Running Head: PRENATAL ENVIRONMENT AND MENTAL HEALTH PROBLEMS

**The association between prenatal environment and children's mental health trajectories
from 2-14 years**

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Abstract

The prenatal period is recognised as a critical period for later behavioural development. This study aimed to elucidate how an adverse prenatal environment, as defined by the presence of a number of known prenatal risk factors, would influence mental health trajectories in children to 14 years of age. The Raine Study provided comprehensive data from 2 900 pregnancies. Offspring were followed up at ages two, five, eight, 10, and 14 years using the Child Behaviour Checklist (CBCL). We used linear mixed regression models with random intercept and slope (random effects models) to examine the extent to which the predictor variables considered influenced changes in continuous CBCL total, internalizing, and externalizing T-scores from ages 2 to 14. In the final multivariate models, increased offspring CBCL T scores were significantly predicted by the mother not finishing high school, smoking during pregnancy, having a total family income below the poverty line, being diagnosed with gestational hypertension and experiencing stressful life events during pregnancy. Conversely, as maternal age increased, CBCL T-scores were significantly decreased. Child age also significantly interacted with maternal education, total family income, and maternal stressful life events, such that these variables predicted increases in CBCL scores from age 2 to age 10, and from age 2 to age 14 years. In the Raine Study sample, children who experienced adverse prenatal environments experienced increased levels of problem behaviours in childhood, and more problematic mental health trajectories. Maternal health risk behaviours and other psychosocial variables more commonly affected child behaviour than obstetric complications.

The association between prenatal environment and children's mental health from 2-14 years

The World Health Organization [1] estimates that one in five children and adolescents experience mental health problems. Mental health problems are a leading cause of health-related burden worldwide, accounting for up to thirty per cent of years lost due to disability during the first three decades of life [2]. It is well established that mental health problems in childhood and adolescence have a significant influence on mental health in later life [3], and mental health problems in childhood are known to predict other negative outcomes in later life, including school non-completion [4], physical health problems [5], drug and alcohol misuse [6], marital difficulties [7], increased mortality [8], injury risk [9], and involvement in the criminal justice system [10]. Prevention and early intervention are thus essential if we are to manage mental health and related morbidities at a societal level.

It is increasingly recognised that many risk factors for poor mental health are present in the prenatal period [11]. Studies have identified two broad components of the fetal environment that relate to later mental health in the child: maternal health risk behaviours and obstetric complications [12-14]. Maternal health risk behaviours may reduce the quality of the fetal environment by altering the supply of oxygen to the fetus, and/or by directly transferring maternal cortisol or other agents to the fetus across the placenta. Obstetric complications are also thought to affect later mental health outcomes via a sub-optimal fetal environment. While gestational hypertension affects the supply of blood and hence nutrition to the fetus [15], intrauterine growth restriction (as indicated by low birthweight for gestational age and spontaneous preterm birth) are indicators of prior disruptions to the fetal environment [16].

A number of maternal health risk behaviors have been identified as predictors of poor offspring mental health. These include maternal cigarette smoking, alcohol consumption, and stress. Maternal cigarette smoking has been associated with increased risk for internalizing and externalizing behaviours over a number of studies [17, 18] as well as specific diagnoses such as Attention Deficit Hyperactivity Disorder [19]. Prenatal exposure to a large amount of alcohol has a known teratogenic effect on the embryo, and has been linked to a range of behavioural problems in offspring [20], most notably Fetal Alcohol Syndrome and Fetal Alcohol Spectrum Disorder. Most inquiry in the area has focused on the impact of heavy drinking on the fetus. The data regarding low to moderate levels of drinking and mental health and behaviour in offspring is mixed, with some studies suggesting adverse behaviour

outcomes in offspring are associated with as little as one alcoholic drink per week [21], while others suggest no increased risk for adverse behaviour outcomes in offspring with light-moderate drinking during pregnancy [22]. Maternal exposure to stress during pregnancy has also been found to influence mental health in offspring, with links to increased risks for difficult infant temperament [23], Attention Deficit/Hyperactivity Disorder (ADHD) in boys [24], and adolescent psychosis [25]. Stress in pregnancy has also been found to predict mental health morbidity in preschool children, and in children from 2-14 years of age [26, 27].

