from wave 1

Parents provided information about several demographic variables. The mother recorded how many cigarettes they smoked each day per trimester and these were averaged to compute the number of cigarettes they smoked (per day) during pregnancy (Stone et al., 2010). Maternal stress during pregnancy was measured by asking mothers if they had problems with stress, anxiety or depression during pregnancy (O'Connor et al., 2007). Child birthweight was converted into four categories: greater than low birthweight (2500g or more), low birthweight

(1500−2499g), very low birthweight (1000g−1499g) and extremely low birthweight (<1000g). Weeks of gestation was converted into three categories: Preterm (<37 weeks), Term (37−41.99 weeks), and Post-term (42 weeks or more) (Davis & Thoman, 1987; Rosen et al., 2003). Combined family income (responses were by categories ranging from Nil or Negative Income to $2400 per week or $124 800 per year or more), maternal age (years), maternal education (El-Sheikh et al., 2013) marital status (married, widowed, divorced, separated, never married), and their child's sex (Shang et al., 2006). These variables were included as covariates due to their reported links with child self-regulation and/or sleep functioning.

2.2.4 Covariate data from waves 2 to 5

See Table 1 for a covariate information. Analyses were adjusted for variables collected at each Wave that have been associated with children's sleep: body mass index (BMI), which was computed based on direct measures of weight and height taken at home visits (Nixon et al., 2008), parents report of their child's asthma (van Maanen et al., 2013) and eczema status (Reid & Lewis-Jones, 1995), family stress (Tsai et al., 2018), and the age of the child (weeks) at each Wave. A count of 21 potential life events was used as an index of family stress (e.g., being assaulted, or experiencing a major financial crisis, legal problems, or domestic violence).

Maternal responses to warm, hostile, and overprotective parenting measures collected via surveys at each Wave were included to control for the effect of the mother-child relationship on child sleep behaviour. Their respective psychometric properties have been described in detail elsewhere (Cooklin, Giallo, D'Esposito, Crawford, & Nicholson, 2013; Zubrick, Lucas, Westrupp, & Nicholson, 2014). The warm parenting scale contained 5 items that tap into how often the parent displays affection towards the child, how often they enjoy spending

time with the child, and how close they feel with the child. The hostile parenting scale

contained 4 items that tap into how often the parent displays anger or shouts at the child,

whether they find their child is crying or upset irritating, and whether they comfort their upset

child. The overprotecting parenting scale contained 3 items that tap into the degree to which

the parent puts their child's needs before their own, wants to protect the child from life's

difficulties, and how upset they become when they separate from the child.

2.3 Missing data

There was missing data across Waves 2 to 5. There was complete sleep data for 2918

(84.65%) children across all 4 Waves. There were 351 children (10.18%) missing 4 sleep

data points and 178 children (5.16%) missing 8 data points. There was complete sleep data

for 3365 (97.62%) children at Wave 2, for 3364 (97.59%) at Wave 3, for 3250 (94.28%) at

Wave 4, and for 3102 (89.99%) at Wave 5. Complete covariate data was reported for 2712

(78.68%) children at Wave 2, 2920 (84.71%) at Wave 3, 3165 (91.82%) at Wave 4, and 3001

(87.06%) at Wave 5.

Wilcoxon rank sums tests indicated that those who were missing data reported significantly

more stressful life events ($r = -0.04$, $p = .006$), lower incomes ($r = -0.09$, $p = < .001$), and

lower levels of education ($r = -0.16$, $p = < .001$) at Wave 1 compared to those with complete

data, and therefore the missing data was considered to be Missing At Random (Sterne et al.,

2009). Missing values were imputed using Multiple Imputation by Chained Equations

imputation chained equations (MICE) package (van Buuren et al., 2019) in "R" (R Core

Team, 2019). All the covariates were included as predictors in the imputation model. Family

stress was included at Wave 1 in the imputation model because levels of stress varied

between non-completers and completers. The count of sleep problems was computed after

imputation to reduce estimate bias (Eekhout et al., 2014). Since 48.06% of cases were

missing at least one data point across Waves 2 to 5 (mode points of missing data = 3), 48

datasets were imputed in order to obtain reliable parameter estimates for the models (van

Buuren, 2018; Von Hippel, 2009). Models were run individually on each imputed data set

and their estimates were pooled to produce the final estimates that are presented in the

Results section.

2.4 Analyses

We used negative binomial regressions to model the effect of PAE on the number of sleep

problems since modelling each of the count outcomes using Poisson distributions lead to

significant over-dispersion (see Table 3, alphas = 0.24−1.67, ps < .05). We examined the

effect of PAE on the total number of sleep problems parents reported from 2−9 years (Waves

2−5), then we examined the effect of PAE on the number of sleep problems reported by

parents at each time point during childhood separately: Wave 2 (2−3 years), Wave 3 (4−5

years), Wave 4 (6−7 years), and Wave 5 (8−9 years). We also used logistic regression to

examine the effect of PAE on the probability of having persistent sleep problems from 2−9

years (at least one sleep problems recorded at three of the four Waves).

For the negative binomial models, we estimated the average partial effects of each level of

PAE on the count of sleep problems multiplying each model coefficient by the average count

of sleep problems for the relevant period (Liao, 1994). Similarly, for the logistic regression

models, we estimated the average partial effect of PAE by computing marginal effects using

the "margins" R package (Leeper, Arnold, & Arel-Bundock, 2018) for each level of PAE in

each of the 48 imputed datasets and then averaging them.

Unadjusted (PAE only predictor) and adjusted (PAE + covariates) analyses were run (Table

4). Analyses were adjusted using several covariates: child sex, child birth weight group

(categorical), child prematurity (categorical), child BMI, child eczema and asthma statuses

(binary), maternal age at Wave 1, maternal marital status at Wave 1 (categorical), maternal cigarette use during pregnancy, maternal stressful pregnancy (binary), maternal warm, hostile and overparenting parenting scale scores, maternal education at Wave 1, the family stress index, and family income. For analyses of sleep problems across childhood (number of sleep problems and persistent sleep problems), child BMI, the family stress index score and maternal warm, hostile, and overparenting parenting scale scores were averaged across all four Waves, while child eczema and asthma statuses were determined by whether eczema and asthma was present for two or more Waves respectively (binary). For analyses at each Wave, variables from the given Wave were used in the models.

Lastly, post-hoc propensity score matching was employed to follow-up the unexpected protective effects of occasional PAE on sleep outcomes. We used the R package "MatchThem" (Pishgar, 2020) to match children from the occasional group with children from the abstinent group. Children were matched across the covariates listed above, which were also used to adjust the original models (see Supplementary Materials for diagnostics). The original models were then re-run using the matched groups as the only predictor.

3. Results

3.1 Maternal alcohol use during pregnancy

The pattern of drinking across each trimester is displayed in Table 2. Of the 3447 mothers in the current study, 61.18% reported abstaining from alcohol throughout pregnancy. Of the 39.63% that reported alcohol consumption at any time during pregnancy, 65.52% reported use in trimester one, 86.75% reported use in trimester two, and 91.22% reported use in trimester three. Overall, the pattern of consuming alcohol in the current sample reflect the pattern reported in the total LSAC sample, which are described elsewhere (Hutchinson, Moore, Breen, Burns, & Mattick, 2013) and similar to patterns of alcohol consumption

during pregnancy reported by another sample of Australian women during a similar period of time (Colvin, Payne, Parsons, Kurinczuk, & Bower, 2007).

3.2 The effect of prenatal alcohol exposure on the number of sleep problems across childhood

Table 3 displays the pooled descriptive statistics of the number of sleep problems across childhood and at each Wave in the overall sample and by PAE category. At 2−3 years the average number of sleep problems (an issue with sleep occurring most of the week) reported by parents was less than one, and this number declined to almost zero by 8−9 years. However, there were clear differences in the mean number of sleep problems across PAE groups with higher rates among the heavy PAE group.

We examined the effect of PAE on the number of sleep problems across childhood after adjusting for a range of potential confounders (2−9 years, see Table 4). Compared to the no-exposure group, occasional exposure significantly reduced the number of sleep problems by 0.22 ($p = 0.029$). Low and moderate exposure did not have significant effects on the number of sleep problems (ps > .05). Heavy exposure significantly increased the number of sleep problems by 1.13 ($p = .011$).

