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Low–moderate prenatal alcohol exposure and risk to child behavioural development: a prospective cohort study

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Objective To examine the association of fetal alcohol exposure during pregnancy with child and adolescent behavioural development.

Design The Western Australian Pregnancy Cohort (Raine) Study recruited 2900 pregnancies (1989–91) and the 14-year follow up was conducted between 2003 and 2006.

Setting Tertiary obstetric hospital in Perth, Western Australia.

Population The women in the study provided data at 18 and 34 weeks of gestation on weekly alcohol intake: no drinking, occasional drinking (up to one standard drink per week), light drinking (2–6 standard drinks per week), moderate drinking (7–10 standard drinks per week), and heavy drinking (11 or more standard drinks per week).

Methods Longitudinal regression models were used to analyse the effect of prenatal alcohol exposure on Child Behaviour Checklist (CBCL) scores over 14 years, assessed by continuous *z*-scores and clinical cutoff points, after adjusting for confounders.

Main outcome measure Their children were followed up at ages 2, 5, 8, 10 and 14 years. The CBCL was used to measure child behaviour.

Results Light drinking and moderate drinking in the first 3 months of pregnancy were associated with child CBCL *z*-scores indicative of positive behaviour over 14 years after adjusting for maternal and sociodemographic characteristics. These changes in *z*-score indicated a clinically meaningful reduction in total, internalising and externalising behavioural problems across the 14 years of follow up.

Conclusions Our findings do not implicate light–moderate consumption of alcohol in pregnancy as a risk factor in the epidemiology of child behavioural problems.

Keywords Alcohol, behaviour, child behaviour checklist, prenatal exposures, Raine Study.

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Introduction

High levels of alcohol consumption during pregnancy have a teratogenic influence on fetal development, resulting in physical, cognitive and behavioural deficits.[1] The devastating impact of extreme levels of exposure to ethanol in pregnancy is evidenced in conditions such as fetal alcohol spectrum disorder and fetal alcohol syndrome.[1] Some studies claim that prenatal exposure to alcohol has a dose–response mechanism, where light drinking shows an effect mainly on behavioural and adaptive function and high levels are associated with more serious developmental impact and problems.[2] These data suggest that alcohol exposure at levels common in nonaddicted individuals, and so-called 'social drinking', may still be associated with long-term risk.[3] Many researchers have noted that most empirical enquiry into the effects of alcohol exposure during pregnancy has focused on and emphasised the devastating effects of high levels of alcohol exposure, often neglecting the influence of light–moderate drinking.[4]

The studies that have examined the effects of low levels of exposure to alcohol and behavioural development have failed to reach consensus, perhaps in part due to a number of methodological limitations.[5] For example, the reliability of retrospective data collected up to 17 years postpregnancy has been questioned.[5] Further, cutoff points used to categorise alcohol consumption (for example, 'low', 'medium' and 'high') have varied across studies,[6,7] and small sample sizes have hindered others.[8]

Maternal alcohol consumption of as little as one alcoholic drink per week has been associated with adverse child behavioural outcomes in a recent study;[7] however, this study placed virtually all alcohol consumption in one category (i.e. greater than or equal to one standard drink per week) so that very different patterns of consumption could not be distinguished within this group.[7] In addition, these results were seen only using clinical cutoff points for problem behaviours rather than across the range of scores, the results were limited to girls and the findings were only demonstrable with overall rather than syndrome-specific scores. Sood *et al.*[6] described alcohol intake in terms of fluid ounces of absolute alcohol consumed per day, and found that mothers who had a daily intake greater than or equal to 0.3 US fl. oz absolute alcohol had children with an increased risk of poor behaviour. Depending on country-specific norms, this amount equates to between half a standard drink and one and a half standard drinks per day;[9] therefore, this study also grouped women at the lower range of alcohol consumption with women who reported much higher patterns of consumption.[6]

Given that almost half of all pregnancies are not planned,[10] with many women consuming alcohol unaware that they are pregnant, alcohol exposure in the first trimester of pregnancy is likely to be common. It is important that women who are pregnant or contemplating becoming pregnant have access to advice on alcohol use that is based on solid empirical evidence. The aim of this study was to use a prospective pregnancy cohort to explore the relationship between alcohol intake that was concurrently assessed during pregnancy and subsequent child total, internalising and externalising behaviour.

Methods

Study design

The Western Australian Pregnancy Cohort (Raine) Study is a prospective longitudinal pregnancy cohort study of 2868 live births. Women were recruited into a randomised controlled trial to evaluate the effects of repeated ultrasound in pregnancy between May 1989 and November 1991 ($n = 2900$) through the public antenatal clinic at King Edward Memorial Hospital (KEMH) and nearby private clinics in Perth, Western Australia.[11] Comprehensive data regarding social and demographic characteristics were collected at 18 weeks of gestation, with further data collection at 34 weeks of gestation. Detailed clinical assessments were performed at birth and the study children and their families were followed up at 1, 2, 3, 5, 8, 10 and 14 years of age by questionnaire, which included sociodemographic and behavioural data (2, 5, 8, 10 and 14 years only).

Participants

Complete details of enrolment methods have been published elsewhere.[11] Briefly, to be eligible for enrolment, the women were required to have a pregnancy between 16 and 20 weeks of gestation (average 18 weeks), sufficient English language skills, an expectation to deliver at KEMH, and an intention to reside in Western Australia to allow for future follow up of their child. The potential for introducing bias by using a tertiary referral centre sample was minimised by enrolling women who booked before 18 weeks of gestation, which excluded those referred with complications.[12] Ninety percent of eligible women agreed to participate in the study and informed consent to participate in the study was obtained from the mother of each child at enrolment and at each subsequent follow up. The Human Ethics Committee at KEMH and/or Princess Margaret Hospital for Children approved all protocols for the study.