Obstetric complications have also been implicated in later offspring mental health and behaviour. Gestational hypertension is hypothesized to act on later child development through changed supply of blood and nutrition to the fetus. There is limited evidence on the relationship between hypertensive diseases of pregnancy and child mental health outcomes, and that which does exist is mixed. Gestational hypertension has been found to predict internalizing and externalizing mental health problems in offspring from age 8 to 14 [28], and difficult infant temperament in the first year of life [29]. In the case of preeclampsia (PE) diagnosis, two studies have found relationships between PE during pregnancy and negative psychological outcomes in offspring [30, 31], one study found no relationship between PE and adverse outcomes [32], and one study found that PE was associated with decreased risk of internalizing problems in children at ages 5 and 8 [28]. Intrauterine growth restriction, as characterized by low birthweight and/or spontaneous preterm birth, may also represent disruption to the fetal environment and thus disrupt child development. A recent meta-analysis concluded that children born very low birthweight (≤ 1500 g) and/or very preterm (≤ 33 weeks' gestation) have moderate to severe deficits in attention, and increased levels of internalizing behaviours [33]. Low gestational age in weeks has been found to be a significant risk factor for behaviour problems at ages 2 and 5 [26], and being born very preterm (< 26 weeks) has been linked to increased risk for diagnoses of emotional disorders, ADHD, and autism spectrum disorders at 11 years of age [34], and higher levels of general internalizing and externalizing problem behaviours at age 10 [35]. In cases of late preterm birth (36-38 weeks gestation), a number of studies have found no difference in behaviour outcomes relative to term births although one of these studies found that children born at 37 weeks gestation were at increased risk of overall and externalizing behaviours [36] compared to children born full-term (> 38 weeks).

Importantly, mental health problems in children are highly dynamic in terms of their onset, persistence, and severity. It is known that the first onset of mental health problems

most often occurs in childhood or adolescence, and that severe disorders occurring later in life are often preceded by less severe problems [37]. However, whilst we have a great deal of information about the onset and severity of mental health problems and the variables that influence them, we know comparatively little about the *course* of mental health problems in childhood and adolescence and the factors that may influence course. Previous studies have indicated that household income at birth can influence rates of depression and antisocial behavior in offspring, and that subsequent increases in income over time can act to reduce child mental health problems [38]. Antisocial behavior in children has also been found to reduce over time when family dysfunction is reduced [39]. It is thus important to understand how socioeconomic and psychological variables, as well as other known predictors of onset of mental health problems, relate to the course of mental health problems across childhood and adolescence.

While the impact of individual prenatal adverse exposures at a single point in time on child mental health problems has previously been examined, the relative impact of these exposures and their interaction with time on the onset, persistence, and severity of mental health problems in children has yet to be examined. This study aimed to elucidate how an adverse prenatal environment, as characterized by the presence of a number of known risk factors, would influence mental health trajectories in children from two to 14 years of age, with attention to the relative importance of different prenatal risks.

Method

Study design and participants

Participants were taken from the Western Australian Pregnancy Cohort (Raine) Study. The methodology and recruitment for this study are described in detail elsewhere [40]. Briefly, 2 900 women were recruited from the public antenatal clinic at King Edward Memorial Hospital in Perth, Western Australia and surrounding private clinics between May 1989 and November 1991. Women were recruited between 16 and 20 weeks gestation (average 18). Ninety percent of those eligible agreed to take part in the study, and there were 2 868 live births. These children were assessed at birth, and were followed up at ages 1, 2, 5, 8, 10, 14, 17, 20, and 23 years of age using questionnaires and physical assessments. This study used data collected at the 2, 5, 8, 10, and 14 year follow ups where comprehensive mental health data were collected. This research was approved by the Human Research Ethics

Committees at KEMH and Princess Margaret Hospital for Children in Perth, Western Australia. Written parental consent was obtained at recruitment and at each follow up.

Cohort attrition

Information on the numbers of participants at each follow up is provided online as supplementary information. Retention to age 14 was achieved for 77% of the sample, with 1860 adolescents (65%) taking part in the 14 year follow up and a further 357 (12%) remaining involved with the study but deferring 14-year participation. By age 14, 207 families (7%) were unable to be contacted, 412 families (14%) had withdrawn, and 32 participants (1%) had died. Detailed information on cohort attrition has been presented elsewhere [41, 42]. Briefly, families that were lost to follow up tended to report greater social disadvantage at the time of recruitment to the study (such as lower maternal education, lower total family income and younger maternal age at conception). However, the initial study oversampled disadvantaged families, and thus the selective attrition resulted in the sample becoming more representative of the Western Australian population over time.