Since PAE had a significant effect across childhood, we then examined the effect of PAE on the number of sleep problems reported at each Wave after adjusting for potential confounders (see Table 4). At 2−3 years, occasional exposure significantly lowered the number of sleep problems by 0.12 ($p = .005$). Low and moderate exposure did not have significant effects on the number of sleep problems (ps > .05). Heavy exposure significantly increased the number of sleep problems by 0.37 ($p = .029$). At 4−5 years, no level of exposure had a significant effect on the number of sleep problems (ps > .05). At 6−7 years, occasional, low and moderate exposure did not have significant effects on the number of sleep problems (ps >

.05). Heavy exposure significantly increased the number of sleep problems by 0.34 ($p =$ .003). At 8−9 years, no level of exposure had a significant effect on the number of sleep problems ($ps > .05$).

3.3 The effect of prenatal alcohol exposure on persistent sleep problems throughout childhood

We also examined the effect of prenatal alcohol exposure on the probability of having persistent sleep problems throughout childhood after adjusting for a range of potential confounders (Table 4). Compared to abstinence, occasional exposure significantly reduced the probability of having persistent sleep problems by 3.73% ($p = .024$). Low and moderate exposure did not have significant effects on the probability of having persistent sleep problems ($ps > .05$). Compared to abstinence, heavy exposure significantly increased the probability of having persistent childhood sleep problems by 22.57% ($p = .010$).

3.4 Post-hoc propensity score matching occasional and abstinent PAE groups

Post-hoc analyses were conducted to explore the unexpected beneficial effects of occasional drinking on child sleep behaviour across childhood and at 2−3 years. We used propensity scores to match children from the abstainer and occasional PAE groups based on the covariates used in the original models (see Supplementary Materials). After matching, the effects of occasional PAE on the number of sleep problems across childhood were non-significant (-0.105, 95% CI -0.232 − 0.023, $p = 0.109$), however the effect at 2−3 years was still significant (-0.152, 95% CI -0.296 − -0.009, $p = 0.037$), suggesting that occasional exposure reduces the number of sleep problems at 2−3 years by 0.11. The effect of occasional PAE on the probability of having persistent sleep problems across childhood was not significant (-0.248, 95% CI 0.503−0.007, $p = 0.056$).

3.5 The effect of covariates on sleep outcomes

Having parents that have never been married at Wave 1 (relative to married; 0.118, 95% CI 0.004–0.231), greater maternal overprotective (0.279, 95% CI 0.198–0.360) and hostile parenting (0.214, 95% CI 0.154–0.274), reporting stress, anxiety or depression during pregnancy (stressful pregnancy; 0.184, 95% CI 0.079–0.290), greater maternal age at Wave 1 (0.011, 95% CI 0.002–0.020), greater family stress (0.118, 95% CI 0.085–0.151), and having eczema (0.139, 95% CI 0.030–0.248) or asthma (0.110, 95% CI 0.016–0.204) for at least half of childhood all predicted significantly more sleep problems reported throughout childhood (2−9 years). Conversely, higher family income at Wave 1 predicted significantly fewer sleep problems across childhood (-0.020, 95% CI -0.038 – -0.001). For brevity, further information about the effects of covariates at each Wave and in the model of persistent sleep problems can be found in the Supplementary Materials. Of note, maternal cigarette-use during pregnancy did not have a significant effect on sleep problems at any period during childhood ($p > .05$).

4. Discussion

The association between prenatal alcohol exposure (PAE) and sleep problems in early and middle childhood is of considerable interest given the impact of sleep on neuropsychological development (Astill et al., 2012). This study assessed the effect of maternal drinking during pregnancy on a) the number of parent-reported sleep problems and b) the probability of having persistent sleep problems across early and middle childhood in a nationally representative sample. Crucially, we controlled for potential confounding variables independently associated with sleep problems in childhood: presence of stress during pregnancy, marital status, maternal education, family income, family stress, maternal parenting styles, prenatal nicotine exposure, child sex, birth weight, gestational age, child asthma and eczema status, and child BMI. It is important to note that the findings were based

on a relatively small number of children with moderate and heavy PAE, resulting in wide confidence intervals around the reported estimates of their respective effects.

We found that children with heavy PAE had 1.13 more sleep problems across childhood (2−9 years) than children whose mothers who did not drink during pregnancy. Specifically, children with heavy PAE had 0.37 more sleep problems at 2−3 years and 0.34 more at 6−7 years relative to children without PAE. None of the other analyses of heavy PAE at other periods during childhood reached statistical significance. Further, we found that children in the heavy PAE group were 22.50% more likely to have sleep problems that persisted across childhood relative to children with no PAE. We also found that children of occasional drinkers had a statistically significant drop of 0.11 of a sleep problem at 2−3 years relative to children with no PAE after propensity score matching.

Our finding that children with heavy PAE have more sleep problems across childhood is consistent with previous research into the effects of PAE in both animal models and human children. Animal models exposed to heavy doses of ethanol, either while in gestation or on postnatal days 4 to 9 (equivalent to PAE in the third trimester in humans), exhibit significantly more hyperactivity throughout the day, more transitions in and out of slow wave sleep, and a reduced proportion of time spent in paradoxical and slow-wave sleep compared to controls (Stone et al., 1996; Volgin & Kubin, 2012; Wilson et al., 2016). In human studies children with PAE have been found to have significantly shorter and fragmented sleep (Pesonen et al., 2009) and significantly more parasomnias (Shang et al., 2006) compared to those without PAE. We extended these findings by showing that heavy PAE leads to more parent-reported sleep problems across 2- to 9-years of age whereas lower doses of PAE do not, even after controlling for the effects of maternal parenting styles and family stress.

When we examined sleep problems at separate time points during childhood, we found that children with heavy PAE were most affected at 2−3 years and 6−7 years. No previous study has tracked how PAE affects the number of sleep problems across childhood in the same cohort. It is important to note that the predicted increases in the number of sleep problems as a result of heavy PAE at these points in childhood were relatively small, each constituting less than half of a sleep problem.

Furthermore, none of the other analyses of heavy PAE at the other time points reached statistical significance. This is potentially at odds with Paavonen et al. (2010), who found an effect of PAE (they did not examine dosage effects) on sleep duration and consolidation at 8 years, which they measured using actigraphy watches. However, as already noted, our estimates were based on a small number of children with moderate and heavy PAE, which is reflected in the wide confidence intervals surrounding each point estimate. We also examined discrete parent-reported sleep problems rather than continuous dimensions of sleep, like duration and consolidation which may have meant our analyses were less sensitive to changes in sleep behaviour. Nevertheless, the estimates at each Wave did follow the expected trend whereby heavy PAE predicted a greater number of sleep problems compared to abstainers (see Graphic Abstract and Table 4). The lack of statistical significance might reflect a genuine absence of an effect or a lack of statistical power to uncover a significant effect of heavy PAE at these time points (O'Leary, Nassar, et al., 2010). Alternatively, the number of sleep problems may not be the best metric of how PAE disrupts sleep in children.

In fact, when the trajectory of sleep problems was examined, rather than the number of different sleep problems, heavy PAE led to a more marked 22.50% increase in the probability of having sleep problems that persisted throughout childhood (2 to 9 years) relative to no PAE. Thus, heavy PAE may not lead to a marked increase in the number of separate

behavioural sleep issues in young children but may instead lead to children developing more chronic sleep problems.

Children with FASD, the neurodevelopmental disorder that results from PAE, have previously been reported to have sleep problems that persist across childhood (Steinhausen & Spohr, 1998). Having chronic sleep problems across childhood can undermine the development of higher-order cognitive abilities that support self-regulation and emotion regulation abilities in adolescents and adults without FASD (Friedman, Corley, Hewitt, & Wright Jr, 2009; Gregory et al., 2005; Gregory et al., 2009). It is well-established that early childhood is a critical period for the development of executive functions since the neural structures that support them, such as the prefrontal cortex, do not mature until later in adolescence (Gogtay et al., 2004). Notably, difficulties with cognitive functions that support self-regulation, executive functions in particular, and emotion regulation are common in people with FASD (Mattson, Bernes, & Doyle, 2019; Mattson, Crocker, & Nguyen, 2011). The degree to which chronic sleep problems across this critical neurodevelopmental period might compound these impairments in children with FASD should be investigated.

