Maternal Cigarette Smoking and Child Psychiatric Morbidity: A Longitudinal Study

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ABSTRACT. Objective. Previous studies have linked maternal smoking during pregnancy with behavioral disturbance in children. However, additional evidence is needed to address the causality of the relationship. The present study analyses result from an Australian cohort of 5342 5-year-old children whose mothers were recruited early in pregnancy.

Methods. Smoking history was gathered for prepregnancy, first clinic visit (FCV), late pregnancy, and when the child was 6 months and 5 years of age. Behavior problems at the age of 5 were assessed using a modified Child Behavior Check List (CBCL) shown to have high agreement with the complete CBCL. This resulted in the formation of three scales: internalizing; social, attentional and thought; and externalizing behavior problems, which were then dichotimized at the 90th percentile in each case. Logistic regression was used to model these outcomes as a function of maternal smoking at five time points during which it was assessed. A series of models explored the effect of additional adjustment for confounding. The predictors of attrition (29.5%) throughout the cohort were also identified by multivariate modeling.

Results. The final analysis was carried out on a cohort of mother-child pairs for whom data and child behavior outcomes were complete. The mean age of children was 5 years, 6 months with a range from 4 to 6 years. The mean age of mothers at the time of birth of the child was 25 years, with a range from 13 to 47 years. Mothers lost to follow-up were more likely to be younger, single, and less well-educated than those who continued participation, although maternal smoking was not an independent determinant.

Unadjusted analyses showed strong associations between externalizing child behavior and maternal smoking during pregnancy and at the 5-year follow-up, with relative risks (RRs) up to 2.6 for children of women smoking at least 20 cigarettes per day at the first antenatal clinic visit. A clear dose-response relationship existed in most relationships with higher levels of smoking being associated with higher rates of externalizing behavior problems. Weaker relationships occurred for internalizing behavior and social, attentional and thought behavior problems.

Multivariate analysis of the timing in more detail that the association between maternal smoking and child behavior problems persisted, although the evidence for dose-response diminished. Moreover, it was primarily associated with smoking as determined by questions asked at the FCV (RR = 1.52, 2.03, 2.16) for 1 to 9, 10 to 19, and ≥20 cigarettes per day, respectively, compared with nonsmoking and secondarily by smoking determined at the 5-year follow-up (RR = 1.52, 1.87, 1.29) for 1 to 9, 10 to 19, and ≥20 cigarettes per day respectively, compared with nonsmoking. This association appeared to be independent of a wide range of possible confounders such as maternal age, education, social class, marital status and mental health, gestation at FCV, complications during pregnancy, the child’s sex, gestational age at birth, and age at last follow-up. Adjustments were also made for the mother’s employment since birth, family structure, and maternal mental health at the time of the CBCL assessment. Associations between externalizing behavior problems and maternal smoking at other times, and those between other behavioral problems examined and maternal smoking were not significant.

Conclusion. Although previous studies have found evidence for an association between maternal smoking and child behavior problems, the strength of this study lies in its size, its detailed and consistent measurement of maternal smoking, and its ability to control for many social and biological factors linked to maternal smoking and child behavior.

The statistical evidence for a causal relationship between maternal smoking as measured at the first antenatal clinic visit and the development of externalizing behavior in children is strongly suggestive, because of the specificity of effect and timing, and the adjustment for a comprehensive range of other risk factors. An alternative explanation that mothers who smoke might be inclined to report behavior problems differently was considered unlikely because the effect was specific to externalizing behavior and the major exposure occurred 5 years before the reported behavior. Additionally, the existence of a factor (beyond those already included in the analysis) that might be related to both behavior problems and any propensity to misreport smoking seems sufficiently implausible to rule out misclassification of smoking status as another alternative explanation for the findings.

The timing of the relationship between smoking in pregnancy and externalizing behavior problems, and its independence of small for gestational age status at birth, suggests that placental insufficiency and oxygen deprivation are not important in the pathogenesis. It is possible that nicotine in the fetal brain derived from maternal smoking may alter gene expression and the nature and
function of the nicotine receptors developing in early pregnancy. The presence of a separate, although slightly weaker, association between concurrent maternal smoking and externalizing child behavior suggests both biological and social explanations, including a direct psychopharmacologic effect of nicotine through passive smoking.