Outcome variable

When children were aged two years, parents completed the Child Behavior Checklist for Ages 2-3 (CBCL/2-3). The CBCL/2-3 is a 99-item parent report measure of child mental health assessed over the past 6 months. When children were aged 5, 8, 10, and 14 years, a parent (usually the mother) completed the Child Behavior Checklist for Ages 4- 18 (CBCL/4-18). The CBCL/4-18 is a 118-item parent-report measure of child mental health assessed over the past six months. Both the CBCL/2-3 and the CBCL/4-18 produce raw scores that can be transformed into summary *T* scores for total behaviour, internalising behaviour (withdrawal, anxious/depressed and somatic), and externalising behaviours (delinquency and aggression), using standardised scoring procedures (Achenbach, 1991). Both of these measures show good internal reliability and validity and have been widely used in literature on child development [43, 44]. United States CBCL norms were used in this study. An Australian clinical calibration has demonstrated good sensitivity (83%) and specificity (67%) of these measures to a clinical diagnosis [45].

Predictor variables

We considered a number of predictor variables present in the prenatal environment that are known from previous research to have some relation to later offspring mental health. We also considered the child's sex and age.

Socio-demographic variables. Maternal age at childbirth in years was included as a continuous variable. Maternal education as recorded at 18 weeks gestation was included as a binary variable (12 or more years of education compared with less than 12 years of education), as was maternal ethnicity (Caucasian compared with non-Caucasian). Total family income was entered as a binary variable (total income $\leq$ 24 000 AUD per annum vs. $>$ 24 000 AUD per annum) in accordance with the poverty line at the time the data were collected.

Prenatal exposures. Mothers were asked at 18 weeks whether they had experienced any of 11 life stress events since they had become pregnant (yes or no), taken from a broader 67-item life stress inventory ('A scale to measure the stress of life events') [46]. The 11 events asked about were: pregnancy problems; death of a close friend or relative; separation or divorce; marital problems; problems with children; involuntary job loss; partner's involuntary job loss; money problems; residential move; and another stressful event not listed. We calculated a total life stress events score by summing all the "yes" responses to the listed events, and included this as a continuous variable.

Maternal alcohol intake per week was measured at 18 weeks gestation to provide an approximate measure of the total number of standard drinks consumed in the first four months of pregnancy. We considered alcohol intake as both a continuous variable, and as a binary variable (10 or fewer standard drinks per week versus 11 or more) to account for the differing literature on low-moderate versus heavy alcohol consumption [20, 42]. The continuous variable was not significantly associated with CBCL scores across all three domains in this analysis ($p > .10$), and only the binary variable was retained for analyses.

Maternal smoking during pregnancy was measured at both 18 and 34 weeks gestation. Previous analysis with Raine Study data has shown a strong correlation between the number of cigarettes smoked daily at 18 weeks and number of cigarettes smoked daily at 34 weeks gestation ($r = .87, p < .001$) [18]. Therefore, we used smoking data collected at 18 weeks to develop a binary variable (no cigarettes smoked versus any cigarettes smoked).

Data on the presence of gestational hypertension (pregnancy induced increase in systolic blood pressure to 140 mmHg and/or an increase in diastolic blood pressure of 90 mmHg or more) and/or PE (gestational hypertension and proteinuria) were collected during

routine antenatal visits. We used a binary variable in analyses which was defined by a normotensive pregnancy or a pregnancy with gestational hypertension. Gestational hypertension in this case was defined as hypertension with or without PE.

Gestational age and weight. Gestational age in weeks was considered as a continuous variable. We also developed a binary variable pertaining to pre-term birth (born at or after 37 weeks gestation versus 36 or fewer weeks' gestation). We included birth weight in grams as a continuous variable. We also considered the percentage of optimal birthweight (POBW) as a continuous variable (a measure of appropriateness of fetal growth for gestational age; value derived using equations cited in Blair et al. [47]).

