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Fergusson DM, Woodward LJ, Horwood LJ. Maternal smoking during pregnancy and psychiatric adjustment in late adolescence. *Archives of General Psychiatry*, 1998; 55: 721-727.

### Maternal Smoking During Pregnancy and Psychiatric Adjustment In Late Adolescence

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Word count: 3,498

## **Maternal smoking during pregnancy and psychiatric adjustment in late adolescence**

### ABSTRACT

**Background:** The aims of this study were to assess the extent to which exposure to maternal smoking during pregnancy was associated with increased risks of psychiatric symptomatology in late adolescence (16-18 years), when due allowance was made for confounding/selection factors associated with maternal smoking in pregnancy.

**Method:** Data were gathered during an 18 year longitudinal study of a birth cohort of 1,265 New Zealand born children. Measures collected included: i) maternal smoking during pregnancy; ii) assessments of psychiatric problems (conduct disorder, major depression, anxiety and substance use disorders) at ages 16 to 18; and iii) measures of potentially confounding social, family and parental factors.

**Results:** Children exposed to maternal smoking during pregnancy had higher psychiatric symptom rates for conduct disorder, alcohol abuse, substance abuse and depression. Those offspring whose mothers smoked at least one pack of cigarettes per day during their pregnancy had symptom rates that were between 1.4 to 2.5 (median = 2.0) times higher than the offspring of non-smokers. However, pregnancy smoking was also associated with a series of adverse or disadvantageous factors that spanned: i) socio-economic disadvantage; ii) impaired childrearing behaviors; and iii) parental and family problems. After adjustment for these confounding and selection factors, pregnancy smoking was significantly associated with an increased rate of conduct disorder symptoms in late adolescence. This effect was more pronounced for males than females.

**Conclusions:** The present study suggests that maternal smoking during pregnancy may contribute to childrens' risk of later externalising problems. There is a need to further explore the moderating effect of child gender and to clarify the underlying pathophysiology of this relationship.

## INTRODUCTION

There has been increasing concern about the effects of maternal smoking during pregnancy on children. Research indicates that maternal smoking during pregnancy is associated with increased risks of miscarriage<sup>1,2</sup>, reduced birthweight<sup>3,4</sup>, compromised perinatal status<sup>4-7</sup>, and reduced intelligence in offspring<sup>8-10</sup>. More recently, a number of studies have suggested that children whose mothers smoke during pregnancy are at an increased risk of developing later childhood externalising problems including; attention deficit<sup>11,12</sup>, oppositional defiant behavior or conduct disorder<sup>13-16</sup>. Furthermore, recent evidence also indicates that the adverse effects of maternal smoking during pregnancy may persist into adolescence<sup>14</sup>.

While there has been increasing research into the relationship between exposure to maternal smoking during pregnancy and later psychological adjustment in childhood and adolescence, a number of features of this association merit further examination. The first concerns the extent to which associations between maternal smoking and adjustment are specific to externalising behaviors, or conversely, the extent to which smoking during pregnancy is associated with generalised increases in risks of disorder. To date, research in this area has focused on the relationship between maternal smoking during pregnancy and externalising behavior problems<sup>11-16</sup>, while virtually no attention has been given to the extent to which smoking during pregnancy may be related to other child and adolescent outcomes, including depression, generalized anxiety and substance misuse.

A second issue in this area concerns the extent to which statistical associations between maternal smoking during pregnancy and later adjustment reflect:

- a) Cause and effect associations in which, by various routes, exposure to cigarette

smoking in utero influences childrens' longer term susceptibility to adjustment difficulties.

b) Non causal or spurious associations between smoking during pregnancy and child psychiatric adjustment that arise because of the social background, behavioral characteristics and childrearing practices of mothers who elect to smoke during pregnancy<sup>16</sup>. To resolve this issue requires that observed associations between maternal smoking during pregnancy and subsequent psychological adjustment in offspring be shown to persist even after selection factors known or suspected to be associated with maternal smoking during pregnancy have been taken into account.

This paper reports the results of an 18 year longitudinal study of the relationships between maternal smoking during pregnancy and psychiatric outcomes in a birth cohort of over 1,000 New Zealand born children. The aims of the study were:

1. To examine the extent to which consistent dose/response relationships could be found between the extent of maternal smoking during pregnancy and rates of psychiatric symptoms in late adolescence (16 -18 years).
2. To examine the extent to which associations between smoking during pregnancy and rates of psychiatric symptoms persisted when due allowance was made for a range of confounding or selection factors that were associated with pregnancy smoking and later risks of disorder.