Our finding that children with confirmed heavy PAE had more chronic sleep problems throughout childhood, after controlling for several potential confounding factors, supports the view that heavy PAE has a direct teratogenic effect on parts of the nervous system involved in sleep regulation (Inkelis & Thomas, 2018). However, the mechanisms that explain the harmful effect of heavy PAE on sleep regulation are unclear. It is possible that PAE might damage the neurobiological systems that underpin the ability to initiate and maintain a low arousal state, such as circuitry in the prefrontal cortex (Fryer et al., 2007; O'Hare et al., 2009), amygdala (Cullen, Burne, Lavidis, & Moritz, 2013; Raineki, Morgan, Ellis, & Weinberg, 2019), and HPA axis (Keiver et al., 2015; McLachlan et al., 2016), along with damage to GABAergic neurons throughout the cortex (Smiley et al., 2015). Melatonin signalling, which

regulates the timing of sleep, in the evening might also be impacted by heavy PAE (Goril et al., 2016). The genetic link between alcohol use problems and insomnia may also play a part (Kranzler et al., 2019). More research is needed to define the behavioural, neurobiological and genetic basis for sleep problems observed in children with heavy PAE, which may in turn lead to the development of more targeted interventions for improving their sleep.

There was no effect of moderate or low levels of PAE in the current study. There are mixed findings with regards to the effect of low and moderate PAE on developmental outcomes (Flak et al., 2014; Robinson et al., 2010; Skogerbø et al., 2012). It may be that, despite using a nationally representative cohort, the present study lacked statistical power to detect a more modest effect. Alternatively, other physical and psychosocial factors may be more powerful drivers of sleep problems in children with moderate PAE (May et al., 2013). It may also suggest a threshold effect of PAE, whereby a sufficiently heavy dose is required before detrimental effects are observed on developmental outcomes.

There was an unexpected significant protective effect of occasional PAE after adjusting for potential confounds. The effect of occasional PAE was relatively small, predicting a drop of 0.11 of a sleep problem at 2−3 years. Previous epidemiological studies of PAE have also found an apparent protective effect of low level PAE (Kelly et al., 2013; Kelly et al., 2009; McCormack et al., 2018; Robinson et al., 2010), even after propensity score matching (Kelly et al., 2013; McCormack et al., 2018). When children with occasional PAE were matched with children who had no PAE on key covariates that reflect adversity using propensity score matching, two of these purported protective effects on sleep behaviour were abolished. The abolishment of two of the three effects in the current study suggests that the positive effect of occasional drinking stems from residual variance associated with being from a higher SES/lower adversity background. This residual variance may not have been fully captured in

previous studies (McCormack et al., 2018) and perhaps was captured better in this study owing to the inclusion of parenting and family stress factors.

Several covariates contributed significantly to the occurrence of sleep problems across the 2- to 9-year period. Consistent with previous work, we found significant detrimental effects of hostile and overprotective parenting, family stress, and lower family income on the number of sleep problems reported throughout childhood (Bell & Belsky, 2008; El-Sheikh et al., 2013; Giallo et al., 2011; Kiel et al., 2015; Whitesell et al., 2018). These findings draw attention to how factors related to the family and material circumstances might contribute to sleep problems in children with FASD, in addition to the teratogenic effects of PAE (May et al., 2013). Reporting the presence of problems due to stress during pregnancy also contributed to the occurrence of sleep problems during childhood, which is in line with evidence of prenatal programming of the HPA axis (Glover, O'Connor, & O'Donnell, 2010; Hellemans, Sliwowska, Verma, & Weinberg, 2010) and highlights the need for antenatal support for families.

Unlike Stone et al. (2010), we did not find an effect of prenatal nicotine exposure on sleep problems. Differences in outcome measures (parent report of discrete sleep problems vs. amalgam of questionnaire items), developmental periods assessed (2−9 years vs 1−12 years), and populations assessed (slightly higher educated sample of population vs. at risk mums) in the current study compared to Stone et al.'s (2010) may underlie these conflicting findings. They may also reflect the difficulty in fully separating prenatal exposure to different substances based on retrospective report.

Finally, the pattern of slight increases in drinking across pregnancy reported in the LSAC may appear counterintuitive as some Australian surveys report that women reduce alcohol consumption as pregnancy progresses (Cameron, Davey, Kendall, Wilson, & McClure, 2013;

O'Keeffe et al., 2015). However, this pattern has also been found in another population study of alcohol use during pregnancy in Australia from a similar period. Hutchinson et al. (2018) found a similar increase (approximately 10%) in low level alcohol consumption from Trimester 1 to 3 in a sample of 1534 women recruited from 2009 to 2013. This pattern of drinking may have been context dependent and may be relate to public health messaging by the National Health and Medical Research Council in Australia from 2001 to 2009 (National Health and Medical Research Council, 2001), which suggested that drinking in small amounts during pregnancy was safe. A stronger abstinence message during pregnancy has occurred across time in Australia (National Health and Medical Research Council, 2009) with a notable increase in abstinence-oriented messaging from media reports in particular, occurring after the data in the above studies were collected (Cook, Leggat, & Pennay, 2020). This may have influenced the patterns of consumption found in Australian studies prior to updated abstinence-oriented public health messaging.

4.1 Limitations

Drinking during pregnancy was assessed through retrospective report, which is common practice in this field (Lange, Shield, Koren, Rehm, & Popova, 2014) and considered reliable (Robles & Day, 1990). Nonetheless, some women may under-report their alcohol use during pregnancy, and this may have led to an underestimation of the rate of heavy drinking during pregnancy. It is also possible that women reported that they abstained when they had not, potentially resulting in an under-estimate of the effects of PAE at all levels (Lange et al., 2014). Further efforts were made to ensure reliability by limiting the sample to the birth cohort, thereby limiting the time between potential drinking episodes and reporting.

Parent-reported sleep problems were used as outcome measures. Parent-report of sleep problems, while not gold standard, have been found to be consistent with recordings of sleep

behaviour and neurophysiology using more objective measures (Byars et al., 2012; Sadeh et al., 2011). While objective measures (e.g., electroencephalography) have been taken on infants with PAE during sleep revealing disrupted arousal regulation (Scher, Richardson, & Day, 2000), implementing objective measures in children with PAE or FASD may be challenging due to their issues with behavioural regulation and polypharmacy, which may in turn impact protocol adherence and the validity of recordings respectively (Chen et al., 2012). We used a nationally representative sample of the Australian population. Despite this, our estimates of the effects of moderate and heavy drinking were based on a relatively small sample, which is common for population studies of the developmental effects of PAE (O'Leary, Nassar, et al., 2010; Pesonen et al., 2009). Future research should attempt to further investigate the effects of heavier PAE in larger samples to obtain more reliable estimates.

5. Conclusion

The present study demonstrates that heavy PAE is associated with 1.13 more parent-reported child sleep problems across childhood (2−9 years), at 2- to 3-years and 6- to 7-years of age in particular. Heavy PAE also significantly increases the probability of having persistent problems across the 2- to 9-year period by 22.57%. Notably, adjusting for confounding factors reduced the effect of PAE, suggesting that greater sleep problems in children with heavy PAE can in part be explained by other factors associated with heavy drinking in pregnancy. Also, when children with occasional PAE were matched with children who had no PAE on key covariates that reflect adversity using propensity score matching, most of the purported protective effects on sleep behaviour were abolished.

Overall, these findings support the argument that sleep problems in children with FASD might stem partially from the teratogenic effects of exposure to alcohol in utero. Thus, parents of young children who present with sleep problems should be asked about their

alcohol use during pregnancy. Young children with heavy PAE should be monitored

throughout childhood as they may not simply "grow out" of their sleep problems, since our

findings suggest they are at a significantly higher risk of developing chronic sleep problems.