Loss to follow up

We achieved a reasonably low rate of attrition over 14 years, with 1860 of the original 2868 live births participating in the 14-year follow up (357 deferred from participating, 412 had withdrawn from the study, 207 were lost to follow up and 32 were deceased). The original cohort more closely reflected those women referred to a tertiary centre in over-representing socially disadvantaged families; however, those who were socially disadvantaged were less likely to remain in the study in the early years.[13] The characteristics of those who participated in the 14-year follow up compared with those who did not participate in the 14-year follow up are presented in Table 1. The selective attrition resulted in the sociodemographic characteristics of the study families participating in the 14-year follow up being equivalent to the characteristics of the general Western Australian population.[14]

Outcome variables

Child behaviour

The Child Behaviour Checklist for Ages 2–3 (CBCL/2-3), a 99-item, empirically validated measure of child behaviour by parent report,[15] was used at the 2-year follow up. At further follow ups the 118-item CBCL for Ages 4–18 (CBCL/4-18) was administered.[16] The CBCL demonstrated good sensitivity (83% overall) and specificity (67% overall)

Table 1. Characteristics of participants in the 14-year follow up (who completed the CBCL) compared with nonparticipants in the 14-year follow up (missing data not shown, column percentages presented)

	Non-participants (*n* = 1124) %	Participants (*n* = 1744) %	*P*-value
Alcohol intake 18 weeks			
No drinking	59.3	51.5	0.028
Occasional drinking	20.0	25.5	
Light drinking	15.4	19.4	
Moderate drinking	3.3	2.1	
Heavy drinking	2.0	1.6	
Maternal age at conception			
<20 years	15.0	6.8	<0.001
20–24.9 years	25.6	18.9	
25–29.9 years	30.1	30.5	
30–34.9 years	21.1	28.1	
35+ years	8.3	15.7	
Maternal education at pregnancy			
<High school completion	74.1	59.6	<0.001
High school completion	25.9	40.4	
Father living with family			
Yes	82.5	90.1	<0.001
No	17.5	9.9	
Low family income in pregnancy			
≤$24 000 per annum	41.9	25.6	<0.001
>$24 000 per annum	58.1	74.4	
Smoking in pregnancy			
None	65.6	77.5	<0.001
1–5 daily	9.6	7.9	
6–10 daily	9.6	5.3	
11–15 daily	7.0	4.5	
16–20 daily	4.9	3.2	
21+ daily	3.3	1.5	
Stress events in pregnancy			
None	20.4	22.9	0.005
1–2 events	38.3	42.2	
3+ events	41.2	34.9	
Year 2 behavioural problems			
Total	13.5	10.8	0.056
Internalising	10.1	8.0	0.077
Externalising	14.4	12.8	0.193
Year 5 behavioural problems			
Total	24.3	20.3	0.032
Internalising	19.0	17.7	0.264
Externalising	23.1	19.4	0.041
Year 8 behavioural problems			
Total	21.0	18.8	0.162
Internalising	19.2	19.4	0.489
Externalising	21.0	17.3	0.043
Year 10 behavioural problems			
Total	18.1	14.4	0.051
Internalising	18.7	17.4	0.310
Externalising	14.9	12.1	0.093
	Non-participants Mean (SD)	**Participants Mean (SD)**	***P*-value**
Gestational age (weeks)	38.69 (2.12)	38.82 (2.15)	0.104
Birthweight (g)	3283 (576)	3333 (591)	0.030

to a clinical psychiatric diagnosis and good test–retest reliability in a Western Australian clinical calibration.[17]

Both CBCL instruments produce a raw score that was transformed into three summary *z*-scores for a) total behaviour, b) internalising (withdrawal, somatic complaints, anxious/depressed) behaviour, and c) externalising (delinquency, aggression) behaviour. The *z*-scores for total, internalising and externalising behaviour were used as continuous scores in this study, with higher scores reflecting more disturbed emotions and behaviours. The raw scores produced by the CBCL were also converted into *T*-scores (standardised by age and sex) for total, internalising and externalising behaviour.[16] The recommended clinical cutoff scores ($T \geq 60$) were applied to the CBCL *T*-scores, to obtain three binary variables indicative of clinically significant total, internalising and externalising problems.[16] By the term 'clinically significant', we are referring to maladaptive behaviour that falls within a defined clinical range for behavioural problems.[16]

Predictor variables

Alcohol

Participants were requested at 18 weeks of gestation to provide an estimate of the total number of drinks consumed per week in the first 3 months of pregnancy. They were asked again at 34 weeks of gestation to provide an estimate of how much they were currently drinking. Participants were informed that the information was being collected for research only and would not be used in any way to make judgements about individuals' behaviour. Participants were asked to indicate the number of a) glasses of wine, b) nips of spirits, c) cans or 375-ml bottles of full-strength beer, and d) cans or 375-ml bottles of low-alcohol beer. These data were converted into a continuous variable representing the total number of standard drinks per week, and from there we used a categorisation of five levels: no drinking; occasional drinking (up to one standard drink per week); light drinking (2–6 standard drinks per week); moderate drinking (7–10 standard drinks per week); and heavy drinking (11 or more standard drinks per week). One standard drink was equivalent to 10 g of absolute alcohol.[18] Given that there were no quantified safe levels of drinking during pregnancy at the time, the categorisations used were based on other recent work in the area[19] and guidelines for alcohol consumption for nonpregnant women at the time.[18]

Control variables

The control variables for adjustment in our analyses included numerous prenatal and perinatal factors known to have some relationship with prenatal alcohol intake and mental health outcomes in children. These variables included maternal sociodemographic information from the prenatal period as follows: maternal age, maternal education, family income, the presence of the biological father in the family home, and maternal experience of stressful events in pregnancy.[20] Maternal smoking during pregnancy (cigarettes per day) was included in the model, as was the child's age at each follow up. The General Functioning Scale from the McMaster Family Assessment Device was applied to measure family functioning at each follow up except at age 2 years (when data were not available).[21]