Assuming the relationship to be causal, it is estimated that maternal smoking in early pregnancy may account for 25% of externalizing (aggressive) behavior while maternal smoking when the child is 5 years old may account for an additional 16%. These findings provide further support for antismoking programs in pregnancy and in young family settings. Pediatrics 1998;102(1). URL: http://www.pediatrics.org/cgi/content/full/102/1/e11; smoking, behavior problems, pregnancy, children.

**TABLE 1. Behavior Scales Derived From the CBCL**

<table>
<thead>
<tr>
<th>Internalizing</th>
<th>SAT</th>
<th>Externalizing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cronbach's $\alpha = 0.76$</td>
<td>Cronbach's $\alpha = 0.75$</td>
<td>Cronbach's $\alpha = 0.84$</td>
</tr>
<tr>
<td>Cries a lot</td>
<td>Acts too young for age</td>
<td>Argues a lot</td>
</tr>
<tr>
<td>Feels worthless or inferior</td>
<td>Cannot concentrate, cannot pay attention for long</td>
<td>Demands a lot of attention</td>
</tr>
<tr>
<td>Likes to be alone</td>
<td>Cannot get mind off certain thoughts</td>
<td>Destroys own things</td>
</tr>
<tr>
<td>Too fearful or anxious</td>
<td>Cannot sit still, restless or hyperactive</td>
<td>Destroys things belonging to others</td>
</tr>
<tr>
<td>Nervous, highly strung or tense</td>
<td>Clings to adults or too dependent</td>
<td>Disobedient at home</td>
</tr>
<tr>
<td>Feels too guilty</td>
<td>Daydreams or gets lost in thoughts</td>
<td>Gets into many fights</td>
</tr>
<tr>
<td>Refuses to talk</td>
<td>Does not get along with other children</td>
<td>Lying or being dishonest</td>
</tr>
<tr>
<td>Sulks a lot</td>
<td>Not liked by other children</td>
<td>Screams a lot</td>
</tr>
<tr>
<td>Withdrawn; does not get involved with others</td>
<td>Poorly coordinated or clumsy</td>
<td>Sudden changes in mood or feeling</td>
</tr>
<tr>
<td>Worrying</td>
<td>Repeats certain acts; has compulsions</td>
<td>Stubborn, sullen, or irritable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Temper tantrums or hot temper</td>
</tr>
</tbody>
</table>

MATERNAL CIGARETTE SMOKING AND CHILD PSYCHIATRIC MORBIDITY

**METHODS**

The Mater Cohort

The Mater University of Queensland Study of Pregnancy involved 8458 pregnant women enrolled between 1981 and 1984. They were recruited at their first antenatal clinic visit to the Mater Misericordiae Hospital in Brisbane, Australia, which serves a population of approximately one half million people and has a major tertiary obstetric unit.

Extensive information regarding social characteristics of the family and psychological characteristics of the mother was collected at enrollment, 1 or 2 days after birth, 6 months after the birth, and again 5 years after delivery. Biological measures relating to pregnancy, delivery, and the neonatal period were extracted from the medical record. At the 5-year follow-up mothers completed a modified Child Behavior Check List (CBCL), and developmental, behavioral, and health information was obtained on the child.

Initial compliance with the study was very high: of 8556 women approached, only 98 refused. Subsequently, 7689 of these mothers were confined at the Mater Hospital, with pregnancies of at least 20 weeks’ gestation. Losses (769) at this stage related to miscarriage or confinement elsewhere. Of those at the Mater Hospital, 112 infants died before discharge, leaving, for the purpose of the present study, a baseline cohort of 7577 infants. Attrition over the following 5 years was 29.5%, resulting in a total contact of 5342 mothers.

Following an approach suggested previously, an analysis was performed to identify those factors, relevant to the present investigation, that predicted attrition from hospital discharge to 5 years of age. This was carried out on the subset of 6989 (of the 7577 discharged infants) for whom information on all variables required measured up to the time of discharge was complete.

The final analysis was performed on the cohort of 4879 mothers and children for whom data on behavioral outcomes and covariates were complete.
Cronbach 0.75; and the externalizing scale consisted of 11 items with a 5-year was used in this analysis.