Statistical analyses

We used linear mixed regression models with random intercept and slope (random effects models) to examine the extent to which the predictor variables influenced changes in continuous CBCL *T*-scores from ages 2 to 14 [48]. Linear mixed models account for the possible correlation between observations on the same subject over time. Initially, univariate analyses were conducted to determine which variables were associated with CBCL outcomes, and those associated at the $p < .10$ level were retained for entry into a multivariate model (this approach has been used in previous publications arising from the Raine Study cohort [49, 50]). We then tested for interactions between each variable and time in order to create a final multivariate model that measured the extent to which each variable impacted upon CBCL total, internalising, and externalising scores, overall (main effects) and in relation to changes in CBCL scores over time (interaction effects with time). Time was treated as a categorical variable in the analysis to avoid placing any arbitrary restrictions on the shape of the relationship between change in CBCL scores and time. Alpha was set at $p < .05$ for the multivariate models. In the case of missing data, the full information available for each participant was included in the analyses. All analyses were conducted in SPSS v20.0.

Results

Frequency characteristics for the cohort are presented in Table 1. Attrition rates for the study are described in detail elsewhere [42, 51]. The average age of mothers at recruitment was 28 years. Approximately one in ten (10.4%) mothers were of ethnicity other than Caucasian, 59.1% did not complete high school, and 38.6% had a total family income that was below the poverty line at the time the data were collected. With regard to prenatal exposures, 25.9 % of mothers were diagnosed with gestational hypertension, 24.5% of the

mothers smoked daily during the first three months of pregnancy, the mean number of standard drinks consumed per week was 1.31, and the mean number of stressful life events experienced in the first three months of pregnancy was 1. The mean gestational age was 39 weeks, and the mean birth weight was 3 299 grams. Across the follow ups to age 14 years, mean total, internalising, and externalising *T*-scores were similar ($T = 48.76$, $T = 48.93$, and $T = 49.25$ respectively).

[TABLE 1]

In univariate analyses, maternal ethnicity, POBW, gestational age in weeks, and alcohol as a continuous variable were not significantly associated with CBCL scores. The binary alcohol variable was significantly associated with externalising CBCL *T*-scores only. Birth weight was significantly associated with total and internalising CBCL *T*-scores. All remaining variables were associated with total, internalising and externalising CBCL *T*-scores at a $p < .10$ level. Table 2 shows the initial multivariate models for total, internalising, and externalising behaviours. For total, internalising, and externalising behaviours, increased offspring CBCL *T* scores were predicted by the mother not finishing high school, smoking during pregnancy, having a total family income below the poverty line, being diagnosed with gestational hypertension, and experiencing stressful life events during pregnancy. Conversely, as maternal age increased, CBCL *T* scores decreased. Birth weight was no longer a significant predictor of total and internalising behaviour outcomes in the multivariate models. Similarly, consuming eleven or more standard drinks per week was no longer a significant predictor of externalising CBCL *T* scores.

[TABLE 2]

We next considered interactions between each prenatal variable and age to see which variables, if any, predicted changes in CBCL scores over time. Significant interactions ($p < .05$) were retained for inclusion in the final multivariate models (Table 3). For total CBCL *T* scores, age was found to significantly interact with total family income, such that living below the poverty line predicted increases in CBCL scores from age 2 to age 14; maternal stressful life events, with a greater number of stressful events in pregnancy associated with increases in CBCL *T* scores from age 2 to age 10, and age 2 to age 14; and maternal education, where eleven or fewer years of maternal education was related to increases in CBCL scores from age 2 to 8, and age 2 to 10.

For internalising CBCL scores, age significantly interacted with total family income and maternal stressful life events, such that living below the poverty line was associated with

significant increases in internalising scores from age 2 to age 14, and a greater number of stressful life events was associated with increases in scores from age 2 to ages 8, 10, and 14.

For externalising CBCL *T* scores, age interacted significantly with total family income, where living below the poverty line predicted increases in CBCL scores from age 2 to age 10, and age 2 to age 14, and there was a trend towards the same relationship from age 2 to age 8 ($p = .051$); and maternal education, where having eleven or fewer years of education predicted increases in CBCL scores from age 2 to ages 8, 10, and 14, with a trend toward the same relationship from age 2 to age 5 ($p = .051$). Stressful life events were not found to predict changes in externalising CBCL scores over time in the final model (see Table 3).