Instead, they should be assessed for FASD, and may require long-term intervention to

improve their sleep regulation. Future research should investigate the pathways that lead

children with heavy PAE to develop persistent sleep problems and how we can effectively

intervene to improve persistent sleep problems and neuropsychological functioning in this

clinical population.

References

Astill, R. G., Van der Heijden, K. B., Van IJzendoorn, M. H., & Van Someren, E. J. (2012). Sleep, cognition, and behavioral problems in school-age children: A century of research meta-analyzed. *Psychol. Bull., 138*(6), 1109.

Australian Bureau Of Statistics. (2006). Census of population and housing. *Australian Government, Canberra.*

Bell, B. G., & Belsky, J. (2008). Parents, parenting, and children's sleep problems: Exploring reciprocal effects. *Br. J. Dev. Psychol., 26*(4), 579-593.

Bernier, A., Beauchamp, M. H., Bouvette-Turcot, A.-A., Carlson, S. M., & Carrier, J. (2013). Sleep and Cognition in Preschool Years: Specific Links to Executive Functioning. *Child Dev., 84*(5), 1542-1553. doi:doi:10.1111/cdev.12063

Byars, K. C., Yolton, K., Rausch, J., Lanphear, B., & Beebe, D. W. (2012). Prevalence, patterns, and persistence of sleep problems in the first 3 years of life. *Pediatrics, 129*(2), e276-e284.

Cameron, C. M., Davey, T. M., Kendall, E., Wilson, A., & McClure, R. J. (2013). Changes in alcohol consumption in pregnant Australian women between 2007 and 2011. *Med. J. Aust., 199*(5), 355-357.

Chen, M. L., Olson, H. C., Picciano, J. F., Starr, J. R., & Owens, J. (2012). Sleep problems in children with fetal alcohol spectrum disorders. *J. Clin. Sleep Med., 8*(04), 421-429.

Colvin, L., Payne, J., Parsons, D., Kurinczuk, J. J., & Bower, C. (2007). Alcohol consumption during pregnancy in nonindigenous west Australian women. *Alcoholism: Clinical and Experimental Research, 31*(2), 276-284.

Cook, M., Leggat, G., & Pennay, A. (2020). Change Over Time in Australian Newspaper Reporting of Drinking During Pregnancy: A Content Analysis (2000–2017). *Alcohol Alcohol.*

Cooklin, A. R., Giallo, R., D'Esposito, F., Crawford, S., & Nicholson, J. M. (2013). Postpartum maternal separation anxiety, overprotective parenting, and children's social-emotional well-being: Longitudinal evidence from an Australian cohort. *J. Fam. Psychol., 27*(4), 618.

Cullen, C. L., Burne, T. H., Lavidis, N. A., & Moritz, K. M. (2013). Low dose prenatal ethanol exposure induces anxiety-like behaviour and alters dendritic morphology in the basolateral amygdala of rat offspring. *PLoS One, 8*(1), e54924.

Dahl, R. E. (1996). The regulation of sleep and arousal: Development and psychopathology. *Dev. Psychopathol., 8*(1), 3-27.

Davis, D. H., & Thoman, E. B. (1987). Behavioral states of premature infants: Implications for neural and behavioral development. *Dev. Psychobiol., 20*(1), 25-38.

Eekhout, I., de Vet, H. C., Twisk, J. W., Brand, J. P., de Boer, M. R., & Heymans, M. W. (2014). Missing data in a multi-item instrument were best handled by multiple imputation at the item score level. *J. Clin. Epidemiol., 67*(3), 335-342.

El-Sheikh, M., Bagley, E. J., Keiley, M., Elmore-Staton, L., Chen, E., & Buckhalt, J. A. (2013). Economic adversity and children's sleep problems: Multiple indicators and moderation of effects. *Health Psychol., 32*(8), 849.

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. *Alcohol. Clin. Exp. Res., 38*(1), 214-226.

Friedman, N. P., Corley, R. P., Hewitt, J. K., & Wright Jr, K. P. (2009). Individual differences in childhood sleep problems predict later cognitive executive control. *Sleep, 32*(3), 323-333.

Fryer, S. L., Tapert, S. F., Mattson, S. N., Paulus, M. P., Spadoni, A. D., & Riley, E. P. (2007). Prenatal alcohol exposure affects frontal–striatal BOLD response during inhibitory control. *Alcoholism: Clinical and Experimental Research, 31*(8), 1415-1424.

Giallo, R., Rose, N., & Vittorino, R. (2011). Fatigue, wellbeing and parenting in mothers of infants and toddlers with sleep problems. *J. Reprod. Infant Psychol., 29*(3), 236-249.

Glover, V., O'Connor, T., & O'Donnell, K. (2010). Prenatal stress and the programming of the HPA axis. *Neurosci. Biobehav. Rev., 35*(1), 17-22.

Gogtay, N., Giedd, J. N., Lusk, L., Hayashi, K. M., Greenstein, D., Vaituzis, A. C., . . . Toga, A. W. (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proceedings of the National Academy of Sciences, 101*(21), 8174-8179.

Goril, S., Zalai, D., Scott, L., & Shapiro, C. M. (2016). Sleep and melatonin secretion abnormalities in children and adolescents with fetal alcohol spectrum disorders. *Sleep Med., 23*, 59-64.

Gregory, A. M., Caspi, A., Eley, T. C., Moffitt, T. E., O'Connor, T. G., & Poulton, R. (2005). Prospective longitudinal associations between persistent sleep problems in childhood and anxiety and depression disorders in adulthood. *J. Abnorm. Child Psychol., 33*(2), 157-163.

Gregory, A. M., Caspi, A., Moffitt, T. E., & Poulton, R. (2009). Sleep problems in childhood predict neuropsychological functioning in adolescence. *Pediatrics, 123*(4), 1171-1176.

Haley, D. W., Handmaker, N. S., & Lowe, J. (2006). Infant stress reactivity and prenatal alcohol exposure. *Alcohol. Clin. Exp. Res., 30*(12), 2055-2064.

Hanlon-Dearman, A., Chen, M. L., & Olson, H. C. (2017). Understanding and managing sleep disruption in children with fetal alcohol spectrum disorder. *Biochem. Cell Biol., 96*(2), 267-274.

Hellemans, K. G., Sliwowska, J. H., Verma, P., & Weinberg, J. (2010). Prenatal alcohol exposure: fetal programming and later life vulnerability to stress, depression and anxiety disorders. *Neuroscience & Biobehavioral Reviews, 34*(6), 791-807.

Hutchinson, D., Moore, E. A., Breen, C., Burns, L., & Mattick, R. P. (2013). Alcohol use in pregnancy: Prevalence and predictors in the Longitudinal Study of Australian Children. *Drug and Alcohol Review, 32*(5), 475-482.

Hutchinson, D., Wilson, J., Allsop, S., Elliott, E., Najman, J., Burns, L., . . . McCormack, C. (2018). Cohort Profile: The Triple B Pregnancy Cohort Study: A longitudinal study of the relationship between alcohol, tobacco and other substance use during pregnancy and the health and well-being of Australian children and families. *Int. J. Epidemiol., 47*(1), 26-27m.

Inkelis, S. M., & Thomas, J. D. (2018). Sleep in Infants and Children with Prenatal Alcohol Exposure. *Alcohol. Clin. Exp. Res., 42*(8), 1390-1405.

Ipsiroglu, O. S., McKellin, W. H., Carey, N., & Loock, C. (2013). "They silently live in terror…" why sleep problems and night-time related quality-of-life are missed in children with a fetal alcohol spectrum disorder. *Soc. Sci. Med., 79*, 76-83.

Ipsiroglu, O. S., Wind, K., Hung, Y.-H. A., Berger, M., Chan, F., Yu, W., . . . Weinberg, J. (2019). Prenatal alcohol exposure and sleep-wake behaviors: exploratory and naturalistic observations in the clinical setting and in an animal model. *Sleep Med., 54*, 101-112.

Kable, J. A., & Coles, C. D. (2004). The impact of prenatal alcohol exposure on neurophysiological encoding of environmental events at six months. *Alcohol. Clin. Exp. Res., 28*(3), 489-496.