Maternal Smoking Status
At the interviews (first clinic visit [FCV], 2 to 4 days after delivery, 6 months after delivery, and at child age 5 years), mothers were asked to quantify their smoking. In the questionnaire administered at the FCV, mothers were asked about their smoking before pregnancy as well as in the past week. In the questionnaire 2 to 4 days after delivery, mothers were asked to recall their smoking level over the last trimester. In the 6-month and 5-year follow-up questionnaires, smoking questions referred to the past smoking level over the last trimester. In the 6-month and 5-year follow-up, owing to difficulties in tracing some children, only its assessment at the FCV and at age 5 years was used in this analysis.

Maternal Anxiety and Depression
Maternal mental health was measured using the Delusions–Symptoms States Inventory of Bedford and Foulds. This measure of mental health was chosen because it assesses symptoms that are not confused easily with those of pregnancy and its consequences. The Delusions–Symptoms States Inventory has been validated extensively, and it has been used in numerous studies. Although maternal mental health was assessed at the first survey and all follow-ups, only its assessment at the FCV and at age 5 years was used in this analysis.

Other Characteristics Potentially Associated With Child Behavior Problems and Maternal Smoking
These included:
1. maternal age at the child’s birth (in 5-year age groups);
2. maternal education level (special school or primary only; started secondary school; left school at age 15 to 16 years; left school at age 17 to 18 years; college or university);
3. marital status (married, single, living together, other);
4. gestation at FCV, estimated from the dates of the FCV and delivery and gestation at delivery (<16 weeks, 16 to 20 weeks, >20 weeks);
5. social class of the mother and her partner at the FCV;
6. country of birth of the mother and her partner;
7. whether the mother or her partner was indigenous;
8. religiosity of the mother, as measured by frequency of church attendance;
9. number of previous pregnancies and miscarriages of the mother;
10. antenatal admissions to hospital;
11. occurrence of bleeding during pregnancy;
12. gender of the child;
13. gestation (in weeks) at delivery;
14. small for gestational age (SGA) at birth (ie, birth weight below the 10th percentile for gestational age and gender);
15. employment since birth;
16. number of children 0 to 2 years, 3 to 6 years, 7 to 12 years, or 13 to 17 years in the family at the 5-year follow-up; and
17. age of child at last follow-up.

The list above contains a mixture of possibly confounding and intervening variables. They were included to determine whether the smoking effect is independent of other well known or presumed effects, so as to eliminate as many alternative explanations as possible. After such extensive adjustment, the survival of an independent smoking effect would strengthen the evidence for the association between maternal smoking and child behavior problems being truly causal.

Statistical Methods
Multivariate analysis of baseline factors predicting attrition was performed using logistic regression on the cohort of the 6989 mothers for whom complete baseline data were available (588 of the 7577 had missing data for at least one of the measures obtained during pregnancy or soon after delivery). This proceeded in two steps: 1) an initial step to eliminate those variables measured at the FCV that were not predictive of attrition, and 2) a second step that added other variables obtained at delivery.

Preliminary analysis of the consequences of maternal smoking behavior was performed by calculating the percentage of children with behavior problems according to smoking at each of the four times. Relative risks (RRs) estimated by odds ratios (OR) were calculated for each smoking category, with nonsmoking as the reference category. Multivariate logistic regression was used to examine the variation in risk of behavior problems according to maternal smoking, after adjusting for smoking at other time periods, and the various sociodemographic and biological characteristics listed above. Computations were performed using the statistical packages SAS and SPSS.

The burden of behavior problems attributable to maternal smoking was calculated according to the standard formula for obtaining population attributable risk (PAR) involving the prevalence (P) of the risk factor (in this case, maternal smoking) and the RR of the outcome:

\[
\text{PAR} = \frac{P(RR - 1)}{1 + P(RR - 1)}
\]

This computation was performed within each stratum of cigarette smoking and aggregated over strata to obtain the total PAR for maternal smoking at each phase.

RESULTS
There were 4879 mothers for whom data on smoking and child behavior outcomes were complete. The mean age of these mothers at the time of birth was 25 years, with a range of 13 to 47 years. Children in this cohort were assessed at a mean age of 5 years 6 months, with a range of 4 to 6 years at the last follow-up, owing to difficulties in tracing some children; however, 83.6% of children were 5 years old at follow-up.