Statistical analyses

Frequency distributions were compared for all outcome, predictor and control variables and cross-tabulations determined the relationships between the outcome and predictor variables. We used a linear regression model with a random intercept (random effects model) to examine the ability of our predictor variables to effect changes on the continuous CBCL *z*-score and generalised estimating equations (GEE; a random effect logistic regression model) to assess whether such changes in score reflected clinically meaningful differences in child behavioural problems (i.e. CBCL ≥ 60). Both models account for repeated observations of the same individuals over time. Firstly, the predictor variables were included in the random effects model and analysed using continuous CBCL *z*-scores for total, internalising and externalising behaviour at each year as outcomes. We followed this analysis with the inclusion of all control variables into the model for multivariable analysis. We examined family functioning as a potential mediator of the relationship between alcohol intake in pregnancy and later behavioural outcomes but it did not alter our results and therefore it was left out of the final model. The interaction between alcohol consumption and the child's age (years) was examined to look for associations between consumption and trajectories of CBCL scores; however, this was not significant. To examine the association between the predictor variables and clinically significant *T*-scores (binary indicator), we included the predictor and the control variables into GEE models with an unstructured working correlation matrix specification. This provided the best goodness-of-fit compared with other correlation structures to estimate the prevalence of child behaviour problems over time using odds ratios (OR). We accounted for nonlinear dependence of behaviour problems on age by adjusting for age and age-squared in the multivariable model. SPSS 15.0 (Chicago, IL, USA) was used for the analyses.

Results

A total of 2370 children contributed some data to the follow-up analyses. There was good consistency between

alcohol intake reported at 18 and 34 weeks of gestation, with the majority either remaining the same or reducing their intake (Table 2). The percentage of children with behavioural problems at each follow up was reasonably consistent across all groups of maternal alcohol intake at 18 weeks (Table 3). Higher alcohol intake in the first 3 months of pregnancy was significantly associated with an older maternal age, the absence of the biological father in the family home and increased smoking in pregnancy ($P < 0.001$) (Table 4). Maternal education and family income at 18 weeks of gestation did not show significant associations with increasing intake of alcohol in pregnancy, and the total number of stress events in pregnancy also showed no significant trend in relation to alcohol intake.

Alcohol intake and CBCL *z*-scores

We examined the mean difference in CBCL *z*-scores according to maternal alcohol intake status compared with the children of women who did not drink at all. In the unadjusted analysis, the children of mothers who consumed alcohol in the first 3 months of pregnancy were not significantly different from those born to mothers who did not drink alcohol in terms of behavioural development (Table 5). Although not significant in the unadjusted model, the direction of effect showed decreasing CBCL total, internalising and externalising *z*-scores for the children of mothers who reported consuming up to ten standard drinks per week at 18 weeks of gestation, representing better behaviour, while heavy drinking was associated with increased CBCL scores, representing poorer behaviour. Following adjustment for confounders, mothers who were light drinkers (2–6 standard drinks per week) in the first 3 months of gestation had children with significantly lower total and internalising *z*-scores across the 14 years of data collection compared with those who did not consume alcohol in the first months of pregnancy. The size of the effect increased following the adjustment for confounders in each of those alcohol consumption categories.

Prior to the adjustment for confounders, mothers who were light drinkers in pregnancy at 34 weeks of gestation had children with significantly lower total CBCL *z*-scores, but this result was not significant after adjustment, and there were no other associations between CBCL scores and alcohol consumption at 34 weeks of gestation with the exception of occasional drinking, which was significantly associated with higher total and externalising behaviour scores. The direction of risk in the adjusted model showed decreasing CBCL scores associated with light and moderate drinking. The interaction of age with alcohol consumption groups was not significant ($P = 0.2$), indicating that the difference in scores between groups was more or less the same at all ages.

Alcohol intake and CBCL behavioural problems

The CBCL problem data for the four drinking groups were compared (using odds ratios) with CBCL problems for the children of mothers who did not drink alcohol, and odds ratios <1 indicate that the group has fewer children reaching the clinical cutoff point than the nondrinking baseline group. The children of mothers who were light drinkers in the first 3 months of pregnancy had significantly fewer behavioural problems over the first 14 years of life than those whose mothers did not drink at all during pregnancy (Table 6). This effect was evident across all three domains in both the unadjusted and adjusted models. Drinking seven to ten standard drinks per week was also significantly associated with fewer total, internalising and externalising problems in the adjusted analyses, although the wider confidence intervals reflect the smaller numbers in this group. Once again, the direction of effect for the nonsignificant results (occasional drinking and heavy drinking) showed that alcohol intake in pregnancy was associated with fewer

Table 2. Comparison of reported alcohol intake group at 18 and 34 weeks of gestation*

	34-week data				
18-week data	**No alcohol (*n* = 1579) *n* (%)**	**Occ. drinking (*n* = 427) *n* (%)**	**Light drinking (*n* = 310) *n* (%)**	**Mod. drinking (*n* = 38) *n* (%)**	**Heavy drinking (*n* = 16) *n* (%)**
No alcohol (*n* = 1310) *n* (%)	1132 (86.4)	110 (8.4)	55 (4.2)	8 (0.6)	5 (0.4)
Occasional drinking (*n* = 539) *n* (%)	264 (49.0)	183 (34.0)	82 (15.2)	8 (1.5)	2 (0.4)
Light drinking (*n* = 419) *n* (%)	141 (33.7)	115 (27.4)	143 (34.1)	14 (3.3)	6 (1.4)
Moderate drinking (*n* = 60) *n* (%)	25 (41.7)	11 (18.3)	20 (33.3)	3 (5.0)	1 (1.7)
Heavy drinking (*n* = 42) *n* (%)	17 (40.5)	8 (19.0)	10 (23.8)	5 (11.9)	2 (4.8)

Kendall's tau-b = 0.44 (95% CI = 0.41, 0.47).
*Missing data not shown, row percentages presented.

behavioural problems in comparison with no alcohol intake in pregnancy in the first 3 months.