Kambeitz, C., Klug, M. G., Greenmyer, J., Popova, S., & Burd, L. (2019). Association of adverse childhood experiences and neurodevelopmental disorders in people with fetal alcohol spectrum disorders (FASD) and non-FASD controls. *BMC Pediatr., 19*(1), 1-9.

Keiver, K., Bertram, C. P., Orr, A. P., & Clarren, S. (2015). Salivary cortisol levels are elevated in the afternoon and at bedtime in children with prenatal alcohol exposure. *Alcohol, 49*(1), 79-87.

Kelly, Y., Iacovou, M., Quigley, M. A., Gray, R., Wolke, D., Kelly, J., & Sacker, A. (2013). Light drinking versus abstinence in pregnancy–behavioural and cognitive outcomes in 7-year-old children: a longitudinal cohort study. *BJOG, 120*(11), 1340-1347.

Kelly, Y., Sacker, A., Gray, R., Kelly, J., Wolke, D., & Quigley, M. A. (2009). Light drinking in pregnancy, a risk for behavioural problems and cognitive deficits at 3 years of age? *Int. J. Epidemiol., 38*(1), 129-140.

Kiel, E. J., Hummel, A. C., & Luebbe, A. M. (2015). Cortisol secretion and change in sleep problems in early childhood: moderation by maternal overcontrol. *Biol. Psychol., 107*, 52-60.

Kranzler, H. R., Zhou, H., Kember, R. L., Smith, R. V., Justice, A. C., Damrauer, S., . . . Reid, J. (2019). Genome-wide association study of alcohol consumption and use disorder in 274,424 individuals from multiple populations. *Nature communications, 10*(1), 1-11.

Lam, P., Hiscock, H., & Wake, M. (2003). Outcomes of infant sleep problems: a longitudinal study of sleep, behavior, and maternal well-being. *Pediatrics, 111*(3), e203-e207.

Lange, S., Shield, K., Koren, G., Rehm, J., & Popova, S. (2014). A comparison of the prevalence of prenatal alcohol exposure obtained via maternal self-reports versus meconium testing: a systematic literature review and meta-analysis. *BMC Pregnancy Childbirth, 14*(1), 127.

Leeper, T. J., Arnold, J., & Arel-Bundock, V. (2018). Package 'margins' (Version 0.3.23). Retrieved from https://github.com/leeper/margins

Liao, T. F. (1994). *Interpreting probability models: Logit, probit, and other generalized linear models*: Sage.

Luppi, P.-H., & Fort, P. (2018). Neuroanatomical and neurochemical bases of vigilance states. In *Sleep-Wake Neurobiology and Pharmacology* (pp. 35-58): Springer.

Mattson, S. N., Bernes, G. A., & Doyle, L. R. (2019). Fetal alcohol spectrum disorders: a review of the neurobehavioral deficits associated with prenatal alcohol exposure. *Alcoholism: Clinical and Experimental Research, 43*(6), 1046-1062.

Mattson, S. N., Crocker, N., & Nguyen, T. T. (2011). Fetal alcohol spectrum disorders: neuropsychological and behavioral features. *Neuropsychol. Rev., 21*(2), 81-101.

May, P. A., Tabachnick, B. G., Gossage, J. P., Kalberg, W. O., Marais, A.-S., Robinson, L. K., . . . Hoyme, H. E. (2013). Maternal factors predicting cognitive and behavioral characteristics of children with fetal alcohol spectrum disorders. *J. Dev. Behav. Pediatr., 34*(5), 314.

McCormack, C., Hutchinson, D., Burns, L., Youssef, G., Wilson, J., Elliott, E., . . . Rossen, L. (2018). Maternal and partner prenatal alcohol use and infant cognitive development. *Drug Alcohol Depend., 185*, 330-338.

McLachlan, K., Rasmussen, C., Oberlander, T. F., Loock, C., Pei, J., Andrew, G., . . . Weinberg, J. (2016). Dysregulation of the cortisol diurnal rhythm following prenatal alcohol exposure and early life adversity. *Alcohol, 53*, 9-18.

Mughal, R., Joyce, A., Hill, C., & Dimitriou, D. (2020). Sleep disturbance as a predictor of anxiety in children with Fetal Alcohol Spectrum Disorders and typically developing children. *Res. Dev. Disabil., 101*, 103610.

National Health and Medical Research Council. (2001). *Australian Alcohol Guidelines: Health Risks and Benefits*. Canberra: Commonwealth of Australia

National Health and Medical Research Council. (2009). *Australian Guidelines to Reduce Health Risks from Drinking Alcohol*. Canberra: Commonwealth of Australia

Nixon, G. M., Thompson, J. M., Han, D. Y., Becroft, D. M., Clark, P. M., Robinson, E., . . . Mitchell, E. A. (2008). Short sleep duration in middle childhood: risk factors and consequences. *Sleep, 31*(1), 71-78.

O'Connor, M. J., Kogan, N., & Findlay, R. (2002). Prenatal alcohol exposure and attachment behavior in children. *Alcohol. Clin. Exp. Res., 26*(10), 1592-1602.

O'Connor, T. G., Caprariello, P., Blackmore, E. R., Gregory, A. M., Glover, V., Fleming, P., & Team, A. S. (2007). Prenatal mood disturbance predicts sleep problems in infancy and toddlerhood. *Early Hum. Dev., 83*(7), 451-458.

O'Hare, E. D., Lu, L. H., Houston, S. M., Bookheimer, S. Y., Mattson, S. N., O'connor, M. J., & Sowell, E. R. (2009). Altered frontal-parietal functioning during verbal working memory in children and adolescents with heavy prenatal alcohol exposure. *Hum. Brain Mapp., 30*(10), 3200-3208.

O'Keeffe, L. M., Kearney, P. M., McCarthy, F. P., Khashan, A. S., Greene, R. A., North, R. A., . . . Dekker, G. A. (2015). Prevalence and predictors of alcohol use during pregnancy: findings from international multicentre cohort studies. *BMJ open, 5*(7).

O'Leary, C. M., Bower, C., Zubrick, S. R., Geelhoed, E., Kurinczuk, J. J., & Nassar, N. (2010). A new method of prenatal alcohol classification accounting for dose, pattern and timing of exposure: improving our ability to examine fetal effects from low to moderate alcohol. *J. Epidemiol. Community Health, 64*(11), 956-962.

O'Leary, C. M., Nassar, N., Zubrick, S. R., Kurinczuk, J. J., Stanley, F., & Bower, C. (2010). Evidence of a complex association between dose, pattern and timing of prenatal alcohol exposure and child behaviour problems. *Addiction, 105*(1), 74-86.

Paavonen, E. J., Räikkönen, K., Pesonen, A.-K., Lahti, J., Komsi, N., Heinonen, K., . . . Porkka-Heiskanen, T. (2010). Sleep quality and cognitive performance in 8-year-old children. *Sleep Med., 11*(4), 386-392.

Patten, A. R., Fontaine, C. J., & Christie, B. R. (2014). A Comparison of the Different Animal Models of Fetal Alcohol Spectrum Disorders and Their Use in Studying Complex Behaviors. *Frontiers in Pediatrics, 2*(93). doi:10.3389/fped.2014.00093

Pesonen, A.-K., Räikkönen, K., Matthews, K., Heinonen, K., Paavonen, J. E., Lahti, J., . . . Kajantie, E. (2009). Prenatal origins of poor sleep in children. *Sleep, 32*(8), 1086-1092.

Pishgar, F. (2020). Package 'MatchThem' (Version 0.9.3): CRAN. Retrieved from https://github.com/FarhadPishgar/MatchThem

Quach, J., Hiscock, H., & Wake, M. (2012). Sleep problems and mental health in primary school new entrants: Cross-sectional community-based study. *J. Paediatr. Child Health, 48*(12), 1076-1081.

Quach, J. L., Nguyen, C. D., Williams, K. E., & Sciberras, E. (2018). Bidirectional associations between child sleep problems and internalizing and externalizing difficulties from preschool to early adolescence. *Arch. Pediatr. Adolesc. Med., 172*(2), e174363-e174363.