Mothers lost to follow-up at 5 years tended to be younger, single, and less educated than those who continued participation (Table 2). They also were more likely to have presented later in their pregnancy, to have been smokers, and to have had higher...
rates of mental health problems early in pregnancy. Their infants were more likely to have been born of earlier gestation and be of SGA status. However, important from the scope of this paper, multivariate analysis showed that the higher rates of attrition among smokers (prepregnancy and during pregnancy) appear to be a consequence of smokers being younger and less well educated rather than an independent effect of smoking itself. This is evidenced by the reduction to nonsignificance of the association between maternal smoking and attrition.

The percentage of children with behavior problems and estimated RR (compared with nonsmokers) was calculated for each category of maternal smoking on each occasion (Table 3).

This analysis demonstrated that the higher the level of maternal smoking at each of the four times, the greater the risk of behavior problems as assessed by each of the three subscales. The strongest association was between externalizing child behavior at the 5-year follow-up and maternal smoking during pregnancy. A clear dose–response relationship existed in most relationships, with higher levels of smoking being associated with higher rates of child behavior problems.

To determine the relative contribution of maternal smoking at different time periods to child behavior problems at 5 years, three separate logistic regression models were fitted to each of the three scales, with the presence of behavior problems at 5 years as the dependent variable.

Before pregnancy, 46.5% of the cohort were cigarette smokers. This declined to 35.4% at the FCV and 37.3% at the 5-year follow-up. It also was common for women to reduce their consumption levels (as opposed to complete cessation of smoking) at the FCV. Given this amount of changing behavior, analysis can be directed toward differentiating the times when smoking may have a greater or lesser impact on child behavior problems.

RR of child behavior problems by level of maternal smoking was estimated, adjusting for mother’s smoking at each other occasion (Table 4). In the first analysis, smoking early in pregnancy was strongly related to later child behavior problems, and this relationship was with externalizing child behaviors rather than with the other scales. There was no statistically significant relationship between smoking later in pregnancy and subsequent child behavior problems (after adjustment for smoking at other times). Behavior problems were related to concurrent maternal smoking at 5 years, although this relationship was weaker than that with smoking at the FCV.

To distinguish the influence of maternal smoking from other factors that may be independent determinants of behavior problems and that may predispose a woman to smoking, a variety of sociodemographic, biological, and maternal mental health variables was added to the analysis as listed earlier. The findings from this analysis were almost identical to the first, indicating that these factors were not further confounding the relationship between either maternal smoking at the FCV or at 5 years and child behavior problems.

The third analysis adds measures of maternal anxiety and depression at the FCV and at 5 years to the model. RRs altered slightly for the phases when mental health was measured, but the levels of statistical significance generally were maintained. In particu-
lar, after all adjustments, the RR associated with the smoking behavior producing highest risk for externalizing behavior problems at age 5 years (smoking at least 20 cigarettes per day in early pregnancy) declined from 2.41 \((P = .01)\) to 2.16 \((P = .03)\). To test this relationship further, self-reported measures of subjective stress were added to the model for externalizing behavior problems. Risk estimates for maternal smoking factors at phase were virtually unchanged.

Smoking at the FCV and, to a lesser extent, at 5 years therefore is associated with increased externalizing behaviors in the child at 5 years. This relationship is independent of the many additional factors examined in this analysis. Contrary to findings in the unadjusted analysis, there was little evidence of a dose–response relationship between smoking at the FCV and externalizing child behavior.

The PAR percent for maternal smoking in early pregnancy, derived from the adjusted RRs (RR) and the prevalence of smoking in each dose category was 7.6\%, 10.4\%, and 7.4\%, giving a total of 25.4\% of externalizing problems attributable to smoking in early pregnancy. A similar calculation for smoking at age 5 years yielded a total PAR of 15.5\%.