There were no significant relationships between any of the 34-week categories of alcohol intake and subsequent child behavioural problems between 2 and 14 years in the adjusted model. For light and moderate drinkers, the direction of effect was a reduction in problems; however, for heavy drinkers at 34 weeks of gestation, the multivariable results showed an increase in internalising and externalising problems compared with nondrinkers. Although not significant, occasional drinking at 34 weeks of gestation showed an association with increased problems across all three domains. The confidence intervals show a large range of effect, most likely because of the smaller sample sizes in the moderate and heavy categories.

Discussion

In this study we have shown that mothers who consumed light levels of alcohol (2–6 standard drinks per week) in the first 3 months of pregnancy had children with significantly lower total and internalising CBCL scores over 14 years, representing more positive behaviour, than nondrinkers at 3 months of gestation. These data also indicate that the children of light to moderate drinkers (2–10 standard drinks per week) were at a clinically meaningful lower risk of total, internalising and externalising behavioural problems than the children of women who did not drink.

Previous studies have suggested that drinking early in pregnancy was found to be associated with the highest risk of poor developmental outcomes for offspring when compared with alcohol intake later in pregnancy;[2] however, our results suggest that low–moderate alcohol intake early in pregnancy is not associated with poor behavioural outcomes for children. These data support other recent data that show low levels of alcohol exposure may not be associated with developmental risks.[19] Some studies that have suggested that low levels of alcohol intake may be a risk factor for poor behavioural outcomes have also included acknowledgements that across multiple domains of behaviour there are few significant results.[2,22] In studies where lower levels of alcohol consumption have been associated with increased risk, adjustment for relevant covariates has often diminished the strength of this effect.[23] Further, the complexity of alcohol consumption over time in quantity and pattern makes it very difficult to speculate as to safe levels of alcohol consumption and this may have led authors to err on the side of caution.[4] Our finding that heavy alcohol consumption was not significantly associated with poorer behavioural outcomes was unexpected. We suggest that this finding was influenced by the small number of heavy drinkers in this cohort.

Table 3. Percentage of participants with total, internalising (int) and externalising (ext) behavioural problems at each follow up according to their mother's alcohol intake at 18 weeks of gestation*

	Year 2 problems *n* (%) (*n* = 1952)			Year 5 problems *n* (%) (*n* = 2127)			Year 8 problems *n* (%) (*n* = 2037)			Year 10 problems *n* (%) (*n* = 1977)			Year 14 problems *n* (%) (*n* = 1744)		
	Total	Int	Ext	Total	Int	Ext	Total	Int	Ext	Total	Int	Ext	Total	Int	Ext
No alcohol *n* (%)	117 (11.3)	96 (9.3)	126 (12.2)	252 (22.6)	207 (18.6)	234 (21.0)	214 (20.0)	207 (19.3)	212 (19.9)	183 (17.8)	214 (20.8)	142 (13.8)	145 (16.2)	127 (14.2)	159 (17.7)
Occasional drinking *n* (%)	66 (13.6)	39 (8.1)	80 (16.5)	97 (18.5)	89 (17.0)	99 (18.9)	90 (18.2)	98 (19.8)	76 (15.4)	65 (13.0)	78 (15.6)	58 (11.6)	56 (12.6)	55 (12.4)	58 (13.1)
Light drinking *n* (%)	33 (9.3)	26 (7.4)	41 (11.6)	76 (19.1)	67 (16.8)	75 (18.8)	72 (18.6)	72 (18.6)	64 (16.5)	42 (11.3)	47 (12.6)	40 (10.8)	39 (11.5)	32 (9.5)	45 (13.3)
Moderate drinking *n* (%)	6 (10.9)	5 (9.1)	7 (12.7)	17 (29.8)	12 (21.1)	13 (22.8)	7 (13.5)	8 (15.4)	6 (11.5)	3 (5.9)	5 (9.8)	4 (7.8)	2 (5.6)	2 (5.6)	5 (13.9)
Heavy drinking *n* (%)	3 (12.0)	1 (4.0)	5 (20.0)	10 (31.3)	8 (25.0)	11 (34.4)	9 (29.0)	9 (29.0)	10 (32.3)	5 (19.2)	5 (19.2)	5 (19.2)	3 (10.7)	4 (14.3)	4 (14.3)

*Percentages represent those participants with behavioural problems compared with those without behavioural problems at each follow up.

Table 4. Frequency data for alcohol intake pattern reported at 18 weeks of gestation and control variables (n = 2370)*

	Alcohol in pregnancy					*P*-value
	No alcohol %	Occ. drinking %	Light drinking %	Moderate drinking %	Heavy drinking %	
Maternal age at conception						
<20 years	11.5	6.9	7.6	10.0	11.9	<0.001
20–24.9 years	23.5	18.2	16.7	13.3	14.3	
25–29.9 years	30.2	32.9	28.6	26.7	28.6	
30–34.9 years	23.7	26.8	29.4	28.3	40.5	
35+ years	11.0	15.2	17.7	21.7	4.8	
Maternal education at pregnancy						
<High school completion	67.0	59.3	61.1	66.7	71.4	0.099
High school completion	33.0	40.7	38.9	33.3	28.6	
Father living with family						
Yes	89.8	87.2	84.5	68.3	85.7	<0.001
No	10.2	12.8	15.5	31.7	14.3	
Low family income in pregnancy						
≤$24 000 per annum	32.8	28.4	28.9	29.8	32.5	0.163
>$24 000 per annum	67.2	71.6	71.1	70.2	67.5	
Smoking in pregnancy						
None	78.0	74.6	64.4	55.0	47.6	<0.001
1–5 daily	7.4	8.7	10.5	16.7	14.3	
6–10 daily	6.3	5.8	7.9	8.3	9.5	
11–15 daily	4.2	5.4	8.8	13.3	4.8	
16–20 daily	2.4	3.5	5.7	1.7	11.9	
21+ daily	1.8	2.0	2.6	5.0	11.9	
Stress events in pregnancy						
None	21.8	21.0	25.2	13.3	21.4	0.364
1–2 events	42.4	41.1	36.7	45.0	33.3	
3+ events	35.7	37.9	38.1	41.7	45.2	