R Core Team. (2019). R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from http://www.R-project.org/.

Raineki, C., Morgan, E. J., Ellis, L., & Weinberg, J. (2019). Glucocorticoid receptor expression in the stress-limbic circuitry is differentially affected by prenatal alcohol exposure and adolescent stress. *Brain Res., 1718*, 242-251.

Reid, P., & Lewis-Jones, M. (1995). Sleep difficulties and their management in preschoolers with atopic eczema. *Clin. Exp. Dermatol., 20*(1), 38-41.

Robinson, M., Oddy, W., McLean, N., Jacoby, P., Pennell, C., De Klerk, N., . . . Newnham, J. (2010). Low–moderate prenatal alcohol exposure and risk to child behavioural development: a prospective cohort study. *BJOG, 117*(9), 1139-1152.

Robles, N., & Day, N. L. (1990). Recall of alcohol consumption during pregnancy. *J. Stud. Alcohol, 51*(5), 403-407.

Rosen, C. L., Larkin, E. K., Kirchner, H. L., Emancipator, J. L., Bivins, S. F., Surovec, S. A., . . . Redline, S. (2003). Prevalence and risk factors for sleep-disordered breathing in 8- to 11-year-old children: association with race and prematurity. *J. Pediatr., 142*(4), 383-389.

Sadeh, A., Mindell, J., & Rivera, L. (2011). "My child has a sleep problem": a cross-cultural comparison of parental definitions. *Sleep Med., 12*(5), 478-482.

Scher, M. S., Richardson, G. A., & Day, N. L. (2000). Effects of prenatal cocaine/crack and other drug exposure on electroencephalographic sleep studies at birth and one year. *Pediatrics, 105*(1), 39-48.

Shang, C. Y., Gau, S. S. F., & Soong, W. T. (2006). Association between childhood sleep problems and perinatal factors, parental mental distress and behavioral problems. *J. Sleep Res., 15*(1), 63-73.

Skogerbø, Å., Kesmodel, U. S., Wimberley, T., Støvring, H., Bertrand, J., Landrø, N. I., & Mortensen, E. L. (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.

Smiley, J. F., Saito, M., Bleiwas, C., Masiello, K., Ardekani, B., Guilfoyle, D. N., . . . Vadasz, C. (2015). Selective reduction of cerebral cortex GABA neurons in a late gestation model of fetal alcohol spectrum disorder. *Alcohol, 49*(6), 571-580.

Soloff, C., Lawrence, D., & Johnstone, R. (2005). *Growing up in Australia: the longitudinal study of Australian children* . *LSAC Technical Paper Number 1: Sample Design*. Retrieved from http://www.aifs.gov.au/growingup/pubs/technical/tp1.pdf

Spruyt, K., Ipsiroglu, O., Stockler, S., & Reynolds, J. N. (2018). Challenging sleep-wake behaviors reported in informal, conversational interviews of caregivers of children

with fetal alcohol spectrum disorder. *International Journal of Developmental Disabilities, 64*(2), 65-74.

Steinhausen, H. C., & Spohr, H. L. (1998). Long-term outcome of children with fetal alcohol syndrome: Psychopathology, behavior, and intelligence. *Alcohol. Clin. Exp. Res., 22*(2), 334-338.

Stéphan-Blanchard, E., Telliez, F., Léké, A., Djeddi, D., Bach, V., Libert, J.-P., & Chardon, K. (2008). The influence of in utero exposure to smoking on sleep patterns in preterm neonates. *Sleep, 31*(12), 1683-1689.

Sterne, J. A., White, I. R., Carlin, J. B., Spratt, M., Royston, P., Kenward, M. G., . . . Carpenter, J. R. (2009). Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ, 338*, b2393.

Stone, K. C., LaGasse, L. L., Lester, B. M., Shankaran, S., Bada, H. S., Bauer, C. R., & Hammond, J. A. (2010). Sleep problems in children with prenatal substance exposure: the Maternal Lifestyle study. *Arch. Pediatr. Adolesc. Med., 164*(5), 452-456.

Stone, W. S., Altman, H. J., Hall, J., Arankowsky-Sandoval, G., Parekh, P., & Gold, P. E. (1996). Prenatal exposure to alcohol in adult rats: relationships between sleep and memory deficits, and effects of glucose administration on memory. *Brain Res., 742*(1-2), 98-106.

Streissguth, A. P., Bookstein, F. L., Barr, H. M., Sampson, P. D., O'Malley, K., & Young, J. K. (2004). Risk factors for adverse life outcomes in fetal alcohol syndrome and fetal alcohol effects. *J. Dev. Behav. Pediatr., 25*(4), 228-238.

Tsai, K. M., Dahl, R. E., Irwin, M. R., Bower, J. E., McCreath, H., Seeman, T. E., . . . Fuligni, A. J. (2018). The roles of parental support and family stress in adolescent sleep. *Child Dev., 89*(5), 1577-1588.

Turnbull, K., Reid, G. J., & Morton, J. B. (2013). Behavioral sleep problems and their potential impact on developing executive function in children. *Sleep, 36*(7), 1077-1084.

van Buuren, S. (2018). *Flexible imputation of missing data*: Chapman and Hall/CRC.

van Buuren, S., Groothuis-Oudshoorn, K., Robitzsch, A., Vink, G., Doove, L., Jolani, S., . . . Gray, B. (2019). Multivariate Imputation by Chained Equations (Version 3.7.0). Retrieved from https://CRAN.R-project.org/package=mice

van Maanen, A., Wijga, A. H., Gehring, U., Postma, D. S., Smit, H. A., Oort, F. J., . . . Meijer, A. M. (2013). Sleep in children with asthma: results of the PIAMA study. *Eur. Respir. J., 41*(4), 832-837.

Volgin, D. V., & Kubin, L. (2012). Reduced sleep and impaired sleep initiation in adult male rats exposed to alcohol during early postnatal period. *Behav. Brain Res., 234*(1), 38-42.

Von Hippel, P. T. (2009). How to impute interactions, squares, and other transformed variables. *Sociol. Methodol., 39*(1), 265-291.

Wengel, T., Hanlon-Dearman, A. C., & Fjeldsted, B. (2011). Sleep and sensory characteristics in young children with fetal alcohol spectrum disorder. *J. Dev. Behav. Pediatr., 32*(5), 384-392.

Whitesell, C. J., Crosby, B., Anders, T. F., & Teti, D. M. (2018). Household chaos and family sleep during infants' first year. *J. Fam. Psychol., 32*(5), 622.

Williams, K. E., Berthelsen, D., Walker, S., & Nicholson, J. M. (2017). A developmental cascade model of behavioral sleep problems and emotional and attentional self-regulation across early childhood. *Behav. Sleep Med., 15*(1), 1-21.

Williamson, A. A., Mindell, J. A., Hiscock, H., & Quach, J. (2019). Child sleep behaviors and sleep problems from infancy to school-age. *Sleep Med., 63*, 5-8.

Wilson, D., Masiello, K., Lewin, M., Hui, M., Smiley, J., & Saito, M. (2016). Developmental ethanol exposure-induced sleep fragmentation predicts adult cognitive impairment. *Neuroscience, 322*, 18-27.

Zubrick, S. R., Lucas, N., Westrupp, E. M., & Nicholson, J. M. (2014). Parenting measures in the Longitudinal Study of Australian Children: Construct validity and measurement quality, Waves 1 to 4. *Canberra: Department of Social Services*.