[TABLE 3]

Discussion

This study aimed to examine (i) the relative impact of a number of prenatal exposures on later offspring mental health, and (ii) how these variables interact with time to influence children's mental health trajectories. Whilst there are many studies looking at these factors individually, relatively few studies have been able to examine these variables in a single sample followed over an extended time period. Extending existing literature, maternal non-completion of high school, smoking during pregnancy, having a family income below the poverty line, being diagnosed with gestational hypertension, and experiencing stressful life events during pregnancy were all associated with elevations in overall, internalizing, and externalizing problems in offspring in the final multivariate models. When considering mental health trajectories (i.e., *changes* in mental health over time), maternal non completion of high school, family income below the poverty line, and stressful life events during pregnancy predicted increasing CBCL scores across childhood. Thus, children born to families with low maternal education, low family income, and stressful life events appear to begin life at a disadvantage, and show worsening mental health trajectories through to adolescence. This study is a novel point of extension from previous research considering single associations between prenatal exposures and children's mental health.

Socio-demographic variables showed a stronger relationship with adverse child behaviour outcomes than did obstetric outcomes. It is plausible that these socio-demographic / environmental variables are the observable measures of a broader latent construct relating to social disadvantage and a lack of family resources, which impacts negatively on the

development of the fetus and child. We suggest that these variables might be used as markers in identifying at risk families prior to or soon after conception. The variables in question are predictable, easily identifiable, and in at least some cases (e.g., maternal smoking, hypertension) amenable to intervention and change. Where variables are less easily changed (e.g., maternal age, family income) targeted family support may help to attenuate risk. This form of early prevention may result in more positive mental health outcomes for at-risk children in later life.

Our findings also highlight the importance of early intervention for reducing rates of child and adolescent mental health problems. The quality of the fetal environment was found to impact not only on overall levels of internalizing and externalizing behaviour problems in childhood, but on trajectories of problems from early childhood through to adolescence. Key exposures (low maternal education, low family income, and family stress) in utero placed children at risk for ongoing and worsening mental health problems over the next 14 years. Clearly, efforts to decrease mental health problems in young people need to commence from the very onset of life - even before birth.

The data presented in this study highlight a trend toward decreasing risk of behaviour problems as children age, with lower numbers of parent-reported behaviour problems at age 14 than at age two. There are a number of possible explanations for these findings. The nature of *T*-score scaling is such that if children with more mental health problems are lost to follow up over time, then *T*-scores will decrease on average over time with attrition. We suggest that attrition is a likely explanation for the reduction observed at 14 years in our sample, consistent with previous reports showing Raine Study families lost to follow-up were more disadvantaged in the early years of the study than those retained to adolescence [42]. Further, these results may also be a product of changes in parents' capacity to report on their child's behaviour over time. Parents may have less contact with their children as they age, and thus are less able to make accurate comment on their child's behaviour. It has been found previously in a study of 11-19 year olds that discrepancies in parent and child reported CBCL-scores increase as the age of the child increases [52]. The results could also be a result of the upper age limit of the children in the study, 14 years.

Our findings have significant implications for both future research and the development of public policy. Our results indicate that the antenatal and preconception environments are important for the behavioural and emotional development of the child, and that mental health prevention can begin during pregnancy. This study contributes to a growing body of evidence pointing toward the need for early intervention as a mechanism of

dealing with mental health problems, as opposed to treating problems after they have developed. A move toward early intervention may ease the burden on the health system by preventing problems before they occur, or lessening their impact, and by freeing up resources in the health system. Results also suggest that researchers interested in prenatal predictors of mental health may benefit from considering family income, family stress, and maternal education as key prenatal predictors of worsening mental health problems over childhood. Family income, family stress, maternal education, maternal smoking, and gestational hypertension may relate to overall levels of mental health problems in childhood, whilst maternal ethnicity, maternal alcohol consumption, gestational age, and birth weight are not strong predictors of mental health outcomes when other variables are considered.

A major strength of this study is the use of a longitudinal pregnancy cohort study that has provided detailed information from 18 weeks gestation, allowing for consideration of a wide range of psychosocial, sociodemographic, and health related prenatal exposures. The collection of CBCL data on the Raine Study children from ages 2 to 14 is another strength, allowing for analysis of mental health trajectories as well as the impact of exposures at particular points during childhood. Conversely, the exposures considered, while comprehensive, are not exhaustive, and there may be other important risk factors we have not been able to consider in our analyses. The use of caretaker (parent) report for the CBCL has been validated as a useful detector of behavioural problems in youth to 18 years of age [53], but we also acknowledge the difficulties with using of parent report data into adolescence and young adulthood [52], and as a consequence analysed data from two to 14 years of age only. Finally, socially disadvantaged participants were less likely to remain in the study [42], and given that this construct appeared to be an important predictor of outcome, our findings may be attenuated.