*Missing data not shown, column percentages for each variable presented.

One of the strengths of this study was the longitudinal design that allowed for assessment of behavioural development at multiple time-points in the developmental trajectory through childhood and into adolescence. A prospective pregnancy cohort is essential for research of this nature to be unaffected by retrospective recall. Any study that intends to examine the effect of the prenatal environment on later behavioural outcomes needs to give careful consideration to the impact of a range of sociodemographic and family characteristics that could confound this effect. We were able to measure and adjust for a range of variables with the potential to influence behavioural outcomes. The administration of the CBCL at each of the follow ups is also a study strength because it is a well-validated behavioural assessment instrument with good internal consistency in the diagnosis of psychopathology.[24] We were able to avoid the problem of dichotomised predictors used in some studies that have the potential to hide dose–response patterns and threshold values (although the categorisation of predictor variables does retain the potential for some level of measurement error),[5] our study had adequate statistical power, and we used a tertiary maternity hospital catchment cohort rather than clinical samples as in previous studies.[25]

We used maternal self-report data for alcohol intake, as have the majority of studies on alcohol consumption and health outcomes.[22] We took steps to reassure the participants that they would not be judged on the information they provided on their drinking habits. Further, self-reported alcohol consumption data for the first trimester, where most results were observed, is likely to be more accurate than data collected later in pregnancy.[22] If there were self-report biases or issues with accurate retrospective recall for the first months of pregnancy at the 18-week assessment in this study, the alcohol consumption may be higher than reported, which could further strengthen our results. A limitation of the study was that our data could not reliably reflect the presence of binge drinking, given that the consumption of drinks per week at each time point was averaged, and patterns of

Table 5. Relationship between alcohol in pregnancy and CBCL *z*-scores [*n* (surveys) = 8531]*

Predictor variables	Linear random effects model—years 2 to 14 inclusive					
	Estimate of effects, 95% confidence interval, significance (*P*-value)					
	Unadjusted analysis			Adjusted analysis**		
	Total behaviour	Internalising behaviour	Externalising behaviour	Total behaviour	Internalising behaviour	Externalising behaviour
Alcohol 18 weeks†						
Occasional drinking	−0.05	−0.06	−0.03	−0.03	−0.05	−0.01
(≤1 drink per week)	−0.13, 0.03	−0.14, 0.01	−0.11, 0.05	−0.12, 0.07	−0.14, 0.04	−0.11, 0.08
n (women) = 539	0.238	0.101	0.441	0.581	0.267	0.788
Light drinking	−0.06	−0.04	−0.06	−0.12***	−0.11***	−0.10
(2–6 drinks per week)	−0.15, 0.03	−0.13, 0.04	−0.15, 0.03	−0.23, −0.01	−0.21, −0.00	−0.21, 0.01
n (women) = 419	0.195	0.319	0.174	0.031	0.044	0.064
Moderate drinking	−0.08	−0.11	−0.01	−0.27	−0.25	−0.20
(7–10 drinks per week)	−0.29, 0.13	−0.31, 0.09	−0.22, 0.20	−0.55, 0.00	−0.52, 0.02	0.48, 0.08
n (women) = 60	0.464	0.288	0.934	0.053	0.066	0.153
Heavy drinking	0.08	0.00	0.22	−0.04	−0.04	0.05
(11+ drinks per week)	0.20, 0.35	−0.26, 0.26	−0.05, 0.50	−0.36, 0.28	−0.35, 0.27	−0.27, 0.37
n (women) = 42	0.580	0.990	0.112	0.811	0.809	0.751
Alcohol 34 weeks						
Occasional drinking	−0.04	−0.04	−0.04	0.10***	0.06	0.14***
(≤1 drink per week)	−0.13, 0.05	0.13, 0.04	−0.13, 0.05	0.00, 0.21	−0.04, 0.16	0.04, 0.24
n (women) = 427	0.419	0.316	0.425	0.047	0.206	0.008
Light drinking	−0.11***	−0.10	−0.11	−0.05	−0.04	−0.03
(2–6 drinks per week)	−0.22, −0.01	−0.20, 0.00	−0.21, −0.00	−0.17, 0.07	−0.16, 0.07	−0.16, 0.09
n (women) = 310	0.039	0.050	0.050	0.432	0.464	0.575
Moderate drinking	−0.24	−0.23	−0.24	−0.21	−0.17	−0.18
(7–10 drinks per week)	−0.52, 0.04	−0.49, 0.04	−0.51, 0.04	−0.53, 0.11	−0.47, 0.14	−0.50, 0.14
n (women) = 38	0.098	0.090	0.097	0.199	0.294	0.270
Heavy drinking	0.06	−0.02	0.15	0.15	0.12	0.17
(11+ drinks per week)	−0.38, 0.51	−0.44, 0.40	−0.29, 0.59	−0.34, 0.63	−0.35, 0.59	−0.31, 0.66
n (women) = 16	0.790	0.925	0.498	0.557	0.621	0.488