To track the pattern of behavior change and its association with subsequent (5-year) child behavior, the percentage of children with externalizing behavior problems was classified progressively according to maternal smoking status before, during, and after the pregnancy (Figure 1). This has been presented in the form of a tree diagram (Figure). Branches with <100 women and smoking at age 6 months have been excluded for clarity. Of the 2271 prepregnancy smokers, 24.5\% reported that they had quit at the FCV, whereas other groups of women stopped smoking late in pregnancy or started smoking after the birth of the child. Nonsmoking mothers at all points of data collection had a low risk of child behavior problems (8.2\%), compared with mothers who smoked at all points (14.7\%). These observations thus confirm that women who smoke have an increased risk of their child manifesting externalizing behaviors. If they continue to smoke beyond the FCV, however, risk is not increased additionally. Women who had stopped smoking at the FCV and subsequently maintained their nonsmoking status have the risk of child behavior problems reduced to that of continuous nonsmokers (7.9\%). Those women who reported prepregnancy smoking, had quit in early pregnancy, but subsequently began smoking had no increased risk of having children with child behavior problems at 5 years of age, except for the group of women \((n = 159)\) who had resumed smoking after their infant was born and were smoking at age 5 years. Reduction in smoking some time after the FCV does not reduce the prevalence of later externalizing child behavior problems.

Women who had never smoked until after the birth of their infant and were smoking at age 5 years \((n = 113)\) had children with increased rates of externalizing child behavior problems.

No additional statistically significant reduction in behavior problems was observed for those women who continued smoking through pregnancy but were no longer smoking at the 5-year follow up.

**DISCUSSION**

Results from this study support those reported previously.\(^1,\)\(^3\) Externalizing behaviors are specifically affected contrary to a previous report,\(^1\) and smoking at the FCV rather than at other times measured is most strongly associated with later behavior problems. Smoking in late pregnancy does not appear to

<table>
<thead>
<tr>
<th>Cigarettes per day</th>
<th>5 Years</th>
<th>6 Months</th>
<th>Late pregnancy</th>
<th>FCV</th>
<th>None</th>
<th>1–9</th>
<th>10–19</th>
<th>≥20</th>
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<td>5 Years</td>
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TABLE 3. Percent With Child Behavior Problems and RR, as Estimated by the OR, by Maternal Smoking Before, During, and After Pregnancy

<table>
<thead>
<tr>
<th>Cigarettes per day</th>
<th>5 Years</th>
<th>6 Months</th>
<th>Late pregnancy</th>
<th>FCV</th>
<th>None</th>
<th>1–9</th>
<th>10–19</th>
<th>≥20</th>
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<tr>
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<td></td>
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</table>

* 95\% CI excludes unity.
add to the risk of externalizing behaviors. Externalizing behaviors, in this study and others, also are associated with disturbances in parenting, social disadvantage, and marital difficulties.22 However, the association between maternal smoking and these behavior problems remains after a wide range of possible social and biological antecedent/intervening and/or confounding variables have been added to the analysis, strengthening the argument that the maternal smoking effect observed is not mediated through them. The evidence that the association that smoking in early pregnancy is causal appears particularly strong because if an unknown confounder, such as personality type, were responsible for this effect, it would have to be independent of all variables already adjusted for, exhibit higher rates within the women who report quitting smoking in early pregnancy, and be associated with externalizing behavior at age 5.

To examine any modification of these effects by gestation at FCV, a separate stratified analysis of gestation at FCV, and externalizing behavior problems (data not shown) provided results that are consistent with the others obtained.

Although Weitzman and colleagues1 developed their items from the CBCL, they present results separately for six subscales, two of which are broadly comparable with the externalizing scale used in this study. Their study found the largest differences were for antisocial and headstrong behaviors, which corresponded closely to the items in the externalizing scale used in this study. This result also is consistent with the measure of conduct disturbance, attentional disorder, and delinquency reported elsewhere.2–4 In earlier studies, an increased prevalence of disruptive hyperactivity,4 hyperactivity and short attention span,9 and impulsivity with increased level of activity17 has been reported in association with smoking during pregnancy. Such behaviors overlap with the externalizing and SAT scales in the present study.

Several explanations can be suggested for the association between maternal cigarette smoking and child behavior problems. The timing of the relationship at the FCV and its independence of SGA status at birth suggest that placental insufficiency and oxygen deprivation are not important in the pathogenesis. Acetylcholine is an important neurotransmitter in the brain, with nicotinic receptors developing during early pregnancy.19 Receptors are mutable during development,20 and it is possible that nicotine in the fetal brain derived from maternal smoking may alter gene expression and the nature and function of the nicotine receptor. Neurotransmitter levels also influence the development of postsynaptic neurons.21 A suitable animal model and measurement of nicotinic receptors might allow testing of this hypothesis.