## METHOD

### Subjects

The data reported here were collected during the course of the Christchurch Health and Development Study (CHDS). The CHDS is a longitudinal study of a birth cohort of 1,265 children born in the Christchurch (New Zealand) urban region during mid 1977. These children have been studied at birth, 4 months, at annual intervals to 16 years, and again at 18 years of age. The analyses reported in this paper were based on a sample of 1,022 children who had complete data on the maternal smoking and all mental health variables measured at age 18. This sample represented 80.8% of the initial birth cohort and 92.1% of all cohort members still alive and resident in New Zealand at the age of 18 years. Losses to follow up arose because of outmigration from New Zealand (56.3%), refusal to participate in the research (35.4%) and mortality (8.3%). A further 3 (0.2%) subjects were omitted due to missing data for the maternal smoking during pregnancy variable.

To examine the effects of sample losses on the representativeness of the sample, comparisons were made between the 1,022 children included in the analyses and the excluded 243 cohort members on a range of social background measures collected at birth. This analysis suggested that losses to follow-up were not associated with maternal age, ethnicity, family size or gender. However there were small but statistically detectable ( $p < .01$ ) tendencies for this sample to under-represent children from lower socio-economic families. Although these results suggest some bias in the sample, it is unlikely that this bias will materially influence the results reported here, since previous efforts with this cohort to correct for non-random sample loss have in the past shown these effects to be negligible<sup>17, 18</sup>.

### **Maternal Smoking during Pregnancy**

At birth, mothers were questioned about their smoking habits during each pregnancy trimester. Since the number of cigarettes smoked per day across the three trimesters were highly correlated ( $r > .85$ ), a composite measure of the total mean number of cigarettes smoked per day throughout the pregnancy was created. On the basis of this score, mothers were classified into one of four groups. These were: (1) non smoking mothers; (2) mothers who smoked an average of between 1-9 cigarettes per day; (3) mothers who smoked an average of 10-19 cigarettes per day; and (4) mothers who smoked an average of 20 or more cigarettes per day.

### **Psychiatric Outcomes (16-18 years)**

At age 18, sample members were questioned about their substance use and experience of mental health problems during the previous two years using a questionnaire based on the Composite International Diagnostic Interview (CIDI)<sup>19</sup> and the Self-Report Delinquency Inventory (SRDI)<sup>20</sup>. Using this information, DSM-IV<sup>21</sup> criteria were used to construct a series of substance abuse and psychiatric diagnoses for each sample member. These diagnoses included; conduct disorder, alcohol abuse/dependence, nicotine dependence, cannabis and other illicit substance abuse/dependence, generalized anxiety and major depression.

In a preliminary examination of the data, analyses were conducted using DSM-IV diagnoses. This analysis suggested that maternal smoking during pregnancy was unrelated to disorder risk after control for selection factors. To test the robustness of this conclusion, the data were reanalyzed using scale measures of the number of DSM-IV symptoms reported by each subject. This analysis revealed the presence of significant associations between

maternal smoking during pregnancy and psychiatric outcome even after control for the effects of selection factors. The differences between the results for categorical and dimensional analyses suggested that a dimensional scoring approach led to greater predictive precision. This is consistent with a previous analysis of the predictive validity of categorical and dimensional scaling approaches to the measurement of psychiatric disorder within this cohort<sup>22</sup>. Therefore for the purposes of this paper, the variability in symptom levels were analyzed as dimensional variables reflecting the number of DSM-IV symptoms reported. The reliability of each symptom scale was assessed using Cronbach alpha which suggested that the measures used were of moderate to high reliability (conduct disorder,  $\alpha = .72$ ; alcohol abuse/dependence,  $\alpha = .84$ ; nicotine dependence,  $\alpha = .85$ ; illicit substance abuse/dependence,  $\alpha = .89$ ; generalized anxiety,  $\alpha = .97$ ; and major depression,  $\alpha = .92$ ).

## **Selection Factors**

To control for selection factors associated with maternal smoking during pregnancy a range of social background, pregnancy and family factors were selected for inclusion in the study. These factors were chosen because of their statistical associations with maternal smoking during pregnancy and their availability in the study database.