Table 1. Demographic information by prenatal alcohol exposure category

	Overall	Prenatal Alcohol Exposure Category				
		Abstainer	Occasional	Low	Moderate	Heavy
N (%)	3447 (100)	2081 (60.37)	906 (26.28)	402 (11.66)	33 (0.96)	25 (0.73)
Wave 1 Variables (0-1 year)						
Child sex = Male (%)	1763 (51.1)	1048 (50.4)	445 (49.1)	237 (59.0)	20 (60.6)	13 (52.0)
Child birth weight (%)						
Extremely low birthweight (< 1000g)	8 (0.2)	7 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Very low birthweight (1000g-1499g)	13 (0.4)	9 (0.4)	2 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)
Low birthweight (1500g-2499g)	159 (4.6)	111 (5.3)	32 (3.5)	13 (3.2)	1 (3.0)	2 (8.0)
Greater than low birthweight (2500g or more)	3267 (94.8)	1954 (93.9)	871 (96.1)	387 (96.3)	32 (97.0)	23 (92.0)
Child gestational age (%)						
Pre-term (<37 weeks)	216 (6.3)	139 (6.7)	46 (5.1)	26 (6.5)	2 (6.1)	3 (12.0)
Term (37-41.99 weeks)	3082 (89.4)	1863 (89.5)	822 (90.7)	344 (85.6)	31 (93.9)	22 (88.0)
Post-term (42 weeks or more)	149 (4.3)	79 (3.8)	38 (4.2)	32 (8.0)	0 (0.0)	0 (0.0)
Ave daily cigarettes during pregnancy (mean (SD))	1.10 (3.64)	1.09 (3.46)	0.88 (3.30)	0.80 (2.95)	6.17 (9.02)	7.27 (10.99)
Maternal age Wave 1 (mean (SD))	31.41 (5.08)	30.74 (5.31)	32.13 (4.42)	33.23 (4.55)	29.36 (5.44)	34.04 (3.62)
Maternal marriage status Wave 1 (%)						
Married	2668 (77.4)	1568 (75.3)	751 (82.9)	322 (80.1)	13 (39.4)	14 (56.0)
Divorced	92 (2.7)	54 (2.6)	22 (2.4)	13 (3.2)	1 (3.0)	2 (8.0)
Separated	47 (1.4)	37 (1.8)	4 (0.4)	4 (1.0)	2 (6.1)	0 (0.0)
Widowed	8 (0.2)	6 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	1 (4.0)
Never Married	632 (18.3)	416 (20.0)	128 (14.1)	63 (15.7)	17 (51.5)	8 (32.0)
Family income category (%)						
Up to $25 999	492 (14.3)	369 (17.7)	69 (7.6)	34 (8.5)	10 (30.3)	10 (40.0)
Between $26 000 and $41 599	927 (26.9)	618 (29.7)	223 (24.6)	74 (18.4)	9 (27.3)	3 (12.0)
$41 600 and over	2028 (58.8)	1094 (52.6)	614 (67.8)	294 (73.1)	14 (42.4)	12 (48.0)

Maternal education (%)						
Completed up to Year 11	917 (26.6)	620 (29.8)	194 (21.4)	77 (19.2)	19 (57.6)	7 (28.0)
Completed up to Year 12	1259 (36.5)	798 (38.3)	317 (35.0)	124 (30.8)	11 (33.3)	9 (36.0)
Completed a Tertiary Degree or Diploma	1271 (36.9)	663 (31.9)	395 (43.6)	201 (50.0)	3 (9.1)	9 (36.0)
Wave 2 Variables (2-3 years)						
Child BMI Wave 2 (mean (SD))	16.81 (1.58)	16.82 (1.63)	16.78 (1.49)	16.80 (1.46)	17.11 (2.14)	17.00 (1.13)
Child age (months) Wave 2 (mean (SD))	149.03 (12.51)	149.69 (12.73)	147.59 (11.80)	148.99 (12.71)	147.00 (12.34)	149.96 (12.51)
Stressful life index score Wave 2 (mean (SD))	1.27 (1.35)	1.26 (1.40)	1.29 (1.32)	1.23 (1.18)	1.50 (1.65)	1.41 (1.53)
Child asthma status Wave 2 = Yes (%)	449 (13.4)	288 (14.3)	108 (12.2)	44 (11.3)	5 (16.1)	4 (16.0)
Child eczema status Wave 2 = Yes (%)	608 (18.1)	351 (17.3)	168 (18.9)	80 (20.3)	4 (12.9)	5 (20.0)
Mother warm parenting Wave 2 (mean (SD))	4.62 (0.41)	4.64 (0.40)	4.60 (0.41)	4.58 (0.42)	4.69 (0.33)	4.59 (0.34)
Mother hostile parenting Wave 2 (mean (SD))	3.21 (1.34)	3.15 (1.33)	3.25 (1.30)	3.39 (1.41)	3.11 (1.59)	3.36 (1.50)
Mother overprotective parenting Wave 2 (mean (SD))	3.64 (0.68)	3.72 (0.69)	3.53 (0.66)	3.52 (0.62)	3.69 (0.75)	3.53 (0.60)
Wave 3 Variables (4-5 years)						
Child BMI Wave 3 (mean (SD))	16.31 (1.72)	16.34 (1.81)	16.25 (1.60)	16.26 (1.55)	16.26 (1.51)	16.53 (0.99)
Child age (months) Wave 3 (mean (SD))	252.05 (12.24)	252.46 (12.49)	250.90 (11.54)	252.62 (12.30)	250.55 (13.12)	252.22 (11.46)
Stressful life index score Wave 3 (mean (SD))	0.98 (1.25)	0.98 (1.24)	0.99 (1.30)	0.89 (1.14)	1.52 (1.29)	1.09 (1.44)
Child asthma status Wave 3 = Yes (%)	682 (20.3)	423 (21.0)	171 (19.2)	74 (18.7)	8 (25.8)	6 (26.1)
Child eczema status Wave 3 = Yes (%)	486 (14.4)	278 (13.7)	136 (15.3)	64 (16.1)	4 (12.9)	4 (17.4)
Mother warm parenting Wave 3 (mean (SD))	4.50 (0.47)	4.52 (0.48)	4.48 (0.45)	4.46 (0.47)	4.65 (0.37)	4.40 (0.57)
Mother hostile parenting Wave 3 (mean (SD))	3.17 (1.26)	3.13 (1.28)	3.20 (1.19)	3.30 (1.28)	3.33 (1.53)	3.18 (1.33)
Mother overprotective parenting Wave 3 (mean (SD))	3.56 (0.69)	3.65 (0.70)	3.47 (0.65)	3.34 (0.61)	3.71 (0.65)	3.58 (0.76)
Wave 4 Variables (6-7 years)						
Child BMI Wave 4 (mean (SD))	16.49 (2.16)	16.57 (2.35)	16.37 (1.97)	16.32 (1.60)	16.82 (1.68)	16.36 (1.35)
Child age (months) Wave 4 (mean (SD))	357.73 (15.31)	358.28 (15.51)	356.86 (15.07)	357.22 (14.92)	354.79 (14.93)	356.92 (12.73)
Stressful life index score Wave 4 (mean (SD))	2.64 (2.30)	2.62 (2.33)	2.70 (2.29)	2.49 (2.13)	3.55 (2.76)	3.17 (2.59)

Child asthma status Wave 4 = Yes (%)	802 (24.8)	490 (25.4)	204 (23.5)	95 (25.0)	6 (21.4)	7 (28.0)
Child eczema status Wave 4 = Yes (%)	430 (13.2)	233 (12.0)	130 (14.9)	62 (16.2)	2 (6.9)	3 (12.0)
Mother warm parenting Wave 4 (mean (SD))	4.54 (0.49)	4.56 (0.50)	4.52 (0.47)	4.51 (0.48)	4.58 (0.57)	4.54 (0.55)
Mother hostile parenting Wave 4 (mean (SD))	1.94 (0.52)	1.91 (0.52)	1.97 (0.52)	2.00 (0.52)	2.06 (0.55)	1.81 (0.58)
Mother overprotective parenting Wave 4 (mean (SD))	3.43 (0.68)	3.53 (0.70)	3.30 (0.63)	3.22 (0.61)	3.47 (0.78)	3.54 (0.72)
Wave 5 Variables (8-9 years)						
Child BMI Wave 5 (mean (SD))	17.52 (2.79)	17.69 (3.01)	17.25 (2.50)	17.23 (2.24)	18.09 (2.20)	17.85 (2.63)
Child age (months) Wave 5 (mean (SD))	465.57 (15.93)	465.66 (16.01)	465.01 (15.54)	466.28 (16.28)	464.50 (16.21)	468.24 (18.10)
Stressful life index score Wave 5 (mean (SD))	2.52 (2.40)	2.50 (2.45)	2.58 (2.36)	2.43 (2.20)	2.75 (2.52)	3.79 (2.43)
Child asthma status Wave 5 = Yes (%)	810 (26.2)	493 (26.9)	203 (24.3)	102 (27.6)	5 (17.9)	7 (28.0)
Child eczema status Wave 5 = Yes (%)	379 (12.2)	215 (11.7)	113 (13.5)	43 (11.7)	4 (14.3)	4 (16.0)
Mother warm parenting Wave 5 (mean (SD))	4.44 (0.54)	4.45 (0.55)	4.41 (0.52)	4.42 (0.52)	4.42 (0.61)	4.41 (0.55)
Mother hostile parenting Wave 5 (mean (SD))	1.96 (0.52)	1.93 (0.52)	2.00 (0.51)	1.99 (0.52)	2.02 (0.51)	1.78 (0.41)
Mother overprotective parenting Wave 5 (mean (SD))	3.39 (0.69)	3.50 (0.70)	3.25 (0.65)	3.17 (0.61)	3.50 (0.72)	3.36 (0.63)

Notes. Family income and maternal education grouped for descriptive purposes. Data from Waves 2-5 based on complete data.