*Number of surveys varied from one to five according to participation in the follow ups.
**Adjusted for maternal age, maternal education, presence of the biological father in the family home, family income, stress in pregnancy, maternal cigarette smoking, and child's age as a random slope.
***$P < 0.05$.
†Reflects drinking patterns in first 3 months of pregnancy, difference from *z*-score for no alcohol.

drinking may be relevant to assessing the influence of alcohol in pregnancy;[26] however, arbitrary definitions of binge patterns used in previous studies (for example, at least four drinks per day compared with fewer than four drinks per day)[26] do not necessarily capture the nature or effect of a binge drinking episode and should be interpreted with caution. We were unable to control for paternal alcohol intake in this study, which has been shown in other studies to moderate the association between intrauterine exposure to alcohol and child IQ.[27] As with any study of this nature it is important to consider that because of the large number of statistical tests performed, some of the significant findings reported may be due to chance. Our results may potentially be influenced by selective attrition given that those who were socially disadvantaged were less likely to remain in the cohort to age 14 years; however, a recent study using a similar cohort found that selective attrition had a minor influence on child behavioural outcomes.[28] Finally, alcohol consumption in pregnancy may be more common in women who experience mental distress in pregnancy[29] and although we were unable to adjust specifically for maternal psychopathology, we were able to control for the mothers' experience of stress, which is a good indicator of psychosocial distress.[30]

Table 6. Relationship between alcohol in pregnancy and CBCL problems ($T \geq 60$) at each age [n (surveys) = 8531]*

Predictor variables	Multivariate logistic GEE model–years 2 to 14 inclusive**					
	Odds ratio (OR), 95% confidence interval, significance (P-value)					
	Unadjusted analysis			Adjusted analysis****		
	Total behaviour	Internalising behaviour	Externalising behaviour	Total behaviour	Internalising behaviour	Externalising behaviour
Alcohol 18 weeks* **						
Occasional drinking	0.86	0.88	0.91	0.82	0.85	0.76*****
(≤1 drink per week)	0.71, 1.05	0.73, 1.06	0.75, 1.11	0.63, 1.06	0.67, 1.07	0.59, 0.99
n (women) = 539	0.140	0.171	0.351	0.133	0.164	0.042
Light drinking	0.77*****	0.80*****	0.80*****	0.63******	0.57******	0.69******
(2–6 drinks per week)	0.62, 0.96	0.65, 0.98	0.65, 1.00	0.46, 0.86	0.42, 0.76	0.51, 0.93
n (women) = 419	0.018	0.034	0.044	0.003	<0.001	0.014
Moderate drinking	0.80	0.75	0.86	0.43*****	0.31*****	0.46*****
(7–10 drinks per week)	0.50, 1.30	0.48, 1.18	0.52, 1.40	0.21, 0.88	0.14, 0.69	0.22, 1.00
n (women) = 60	0.375	0.209	0.535	0.020	0.004	0.049
Heavy drinking	1.14	1.12	1.38	0.68	0.76	0.97
(11+ drinks per week)	0.71, 1.82	0.67, 1.89	0.82, 2.33	0.31, 1.47	0.33, 1.76	0.49, 1.93
n (women) = 42	0.592	0.661	0.222	0.323	0.519	0.931
Alcohol 34 weeks†						
Occasional drinking	0.85	0.89	0.81	1.24	1.06	1.22
(≤1 drink per week)	0.68, 1.06	0.73, 1.09	0.65, 1.01	0.93, 1.65	0.82, 1.37	0.92, 1.62
n (women) = 427	0.141	0.273	0.057	0.137	0.683	0.168
Light drinking	0.75*****	0.81	0.74*****	0.88	0.86	0.77
(2–6 drinks per week)	0.59, 0.97	0.63, 1.03	0.57, 0.95	0.63, 1.23	0.61, 1.20	0.56, 1.05
n (women) = 310	0.029	0.087	0.019	0.460	0.378	0.099
Moderate drinking	0.72	0.52	0.79	0.48	0.49	0.53
(7–10 drinks per week)	0.36, 1.44	0.24, 1.11	0.39, 1.61	0.20, 1.14	0.16, 1.49	0.19, 1.44
n (women) = 38	0.355	0.089	0.520	0.098	0.207	0.210
Heavy drinking	1.29	0.80	1.35	1.19	1.21	1.24
(11+ drinks per week)	0.56, 2.96	0.37, 1.74	0.61, 3.00	0.30, 4.68	0.49, 2.95	0.40, 3.86
n (women) = 16	0.551	0.576	0.466	0.802	0.683	0.713

*Number of surveys varied from one to five according to participation in the follow ups.
**Obtained with binomial distribution, logit link and unstructured working correlation matrix.
***Reflects drinking patterns in first 3 months of pregnancy, reference category no alcohol.
****Adjusted for maternal age, maternal education, presence of the biological father in the family home, family income, stress in pregnancy, child's age at follow up (and child's age at follow-up squared), and maternal cigarette smoking.
*****$P < 0.05$, ******$P < 0.005$.
†Reference category no alcohol.

Possible mechanisms

Our findings could be explained in part by the psychosocial characteristics of mothers who drink in moderation during early pregnancy: more specifically, the characteristics that make these mothers different from mothers who do not drink at all. Substance-use research suggests that moderate drinkers are mentally healthier than both abstainers and addicts,[31] which is attributed to the self-efficacy and behavioural self-management required for moderating substance intake.[32,33] The self-control that allows light–moderate drinkers to contain and manage their drinking quite plausibly enables better parenting and positive child well-being.[34] Numerous socioeconomic and medical factors may also confound the differences between moderate drinkers and abstainers,[35] and our finding that maternal education and family income were not associated with alcohol intake indicates that drinking habits are not easily predicted by measurable sociodemographic variables.