### **1. Family Background Factors**

Measures of maternal education, maternal age and family socio-economic status were obtained at the time of the sample member's birth. Education was coded on a 3-point scale reflecting the highest academic qualification obtained, with 1 = no formal qualifications, 2 = high school qualifications; and 3 = tertiary level qualifications. The third measure was family socio-economic status at the time of the child's birth. This was assessed using the

Elley and Irving<sup>23</sup> scale of socio-economic status for New Zealand. This scale classifies families into six classes on the basis of paternal occupation.

## 2. Pregnancy Related Factors

Measures of mother's pregnancy planning, alcohol consumption and illicit drug use during pregnancy were also collected at the birth assessment. Alcohol use was coded as the mean number of drinks consumed per week across the three pregnancy trimesters. Illicit drug use was coded if mothers reported at any time having used an illicit drug (including; cannabis, hallucinogens, stimulants, sedative and/or opiates) without a doctors prescription during their pregnancy.

## 3. Childrearing Practices

Four measures of maternal childrearing practices were used in this analysis. First, the maternal emotional responsiveness subscale of the HOME Inventory was included as a measure of the frequency with which mothers were observed to make positive emotional responses to their three year old child<sup>24, 25</sup>. Secondly, at age 18, sample members were questioned about the extent to which each parent used physical punishment to discipline them during their childhood (birth to 16 years). A composite measure of exposure to physical punishment was created by taking the highest level of punishment experienced by the sample member<sup>26</sup>. This classification ranged from (1) parent/s never used physical punishment to (4) at least one parent used physical punishment too often or too severely. Thirdly, at age 18, sample members were questioned about their exposure to childhood sexual abuse (CSA) during childhood. Children were classified into four groups ranging from (1) no exposure to CSA to (4) exposure to CSA involving completed or attempted oral, anal or vaginal intercourse<sup>27</sup>.

#### 4. Parental Characteristics and Family Functioning.

Five measures of parental behavior and family functioning were identified. These included; parental separation, parental conflict, parental history of alcohol problems and parental illicit drug use. Children were coded as having experienced a parental separation if their parents had separated or divorced within their first five years of life. The quality of parents' marital relations was coded annually using the following three items: a) whether the parents had engaged in prolonged arguments during the last 12 months; b) whether the child's mother reported being assaulted by her spouse in the last 12 months; and c) whether the child's mother had reported experiencing sexual difficulties in the last 12 months. These items were then combined to produce a scale measure of the extent to which the child was exposed to parental conflict in the period from birth to 5 years<sup>28</sup>. At age 15, parents were asked about their history of criminal offending and alcohol abuse over the last 15 years. Finally, at age 11, parents were questioned about their use of cannabis and other illicit drugs.

#### **Statistical Methods**

The analysis was conducted in four stages:

1. The associations between maternal smoking during pregnancy and DSM-IV symptoms were tabulated and tested for statistical significance using one way analysis of variance and F tests of linear and non linear association. (Table 1).
2. The associations between maternal smoking during pregnancy and a range of confounding and selection factors were then assessed using chi squared tests of independence. (Table 2).
3. The associations between pregnancy smoking and psychiatric symptom rates were then adjusted for confounding and selection by fitting linear regression models to the data. Model fitting was conducted using methods of forward and backward variable elimination to identify

the most parsimonious model. The adjusted dose-response functions were then computed using the parameters of the regression model to estimate the adjusted relationship between symptom rates and pregnancy smoking. (Table 3). An account of this method is provided by Lee<sup>29</sup>.

4. The effects of child gender on the adjusted relationship between maternal smoking during pregnancy and subsequent psychiatric wellbeing was examined using two way analysis of covariance. (Table 4).

## RESULTS

### **Relationship between Maternal Smoking During Pregnancy and Adolescent Psychiatric Adjustment (16-18 years)**

Table 1 shows the relationships between maternal smoking during pregnancy and rates of conduct disorder, substance abuse, anxiety and depression symptoms. For all comparisons except anxiety, there was evidence of significant linear associations between maternal smoking during pregnancy and symptom rates in late adolescence. There were no significant non linear associations. Children whose mothers smoked more than one pack per day during pregnancy had rates of conduct disorder symptoms, nicotine dependence, substance abuse symptoms and depressive symptoms that were between 1.4 to 2.5 (median = 2.0) times higher than the offspring of mothers who did not smoke during pregnancy.