Conclusions

Children who experienced adverse prenatal environments experienced higher levels of problem behaviours in childhood, and more problematic mental health trajectories, highlighting the importance of early intervention as a part of addressing the global burden of mental illness. Demographic factors were more important in predicting child behaviour than obstetric complications. Maternal education, family income, and family exposure to stress were most important in predicting increasing CBCL scores from age 2 to age 14.

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The authors declare that there are no conflicts of interest to report. This research was approved by the Human Research Ethics Committees at KEMH and Princess Margaret Hospital for Children in Perth, Western Australia and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written parental consent was obtained at recruitment and at each follow up.

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Supplementary information

Participants available at each follow up

	Completed	Deferred	Lost	Withdrawn	Died	Total
all or part of follow- up						
2	1988	381	418	51	30	2868
5	2237	339	135	127	30	2868
8	2140	376	124	198	30	2868
10	2047	281	162	348	30	2868
14	1860	357	207	412	32	2868

Table 1.

Frequency characteristics for the cohort.

Continuous variables	<i>N</i>	<i>M</i>	<i>SD</i>
Maternal age at birth of offspring	2 459	27.92	5.84
Weekly maternal alcohol consumption (standard drinks) ¹	2 458	1.31	2.85
Gestational age (in weeks)	2 504	38.71	2.21
Birth weight (in grams)	2 505	3 298.92	601.91
POBW	2 494	97.33	13.87
Total number of stressful life events ¹	2 459	1.18	1.23
CBCL Total <i>T</i> -score ²	2 459	48.76	11.17
CBCL Internalising <i>T</i> -score ²	2 459	48.93	10.44
CBCL Externalising <i>T</i> -score ²	2 459	49.25	10.70
Categorical variables	<i>N</i>	<i>n</i>	%
Maternal ethnicity	2 459		
Caucasian		2 203	89.6
Other		256	10.4
Maternal education	2 459		
12 or more years		1 005	40.9
11 or less years		1 454	59.1
Maternal smoking ¹	2 459		
0 cigarettes daily		1 843	73.3
1 or more cigarettes daily		616	24.5
Total family income ¹	2 459		
< 24 000 AUD per annum		1 387	56.4
≥ 24 000 AUD per annum		948	38.6
Maternal gestational hypertension	2 453		
Normotensive		1 817	74.1
Gestational hypertension		636	25.9

¹ In the first 18 weeks of pregnancy. ² On average from age 2 to 14 years

Table 2. *Initial multivariate estimates of fixed effects for total, internalising and externalising behaviour problems to age 14.*

		Total problems	Internalising problems	Externalising problems
		Estimate (95% CI for estimate)		
Categorical variables				
Sex (ref: M)	F	-1.46** (-2.16, -.77)	-.33 (-.95, .29)	-1.25*** (-1.91, -.59)
Age (ref: 2)	5	4.52*** (4.11, 4.93)	3.12*** (2.68, 3.57)	3.25*** (2.85, 3.65)
	8	2.85*** (2.37, 3.33)	3.41*** (2.91, 3.93)	1.25*** (.78, 1.72)
	10	.46 (-.049, .98)	2.30*** (1.76, 2.83)	-1.03*** (-1.52, -.54)
	14	-.68* (01.22, -.14)	-.66* (-1.22, -.11)	-.50 (-1.01, .024)
	Maternal education in years (ref: 12 or more)	11 or less	1.44*** (.70, 2.17)	.86** (.21, 1.52)
Maternal smoking (ref: 0 daily)	1 or more daily	2.59*** (1.74, 3.44)	1.56** (.80, 2.33)	2.81*** (2.00, 3.62)
Total family income (ref: ≥ 24 000 AUD per annum)	< 24 000	1.73*** (.97, 2.49)	1.11*** (.43, 1.80)	1.83*** (1.10, 2.55)
	AUD per annum			
Gestational hypertension (ref: normotensive)	Hypertensive	1.18** (.39, 1.97)	.79* (.082, 1.50)	1.20** (.45, 1.95)
Maternal alcohol consumption (ref: 10 or fewer)	11 or more drinks per week	n/a	n/a	.97 (-1.69, 3.62)
Continuous variables				
Mother's age		-.17*** (-.23, -.10)	-.11*** (-.17, -.05)	-.19*** (-.26, -.13)
Birth weight		-0.0 (-.00, .00)	-0.0 (-.00, .00)	n/a
Maternal stressful life events		1.50*** (1.21, 1.78)	1.32*** (1.06, 1.58)	1.18*** (.91, 1.46)

Note. Variables were only included in the multivariate model if they entered univariate models with $p < .10$.