We propose that biological mechanisms may also help to explain the results we have observed in this study. Alcohol is easily distributed from the maternal bloodstream to the fetus,[25] and alcohol may affect hypothalamic–pituitary–adrenal axis reactivity which is linked to neonatal behaviour and the development of psychopathology.[25] Given that

maternal prenatal anxiety is a risk for the development of behavioural problems in childhood,[36] low doses of alcohol may have a moderating effect on maternal mood.[32] Further, when considering the biological mechanisms through which a light intake of alcohol in pregnancy may reduce the incidence of child behavioural problems, it is useful to examine the broader literature on alcohol and population health. Increasing alcohol intake is generally found to show a *U*-shaped or *J*-shaped curve in relation to physical health outcomes, for example increased intake of alcohol is thought to be protective against cardiovascular mortality up to a threshold point.[37,38] The recommended quantity of alcohol consumption for women to protect against cardiovascular mortality is one or two drinks daily for 5–6 days a week,[39] and although these findings are not within the context of pregnancy, they are similar amounts to the levels that we found to be associated with a reduction in child behavioural problems. Recent studies also suggest the potential for specific genetic variants to moderate the relationship between maternal cigarette smoking during pregnancy and child behaviour and it is yet to be seen what influence genetic factors may have over the relationship between alcohol intake during pregnancy and child behavioural outcomes.[40–42]

Implications of these findings

The antenatal period is one where women are often advised to give up behaviours that they may have previously enjoyed, including alcohol, smoking, high-fat foods and caffeine.[43] Therefore, enhancing the social and medical supports for those who find this lifestyle change difficult is important. We believe that these findings are important for the community in relation to limiting the overestimation of risk that accompanies emotive subjects such as teratogenic exposure in pregnancy. With up to 50% of pregnancies unplanned, the first 18 weeks of pregnancy are likely to encompass a period of time where the pregnancy is unknown or unconfirmed, and as such may be reflective of women's usual drinking patterns rather than an intentional change in drinking behaviour due to pregnancy. Women who believe their actions before discovering they are pregnant may have harmed their unborn child may experience guilt, anxiety and critical judgement from their peers. As previously mentioned, maternal antenatal anxiety and stress are known to increase the risk of child behavioural problems,[36] highlighting the need for understanding and the reservation of judgement. Given the guilt and anxiety that are associated with the consumption of alcohol during pregnancy it is important to acknowledge that alcohol consumption and behavioural consequences for the child do not necessarily follow a simple linear dose–response pattern. It should be noted that these results relate to low–moderate alcohol consumption and child behavioural outcomes only and there may be other cognitive and neurodevelopmental outcomes that relate to alcohol consumption in different ways.

Conclusion

Our findings, taken together with data from other recent studies, indicate that low levels of alcohol consumption by women in early pregnancy do not appear to be harmful to subsequent mental health of the offspring whereas high levels of alcohol exposure during pregnancy should be discouraged during pregnancy because there are consistent findings across multiple studies that high levels of alcohol exposure during pregnancy are associated with an increase in adverse outcomes for the offspring. Despite the fact that our analyses have controlled for socioeconomic status, the results of our study may still reflect other unmeasured psychosocial differences between women who drink small amounts of alcohol during pregnancy and those who are abstainers, and future studies addressing this issue require a very careful assessment of maternal and paternal alcohol consumption and sociodemographic factors. Our data suggest that women who conceive unexpectedly while consuming limited amounts of alcohol have not placed their unborn child at increased risk of behavioural problems during childhood.

Disclosure of interest

All authors declare that there are no conflicts of interest to disclose.

Contribution to authorship

The contributions of individual authors to this paper are as follows: planning research (Monique Robinson, Craig Pennell, Nicholas de Klerk, Fiona Stanley, John Newnham); executing research (Monique Robinson, Wendy Oddy, Neil McLean, Peter Jacoby, Craig Pennell, Nicholas de Klerk, John Newnham); analysing data (Monique Robinson, Peter Jacoby, Nicholas de Klerk); interpreting data (Monique Robinson, Wendy Oddy, Neil McLean, Peter Jacoby, Craig Pennell, Nicholas de Klerk, Stephen Zubrick, Fiona Stanley, John Newnham); and writing (Monique Robinson, Wendy Oddy, Neil McLean, Peter Jacoby, Craig Pennell, Nicholas de Klerk, John Newnham).

Details of ethics approval

The Human Ethics Committee at KEMH approved the protocols for this study on 18 May 1989. Princess Margaret Hospital for Children approved all subsequent protocols for the study, with the first approval being granted on 23 August 1990 under the reference code RE90-23.4 and the most recent approval for the 14-year follow up granted on 20 March 2003 under the reference code EC03-14.7.

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Commentary on 'Low–moderate prenatal alcohol exposure and the risk to child behavioural development: a prospective cohort study'

Excessive maternal alcohol consumption during pregnancy is associated with various severe growth and neurobehavioral consequences in the offspring (Jones *et al. Lancet* 1973;301:1267–71). More recently, studies have focused on the effects of low to moderate alcohol consumption, which commonly refers to less than one unit per day. Low to moderate levels of maternal alcohol consumption during pregnancy seem not to be consistently associated with fetal growth restriction or increased risks of birth complications (Jaddoe *et al. Ann Epidemiol* 2007;17:834–40, Bakker *et al. Int J Epidemiol* 2010: doi: 10.1093/ije/dyq047). However, exposure to low levels of alcohol during fetal life may still lead to neurodevelopmental maladaptations, without affecting early growth. Most studies suggesting associations between low maternal alcohol consumption during pregnancy and behavioural and cognitive outcomes in children were mainly based on small study samples and only took account of a limited number of covariates.