INSERT TABLE 1 HERE

## **Social, Maternal and Family Characteristics Associated with Smoking During Pregnancy**

Table 2 shows the relationships between maternal smoking during pregnancy and a range of measures of maternal social background, antenatal history, childrearing practices, and parental and family characteristics. For ease of data display all measures have been presented in dichotomous form. Results revealed relatively strong associations between mothers' social background and their tendency to smoke during pregnancy. Mothers who smoked during pregnancy, and particularly those who smoked more than half a pack (10 cigarettes) per day, were younger, less well educated and of lower socio-economic status compared to non-smoking mothers. Compared to non-smoking mothers, mothers who smoked during their pregnancy were less likely to have planned their pregnancy and were also more likely to have consumed alcohol and used illicit drugs whilst pregnant. In terms of early childrearing practices, women who smoked during pregnancy were rated as being significantly less nurturant towards their children at age 3 years. Children whose mothers smoked during pregnancy had greater exposure to child physical abuse and child sexual abuse compared to children whose mothers did not smoke during their pregnancy. Finally, mothers who smoked during pregnancy were more likely to have experienced a separation or divorce and reported higher rates of alcohol abuse/dependence, illicit drug use and criminal offending compared to non-smoking mothers. These findings clearly raise the possibility that the elevated rates of disorder found amongst the adolescent children whose mothers smoked during pregnancy could reflect the social circumstances, personal characteristics and childrearing practices of women who elected to smoke during their pregnancy, rather than the direct causal effect of smoking on childrens' later adjustment.

INSERT TABLE 2 HERE

### **Relationship Between Maternal Smoking During Pregnancy and Psychiatric Symptoms Adjusted for Selection Factors**

Table 3 shows the relationships between maternal smoking during pregnancy and later psychiatric symptoms after adjustment for selection factors associated with maternal smoking. As noted in the methods section these adjustments were obtained using multiple linear regression. For each outcome the Table shows: a) the covariate adjusted dose/response relationship between maternal smoking during pregnancy and rates of symptoms; b) the regression coefficient and standard error for the smoking during pregnancy factor; c) the significance of the association; and d) the significant covariates in the regression adjustment equations.

The Table shows that after control for confounding and selection processes, maternal smoking during pregnancy was not significantly related to symptoms of: alcohol abuse/dependence; nicotine dependence; illicit drug abuse/dependence; major depression or generalised anxiety. However even after adjustment for confounding there was still a clear and significant relationship between conduct disorder symptoms and maternal smoking during pregnancy. After covariate adjustment, children whose mothers smoked one pack or more per day during pregnancy had rates of conduct disorder symptoms that were twice as high as the rate for the offspring of non smokers.

Exploration of the sensitivity of the results in Table 3 to the order and number of control factors included in the analysis indicated that providing the significant covariates identified in Table 3 were included in the analysis, inclusion or exclusion of further covariates

did not materially influence the estimates of the adjusted dose/response functions or the significance level of the associations.

INSERT TABLE 3 HERE

### **Gender Differences**

To examine possible gender differences in the effects of maternal smoking during pregnancy on conduct disorder symptoms, the analysis was extended to an analysis of covariance model in which maternal smoking during pregnancy and gender were included as factors. This analysis produced evidence of a clear pregnancy smoking x gender interaction ( $F(3, 936) = 7.18, p < .001$ ) for conduct problems. This interaction is illustrated in Table 4 which shows the relationship between maternal smoking during pregnancy and conduct problems after adjustment for selection factors for males and females. It is evident from these results that whilst rates of conduct difficulties increase with increasing levels of maternal smoking during pregnancy for both males and females, the rate of increase in conduct disorder symptoms is far more marked for males than for females. These results are consistent with the view that males may be more susceptible than females to the effects of maternal smoking during pregnancy.

INSERT TABLE 4 HERE

## COMMENT

This study has examined the relationship between maternal smoking during pregnancy and psychiatric symptoms in late adolescence within a birth cohort of over 1,000 children studied to the age of 18. The major findings of the study and their implications are reviewed below.

First, there was evidence of pervasive and general associations between maternal smoking during pregnancy and later adolescent adjustment with children whose mothers smoked during pregnancy having elevated rates of psychiatric symptoms of: conduct disorder; alcohol abuse/dependence; nicotine dependence; illicit drug abuse/dependence; anxiety and depression. Furthermore, there was evidence of consistent dose/response relationships in which increasing exposure to cigarette smoke during pregnancy was associated with steadily increasing rates of psychiatric symptoms.