* $p < .05$ ** $p < .01$ *** $p < .001$

Table 3. *Final multivariate model, including interactions with time, for total, internalising and externalising behaviour problems to age 14.*

		Total problems	Internalising problems	Externalising problems
		Estimate (95% CI for estimate)		
Categorical variables				
<i>Sex (ref: M)</i>	F	-1.40*** (-2.08, -.71)	-.25 (-.87, .36)	-1.24*** (-1.90, -.58)
<i>Age (ref: 2)</i>	5	3.57*** (2.84, 4.30)	2.65*** (1.98, 3.32)	2.20*** (1.49, 2.90)
	8	1.55*** (.69, 2.41)	2.62*** (1.85, 3.39)	.054 (-.77, .89)
	10	-1.18* (-2.1, -.27)	1.28** (.48, 2.08)	-2.66*** (-3.54, -1.79)
	14	-2.41*** (-3.34, -1.45)	-2.07*** (-2.91, -1.23)	-2.01*** (-2.93, -1.08)
<i>Maternal education in years (ref: 12 or more)</i>	11 or less	.74 (-.23, 1.69)	.84* (.19, 1.50)	.56 (-.36, 1.48)
<i>Maternal smoking (ref: 0 daily)</i>	1 or more daily	2.59*** (1.75, 3.43)	1.56*** (.81, 2.32)	2.83*** (2.02, 3.64)
<i>Total family income (ref: ≥ 24 000 AUD per annum)</i>	< 24 000 AUD per annum	.95 (-.034, 1.94)	.64 (-.31, 1.58)	.95* (.00, 1.90)
<i>Gestational hypertension (ref: normotensive)</i>	Hypertensive	1.23** (.44, 2.01)	.84* (.13, 1.54)	1.14** (.39, 1.90)
<i>Mother's age</i>		-.17*** (-.23, -.10)	-.11*** (-.17, -.054)	-.19*** (-.26, -.13)
<i>Maternal stressful life events</i>		1.15*** (.76, 1.53)	.85*** (.48, 1.22)	1.07*** (-1.90, -.58)
<i>Family income x Time¹</i>	2	Ref.	Ref.	Ref.
	5	.66 (-.22, 1.54)	.40 (-.53, 1.34)	.59 (-.27, 1.45)

	8	.71 (-.32, 1.74)	.28 (-.78, 1.34)	1.00 (-.005, 2.00)
	10	.86 (-.24, 1.95)	.36 (-.75, 1.47)	1.14* (.087, 2.20)
	14	1.85** (.69, 3.01)	1.40* (.23, 2.56)	1.91*** (.79, 3.03)
<i>Maternal stressful life events x Time</i>	2	Ref.	Ref.	Ref.
	5	.32 (-.028, .67)	.30 (-.079, .68)	.29 (-.047, .63)
	8	.34 (-.069, .75)	.62** (.17, 1.05)	-.003 (-.40, .39)
	10	.61** (.18, 1.05)	.79*** (.34, 1.24)	.26 (-.16, .68)
	14	.60* (.14, 1.06)	.34*** (.34, 1.39)	.09 (-.35, .54)
<i>Maternal education less than 11 years x Time²</i>	2	Ref.	n/a	Ref.
	5	.66 (-.20, 1.50)		.83 (-.00, 1.66)
	8	1.22* (.22, 2.22)		1.43** (.47, 2.40)
	10	1.17* (.11, 2.23)		1.55** (.53, 2.57)
	14	1.25 (-.41, 1.82)		1.21* (.14, 2.29)

¹Relative to family income of \$24 000 AUD or more by time

²Relative to maternal education of twelve or more years by time

Note. Main effects should not be interpreted when included in models with interaction effects. See Table 2 for main effect results.

* $p < .05$ ** $p < .01$ *** $p < .001$