Table 2. Frequency and quantity of alcohol consumption during pregnancy by prenatal alcohol exposure category

Alcohol Consumption	Overall	Prenatal Alcohol Exposure Category				
		Abstainers	Occasional	Low	Moderate	Heavy
Quantity per drinking occasion (%)						
None	2081 (60.4)	2081 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1 or 2 drinks per occasion	1320 (38.3)	0 (0.0)	906 (100.0)	402 (100.0)	0 (0.0)	12 (48.0)
3 or 4 drinks per occasion	41 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	33 (100.0)	8 (32.0)
5 or 6 drinks per occasion	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)
7 to 10 drinks per occasion	2 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.0)
11 or more drinks per occasion	2 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.0)
Frequency Trimester 1 (%)						
Never	2552 (74.0)	2081 (100.0)	333 (36.8)	135 (33.6)	3 (9.1)	0 (0.0)
Occasionally	650 (18.9)	0 (0.0)	573 (63.2)	57 (14.2)	18 (54.5)	2 (8.0)
1-3 days per week	212 (6.2)	0 (0.0)	0 (0.0)	193 (48.0)	11 (33.3)	8 (32.0)
4-7 days per week	33 (1.0)	0 (0.0)	0 (0.0)	17 (4.2)	1 (3.0)	15 (60.0)
Frequency Trimester 2 (%)						
Never	2262 (65.6)	2081 (100.0)	141 (15.6)	35 (8.7)	4 (12.1)	1 (4.0)
Occasionally	839 (24.3)	0 (0.0)	765 (84.4)	55 (13.7)	18 (54.5)	1 (4.0)
1-3 days per week	316 (9.2)	0 (0.0)	0 (0.0)	296 (73.6)	11 (33.3)	9 (36.0)
4-7 days per week	30 (0.9)	0 (0.0)	0 (0.0)	16 (4.0)	0 (0.0)	14 (56.0)

Frequency Trimester 3 (%)						
Never	2201 (63.9)	2081 (100.0)	78 (8.6)	27 (6.7)	13 (39.4)	2 (8.0)
Occasionally	882 (25.6)	0 (0.0)	828 (91.4)	40 (10.0)	13 (39.4)	1 (4.0)
1-3 days per week	324 (9.4)	0 (0.0)	0 (0.0)	308 (76.6)	7 (21.2)	9 (36.0)
4-7 days per week	40 (1.2)	0 (0.0)	0 (0.0)	27 (6.7)	0 (0.0)	13 (52.0)

Table 3. Mean and standard deviations (SD) for each sleep outcome by prenatal alcohol exposure pooled across 48 imputations

Sleep Outcome	Overall		Prenatal Alcohol Exposure Category									
			Abstainers		Occasional		Low		Moderate		Heavy	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Persistent	0.20	0.40	0.22	0.41	0.17	0.38	0.19	0.39	0.15	0.36	0.50	0.51
Count 2-9yrs	2.03	2.45	2.13	2.53	1.82	2.33	1.82	2.11	2.1	1.88	4.00	3.68
Count 2-3yrs	0.73	1.00	0.78	1.04	0.64	0.93	0.69	0.93	0.75	1.01	1.32	1.18
Count 4-5yrs	0.50	0.85	0.52	0.87	0.46	0.82	0.43	0.78	0.51	0.69	0.84	1.07
Count 6-7yrs	0.40	0.75	0.41	0.76	0.37	0.73	0.37	0.69	0.47	0.75	1.08	1.32
Count 8-9yrs	0.40	0.77	0.42	0.79	0.35	0.75	0.33	0.69	0.37	0.67	0.76	0.93

Table 4. Model coefficients for each level of PAE on the number sleep problems across childhood[a], at each Wave[b], and on the odds of having persistent sleep problems relative to abstainers[a]

Outcome time point	Prenatal alcohol exposure category							
	Occasional		Low		Moderate		Heavy	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Negative binomial regression model estimates (95% confidence intervals)								
Childhood 2-9 years	-0.158 (-0.256, -0.059)	-0.109 (-0.207, -0.011)	-0.156 (-0.291, -0.020)	-0.077 (-0.212, 0.058)	-0.017 (-0.449, 0.415)	-0.186 (-0.604, 0.232)	0.628 (0.180, 1.076)	0.557 (0.127, 0.988)
2-3 years	-0.187 (-0.301, -0.074)	-0.162 (-0.277, -0.048)	-0.113 (-0.267, 0.040)	-0.073 (-0.228, 0.082)	-0.035 (-0.534, 0.463)	-0.206 (-0.702, 0.291)	0.533 (0.071, 0.995)	0.504 (0.053, 0.956)
4-5 years	-0.135 (-0.275, 0.005)	-0.091 (-0.232, 0.050)	-0.189 (-0.385, 0.006)	-0.109 (-0.306, 0.089)	-0.031 (-0.645, 0.582)	-0.243 (-0.842, 0.356)	0.468 (-0.132, 1.068)	0.419 (-0.166, 1.005)
6-7 years	-0.102 (-0.254, 0.052)	-0.049 (-0.203, 0.104)	-0.109 (-0.323, 0.105)	-0.027 (-0.243, 0.190)	0.130 (-0.529, 0.789)	-0.099 (-0.740, 0.542)	0.965 (0.402, 1.529)	0.847 (0.299, 1.396)
8-9 years	-0.188 (-0.353, -0.024)	-0.122 (-0.290, 0.045)	-0.246 (-0.478, -0.013)	-0.131 (-0.366, 0.104)	-0.153 (-0.931, 0.625)	-0.381 (-1.142, 0.381)	0.585 (-0.061, 1.232)	0.470 (-0.172, 1.112)
Logistic regression model estimates (95% confidence intervals)								

Persistent Problems 2-9 years	-0.330 (-0.536, -0.123)	-0.251 (-0.470, -0.033)	-0.195 (-0.474, 0.084)	-0.059 (-0.356, 0.238)	-0.512 (-1.555, 0.529)	-0.916 (-2.015, 0.183)	1.265 (0.458, 2.072)	1.130 (0.274, 1.986)

[a]Models were adjusted using several covariates: child sex, child birth weight group (categorical), child prematurity (categorical), child BMI averaged across childhood, child eczema and asthma status across childhood (binary), maternal age at Wave 1, maternal marital status at Wave 1 (categorical), maternal cigarette use during pregnancy, maternal stressful pregnancy (binary), maternal warm, hostile and overparenting parenting scales averaged across childhood, maternal education at Wave 1, family stress index averaged across childhood, family income

[b]Models were adjusted using several covariates: child sex, child age at the Wave, child birth weight group (categorical), child prematurity (categorical), child BMI at the Wave, child eczema and asthma statuses at the Wave (binary), maternal age at Wave 1, maternal marital status at Wave 1 (categorical), maternal cigarette use during pregnancy, maternal stressful pregnancy (binary), maternal warm, hostile, and overparenting parenting scales at the Wave, maternal education at Wave 1, family stress index at the Wave, family income