Subsequent analyses, however, showed that maternal smoking during pregnancy was correlated with a wide range of social background, pregnancy, parental and family functioning factors that could also have given rise to spurious correlations between maternal smoking during pregnancy and adolescent adjustment. The offspring of women who smoked during pregnancy were exposed to higher levels of social disadvantage, parental deviance, and family dysfunction throughout childhood, compared to the offspring of women who did not smoke during pregnancy. Control for these social and contextual factors explained nearly all of the associations between maternal smoking during pregnancy and self reported psychiatric symptoms, including anxiety, depression, nicotine dependence, alcohol misuse, and illicit drug abuse/dependence. However, even after control for potentially confounding and selection factors, maternal smoking during pregnancy remained significantly associated

with the number of conduct disorder symptoms reported by sample members at age 18. Children whose mothers smoked one pack of cigarettes or more per day during their pregnancy, had mean rates of conduct disorder symptoms that were twice as high as those found amongst children born to mothers who did not smoke during pregnancy.

These findings add to a growing body of evidence that suggests possible causal linkages between exposure to maternal smoking during pregnancy and increased rates of externalising symptoms in later life<sup>11-16</sup>. In support of this causal hypothesis it may be noted that:

- a) A growing number of studies has reported associations between maternal smoking during pregnancy and measures of externalising symptoms during childhood. In all cases these associations have been shown to persist after control for confounding and selection processes.
- b) As illustrated in this study, there is evidence of consistent dose/response relationships in which increasing exposure to maternal smoking during pregnancy is associated with increased rates of externalising symptoms.
- c) The present study also suggests that this association is specific to conduct problems and that similar associations do not exist between pregnancy smoking and other psychiatric symptom patterns.
- d) Additionally, longitudinal evidence from this study suggests that the association is present during both middle childhood<sup>13</sup> and late adolescence.

Collectively, these considerations suggest that the evidence on maternal smoking during pregnancy and later externalising behaviors meets many of the criteria (consistent dose/response; replication; resilience to control for confounding; and specificity of association) that have been proposed as bases for causal inference in non-experimental studies<sup>30</sup>.

Whilst the available evidence clearly suggests a possible causal relationship between maternal smoking during pregnancy and later externalising behaviors, there are still grounds for uncertainty about this conclusion. First, it remains possible that this association reflects uncontrolled confounding factors that are related to smoking during pregnancy and later externalising symptom levels. One source of uncontrolled confounding comes from the possible effects of common genetic factors that are associated with both maternal smoking during pregnancy and later externalising behaviors. A further difficulty in this area has been that of developing a biologically plausible account of the physiological and developmental bases of any causal relationship between exposure to pregnancy smoking and later externalising behavior. A number of authors have pointed to possible biological processes and mechanisms that may explain this association<sup>12, 14, 15</sup>. These have included; fetal hypoxia, changes in serotonin uptake, changes in dopaminergic systems and changes in DNA and RNA synthesis in the brain. However, these explanations remain highly speculative. The uncertainties about the adequacy of control of confounding factors and the absence of compelling evidence about the mechanisms that might lead to causal links between maternal smoking during pregnancy and later outcomes continue to pose threats to the validity of causal inferences in this area<sup>16</sup>. Finally, the results of the present study may suggest that the effects of maternal smoking during pregnancy on externalising behavior are modified by the child's gender, with the evidence suggesting that whilst boys show increases in externalising symptoms with increasing exposure to maternal pregnancy smoking, the same may not be true for girls.

## ACKNOWLEDGMENTS

This research was funded by grants from the Health Research Council of New Zealand, the National Child Health Research Foundation, the Canterbury Medical Research Foundation and the New Zealand Lottery Grants Board.