The article by Robinson *et al.* (*BJOG* 2010; doi: 10.1111/j.1471-0528.2010.02596.x) adds important information to this topic. They examined the associations of fetal alcohol exposure at the gestational ages of 18 and 34 weeks with child and adolescent behavioural development in a prospective cohort study. Childhood behavioural development was measured at the ages of 2, 5, 8, 10 and 14 years by means of the standardised and validated Child Behaviour Checklist questionnaire, which enables assessment of total, internalising and externalising problem behaviour. They did not observe any adverse effect of low to moderate alcohol consumption during pregnancy at either 18 or 34 weeks, on behavioural outcomes in childhood. Their findings suggest that light and moderate drinking in the first 3 months of pregnancy was associated with a reduction in total, internalising and externalising behavioural problems during childhood and adolescence. These results are in line with two recent large population-based cohort studies. A recent study among more than 20 000 children showed no association of low doses of maternal alcohol consumption during pregnancy with the risks of attention deficit and hyperreactivity disorder after adjustment for social adversity and smoking (Rodriguez *et al. J Child Psychol Psychiatry* 2009;50:1073–83). Similarly, results from the nationally representative prospective UK Millennium Cohort study showed no effects of low alcohol consumption during pregnancy on behavioural and cognitive outcomes in more than 9000 preschool children (Kelly *et al. Int J Epidemiol* 2009;38:129–40). Interestingly, like the study by Robinson *et al.*, results from this study suggested even a protective effect of low to moderate alcohol consumption for development of behavioural problems. Although several biological explanations for these associations have been proposed, residual confounding due to, for example, social and dietary circumstances, should be considered. In many contemporary Western populations, low to moderate alcohol consumption during pregnancy is common in socially advantaged, higher educated and healthier women.

Although current evidence from epidemiological studies does not strongly suggest that low to moderate maternal alcohol consumption during pregnancy adversely affects the health of their children, more information is needed on specific critical periods during fetal life and threshold levels above which alcohol consumption might have adverse effects. This information is needed for updating recommendations for safe low alcohol consumption during pregnancy.

Disclosure of interests

No conflict of interest. ■

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Commentary on 'Low–moderate prenatal alcohol exposure and risk to child behavioural development: a prospective cohort study'

Robinson *et al.* (*BJOG* 2010; doi: 10.1111/j.1471-0528.2010.02596.x) use data from the Western Australian Pregnancy Cohort to show that children exposed prenatally to low–moderate alcohol actually do better on the Child Behaviour Checklist (CBCL) than those born to mothers who abstain. This finding was unexpected and is inconsistent with a substantial body of evidence from large, prospective, longitudinal studies that have documented a broad range of adverse effects on growth, cognition and behaviour in children exposed at low-to-moderate levels using measures that are more sensitive than the CBCL (e.g. Day *et al. Alcohol Clin Exp Res* 2002;26:1584–91; Jacobson *et al. Alcohol Clin Exp Res* 2004;28:1732–45; Holmgren. Swedish National Institute of Public Health, 2009).

A major limitation of the Robinson *et al.* study is the use of abstainers as the reference control group. Light–moderate drinkers are often socioeconomically more advantaged than abstainers, and their children are, therefore, likely to exhibit more optimal behavioural outcomes (http://pubs.niaaa.nih.gov/publications/ModerateDrinking-03.htm, 2003; www.fasdsg.org/News_Publications.php?topic=1&category=1, 2008). Given that the abstainers' income and education are markedly lower compared with the occasional–light drinkers in the Robinson *et al.* study, combining the abstainers and occasional–light drinkers would have provided a more appropriate reference group.

The absence of significant adverse effects in the heavily exposed children also raises questions about the utility of the parental CBCL for detecting subtle effects in this population. To determine a threshold, one must first confirm the adverse effect on the outcome being examined and then determine the lowest dose at which the effect continues to be evident. The data from studies examining the CBCL in relation to prenatal alcohol exposure have been inconsistent (Mattson and Riley. *Alcohol Clin Exp Res* 2000;24:226–31). By contrast, teacher ratings on this instrument reliably detect adverse effects at low–moderate exposures (Jacobson *et al. J Pediatr* 2006;148:30–7).

In addition, the Robinson *et al.* data were not analysed to assess the effects of binge drinking (at least four drinks/occasion for women). Studies in animals and in humans have found that dose/occasion is often more important than mean amount of alcohol/week in determining adverse effects (Bonthius and West. *Teratology* 1991;44:147–63; Jacobson *et al. Alcohol Clin Exp Res* 1998;22:345–51). Most women do not drink daily but concentrate their drinking on 1 or 2 days/week, thereby exposing the fetus to levels found to be harmful, even when maternal average volume of alcohol/week is low (Jacobson and Jacobson. In Nelson CS, editor, *Minnesota Symposia on Child Psychology*. Mahwah, NJ: Lawrence Erlbaum; 2000).

Women who drink at low levels 'may experience [unwarranted] guilt, anxiety and critical judgement from their peers'. Nevertheless, it is not appropriate to reassure them or their health providers, based on the limited findings reported in this paper, that low–moderate doses of alcohol during pregnancy may be beneficial. Also, advice that low doses of alcohol in pregnancy could be beneficial may encourage drinking by pregnant women with a propensity for alcohol abuse who may not recognise when their drinking becomes excessive. In our research we have found evidence of substantial individual differences in vulnerability to the adverse effects of fetal alcohol exposure based on maternal age, alcohol abuse history and genetic make-up (Jacobson *et al.*, 2004, 2006 cited above). For this reason, even light drinking could put the fetus at risk where the mother or infant is particularly vulnerable. Although there is no

evidence that an occasional drink during pregnancy is consequential, abstaining from alcohol during pregnancy is still the best advice the obstetrician can offer.

Disclosure of interests

Neither of the authors have any conflicts of interest that would bias the commentary or interpretation of the findings presented here. ■

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