The suggestion that mothers who smoke report the behaviors of their children differently is less likely given that the association is observed for externalizing but not for other behaviors. Specifically, it is unlikely that nicotine effects occurring in early pregnancy would affect a mother’s perception of externalizing behaviors, particularly some 5 years later. Similar considerations would apply to a hypothesis that external factors such as psychosocial stress

TABLE 4. Adjusted Estimated RR of Child Behavior Problems, as Estimated by the OR, by Maternal Smoking Before, During, and After Pregnancy

<table>
<thead>
<tr>
<th>Cigarettes per day</th>
<th>Internalizing</th>
<th>SAT</th>
<th>Externalizing</th>
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<tr>
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<td>≥20</td>
<td>1.42</td>
<td>1.31</td>
<td>1.08</td>
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Abbreviations: RR1 adjusted for smoking at other times; RR2 adjusted for smoking at other times and social and biological factors listed in text; RR3, adjusted for smoking at other times, social, and biological factors listed in text and maternal mental health at first antenatal visit and at 5 years.

* 95% CI excludes unity.
might simultaneously lead to a woman smoking and influence her perception of her child’s behavior.

The presence of a separate although slightly weaker independent association between concurrent maternal smoking and externalizing child behaviors at 5 years again suggests both biological and social explanations, including a direct psychopharmacologic effect of nicotine through passive smoking. Nicotine effects operating as a result of maternal smoking at age 5 years might have such an effect; however, we have no way of discerning this and there is no published literature suggesting this. Although the subgroup of women who began smoking after the birth of their child is a relatively small proportion of the study sample, the finding that their children had higher rates of behavior problems could reflect either biological factors associated with passive cigarette smoking or social learning and/or childbearing processes associated with mothers who smoke cigarettes. This latter possibility is rendered less plausible by the finding that controlling for a wide variety of maternal social variables does not eliminate the associations observed in this study (Table 4).

Based on the rate and level of smoking early in pregnancy and the adjusted RRs presented in Table 4 (and assuming a cause–effect association), it is estimated that up to 25% of behavior problems in children can be attributed to maternal smoking early in pregnancy. A somewhat lesser amount could be attributed to concurrent smoking.

Three methodologic issues could possibly affect
the interpretation of these findings. First, no independent measures of maternal smoking or child behaviors were made to confirm the questionnaire information. Various studies, however, confirm that self-reports of smoking have high reliability and validity. Bias in self-reports of smoking would only be misleading if misclassification of smoking was differential with respect to the reporting of child behavior problems. Moreover, if deceptive responses (presumably false-negative) were responsible for the early-pregnancy effect, one would need to posit that the factor actually responsible for the lower rate of externalizing behavior in this group was more frequent in those with a propensity to misreport non-smoking status in early pregnancy specifically. The existence of such a factor (beyond those already adjusted for) seems implausible. Second, attrition was differential for certain groups, as described previously. This would produce misleading results if there were a systematic association between loss to follow-up and the measurement of child behavior problems. Third, it could be argued that maternal smoking is a marker or is associated with some aspects of maternal child-rearing practices. Perhaps there is some other characteristic of the mother that, on the one hand, is associated with the decision to smoke early in pregnancy or after the child is born and, on the other, influences child-rearing practices. If this were so, it would be difficult to explain why smoking at the first trimester is a more important predictor variable than smoking at the 5-year follow-up. The association between maternal smoking during early pregnancy is strong, and there is some evidence that it is dose-related; it involves specific behaviors and is independent of measured confounding.

The attributable risk is large and, although additional investigation is required, these findings provide further support for antismoking programs in pregnancy and in young family settings.

ACKNOWLEDGMENT

The Mater–University Study of Pregnancy was supported by the National Health and Medical Research Council of Australia.

REFERENCES

16. Statistical Package for the Social Sciences Version 7.0
Maternal Cigarette Smoking and Child Psychiatric Morbidity: A Longitudinal Study
Gail M. Williams, Michael O’Callaghan, Jake M. Najman, William Bor, FRANZCP; Margaret J. Andersen, AIMS¶; David Richards and Chinlyn U, BSc

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Pediatrics 1998;102:e11

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