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Table 1. Mean (standard deviation) rates of DSM-IV symptom criteria (16-18 years) by the extent of maternal smoking during pregnancy

Measure	Number of Cigarettes Per Day				Test for Linear Trend	
	None (N = 691)	1-9 (N = 158)	10-19 (N = 98)	20+ (N = 75)	F (1,1020)	p
<u>Externalising</u>						
Conduct disorder	0.33 (0.90)	0.56 (1.16)	0.57 (1.06)	0.85 (1.83)	21.60	<.0001
Alcohol abuse/dependence	0.59 (1.44)	0.82 (1.81)	0.86 (1.97)	1.07 (2.11)	8.62	<.005
Nicotine dependence	0.41 (1.17)	0.58 (1.32)	0.84 (1.51)	0.83 (1.54)	15.16	<.0001
Illicit substance abuse/ dependence	0.47 (1.44)	0.81 (1.90)	0.68 (1.76)	1.12 (2.49)	12.02	<.001
<u>Internalising</u>						
Major depression	2.05 (3.31)	2.37 (3.57)	2.34 (3.58)	2.93 (3.73)	4.71	<.05
Generalized anxiety	0.66 (1.60)	0.75 (1.60)	1.08 (1.96)	0.61 (1.57)	1.28	>.20

Table 2. Rates (%) of social background, parental and family characteristics by the extent of maternal smoking during pregnancy

Outcomes	Number of Cigarettes Per Day				$\chi^2$	p
	None (N = 691)	1-9 (N = 158)	10-19 (N = 98)	20+ (N = 75)		
<u>Family Social Background Factors</u>						
Mother lacked formal educational qualifications	42.1	57.1	79.1	76.6	93.14	<.001
Mother aged <25 years at birth of child	4.7	55.3	51.9	48.6	23.09	<.001
Family of semi-skilled/unskilled socio-economic status	21.1	30.4	47.0	42.1	49.15	<.001
<u>Pregnancy Factors</u>						
Pregnancy was unplanned	32.7	47.6	50.8	56.1	37.78	<.001
Mother drank 3 or more alcohol drinks/week	9.4	15.2	17.2	20.8	17.6	<.001
Mother used illicit drugs	1.2	5.8	3.7	7.5	18.15	<.001
<u>Childrearing Factors</u>						
In lowest quartile of maternal emotional responsiveness score (3 years)	21.7	21.2	41.3	34.0	20.10	<.001

Outcomes	Number of Cigarettes Per Day				$\chi^2$	p
	None (N = 691)	1-9 (N = 158)	10-19 (N = 98)	20+ (N = 75)		
Parents regularly used physical punishment during childhood	10.3	11.4	16.3	17.3	5.35	<.05
Child sexual abuse reported	8.51	13.9	13.3	17.3	8.27	<.01
<u>Parent and Family Factors</u>						
Parental separation/divorce (0-5 years)	8.1	14.8	19.2	27.4	40.2	<.001
In highest decile of parental conflict score (0-5 years)	6.7	9.5	11.9	26.1	30.57	<.001
Parental history of alcoholism/alcohol problems	9.9	9.8	19.0	26.9	20.42	<.001
Parental history of criminal offending	9.3	19.0	27.4	19.2	23.27	<.001
Parental illicit drug use	20.0	33.8	30.1	42.5	27.00	<.001

Table 3. Mean rates of DSM-IV symptom criteria by maternal smoking during pregnancy after adjustment for confounding and selection factors.

Measure	Number of Cigarettes Per Day				Regression Coefficient (S.E.)	p	Significant Covariates <sup>a</sup>
	None	1-9	10-19	20+			
<u>Externalising</u>							
Conduct disorder	0.35	0.47	0.60	0.72	.124 (.036)	<.001	4-6
Alcohol abuse/dependence	0.63	0.72	0.82	0.91	.093 (.054)	>.05	4, 5
Nicotine dependence	0.48	0.51	0.54	0.57	.030 (.044)	>.50	1-4
Illicit substance abuse/dependence	0.52	0.63	0.74	0.84	.107 (.056)	>.05	4-6
<u>Internalising</u>							
Major depression	2.05	2.18	2.30	2.42	.125 (.116)	>.25	4
Generalized anxiety	0.68	0.70	0.71	0.73	.016 (.054)	>.75	4, 5

<sup>a</sup> Significant covariates: 1 = maternal age; 2 = maternal education; 3 = planned pregnancy; 4 = childhood sexual abuse; 5 = parental use of physical punishment; 6 = parental criminality.

Table 4. Mean rates of DSM-IV symptom criteria for conduct disorder for males and females after adjustment for confounding and selection factors.

	Number of Cigarettes Per Day			
	None	1-9	10-19	20+
Male	0.48	0.76	1.04	1.32
Female	0.20	0.23	0.26	0.28
Total	0.35	0.47	0.60	0.72