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Pediatrics 2006;118;943
DOI: 10.1542/peds.2006-0168

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The authors have indicated they have no financial relationships relevant to this article to disclose.

ABSTRACT

BACKGROUND. Numerous studies have reported that maternal cigarette smoking during pregnancy is related to lower IQ scores in the offspring. Confounding is a crucial issue in interpreting this association.

METHODS. In the US National Longitudinal Survey of Youth 1979, IQ was ascertained serially during childhood using the Peabody Individual Achievement Test, the total score for which comprises results on 3 subtests: mathematics, reading comprehension, and reading recognition. Maternal IQ was assessed by using the Armed Forces Qualification Test. There were 5578 offspring (born to 3145 mothers) with complete information for maternal smoking habits, total Peabody Individual Achievement Test score, and covariates.

RESULTS. The offspring of mothers who smoked ≥1 pack of cigarettes per day during pregnancy had an IQ score (Peabody Individual Achievement Test total) that was, on average, 2.87 points lower than children born to nonsmoking mothers. Separate control for maternal education (0.27-IQ-point decrement) and, to a lesser degree, maternal IQ (1.51-IQ-point decrement) led to marked attenuation of the maternal-smoking–offspring-IQ relation. A similar pattern of results was seen when Peabody Individual Achievement Test subtest results were the outcomes of interest. The only exception was the Peabody Individual Achievement Test mathematics score, in which adjusting for maternal IQ essentially led to complete attenuation of the maternal-smoking–offspring-IQ gradient (0.66-IQ-point decrement). The impact of controlling for physical, behavioral, and other social indices was much less pronounced than for maternal education or IQ.

CONCLUSIONS. These findings suggest that previous studies that did not adjust for maternal education and/or IQ may have overestimated the association of maternal smoking with offspring cognitive ability.
FIRST DESCRIBED >3 decades ago,1 an inverse association between maternal smoking during pregnancy and offspring intelligence (denoted here as IQ) has been reported in cohorts drawn from Finland,2 the United Kingdom,3 Canada,4 Australia,5,6 New Zealand,7,8 the United States,9 and Denmark.10 Taking the findings of these studies together, there is an ~3- to 7-point (0.2–0.5 of an SD) deficit in the IQ scores of children born to mothers who smoke relative to those born to mothers who do not. In addition, in studies that report the amount of cigarettes smoked,9,10 a dose-response relation with offspring IQ has been found. As in many observational studies, the issue of confounding is critical to the interpretation of this association: the characteristics of mothers who smoke (and those of the offspring born to them) differ consistently from those that do not. In most,2–4,7,9–12 but not all,5,6,8 studies the inverse maternal-smoking–offspring-IQ gradient holds after adjustment for a range of social and biological covariates that attempt to capture characteristics of the parents (socioeconomic position, adiposity, alcohol consumption, and illicit drug use), the home environment (cognitive stimulation, emotional support, and quality of child care), and the offspring themselves (prematurity, fetal growth, and infant feeding method).

Persons with lower IQ scores have an increased risk of smoking initiation13,14 and a reduced likelihood of giving up once started.15 Given also the moderately high parent-offspring IQ correlation,16 maternal IQ should also be considered as a potentially important candidate confounder in studies linking maternal smoking with offspring IQ. To our knowledge, only 2 studies9,17 have examined this issue, and they reveal somewhat contradictory findings. Although both demonstrated the expected inverse maternal-smoking–offspring-IQ relation, this effect was robust to adjustment for maternal IQ and other covariates for some, although not all, measures of childhood ability in the Elmira, New York, cohort.9 However, in a larger sample drawn from southeast Michigan, the maternal-smoking–offspring-IQ association was lost.17

To address the relative paucity of evidence and somewhat contradictory findings, we analyzed data from the US National Longitudinal Survey of Youth 1979 (NLSY79), which holds data on a nationally representative sample of >3000 mothers and their offspring. Cognitive ability test results were available for both mothers and children, with repeated assessments made on the latter between the ages of 5 and 14 years. Study participants are also well characterized for a wide range of potentially confounding socioeconomic and behavioral variables.

METHODS

Study Participants
The NLSY799–18 (available at: www.bls.gov/nls/nlsy79.htm) comprises a population-based sample of 12 686 young people aged between 14 and 21 years on January 1, 1979. Selected groups (black and Hispanic people, poor white people, and people in the military) were oversampled. Study participants were resurveyed annually until 1994 and biennially thereafter. From 1986, children born to the female study participants were also incorporated into data collection. The database for these offspring is referred to as the NLSY79 child and young adult sample (“young adult” because some of the children are now of adult age).19

Assessment of Maternal Smoking During Pregnancy
Mothers reported their cigarette smoking as number of packs of 20 cigarettes smoked per day during pregnancy (categorized as none, <1 pack, between 1 and 2 packs, and >2 packs). Because of the small number of mothers who reported the highest level of cigarette smoking, we collapsed the latter 2 groups. Studies in adults show close agreement between self-reported cigarette smoking and its biochemical marker, plasma cotinine.20 In addition, even distant (>30-year) recall of cigarette consumption during pregnancy demonstrates a high level of agreement with archived data on smoking collected during pregnancy.21

Assessment of Offspring IQ
Offspring IQ was based on scores derived from the Peabody Individual Achievement Test (PIAT).19 The PIAT total score comprises results on 3 subtests: mathematics, reading comprehension, and reading recognition. The PIAT mathematics subtest has 84 multiple-choice questions of increasing difficulty, ranging from recognizing numbers to advanced concepts in geometry and trigonometry. Commencing the test at an age-appropriate level, a baseline is established by achieving 5 consecutive correct answers. Testing ceases when 5 mistakes are made of 7 possible answers; scores are age standardized. The PIAT reading-recognition subtest has 84 items involving word recognition and pronunciation. The PIAT reading-comprehension subtest contains 64 items in which the child reads a sentence and chooses which of 4 pictures best represents the description. The PIAT22 is among the most widely used brief measure of academic achievement for children aged 5 and older. Moderate-to-high correlations have been reported when scores from it were compared with the Wechsler Intelligence Scale for Children-Revised.23 In even-numbered years from 1986 to 2002, the PIAT was administered to the female subjects’ offspring who were aged between 5 and 14 years.19 Children were tested repeatedly if they fell within the age range during the test years.

Assessment of Covariates
On the basis of the Armed Services Vocational Aptitude Battery (ASVAB), the mother’s IQ score was derived from the Armed Forces Qualification Test (AFQT),
which was administered in 1980. Four sections of the ASVAB were used to compute the AFQT: arithmetic reasoning, word knowledge, paragraph comprehension, and numerical operations.\textsuperscript{23} Mothers also responded to a range of interviewer-administered inquiries regarding race, infant feeding, gestational age (in weeks), and birth weight (in ounces) of her offspring; alcohol consumption and illicit drug use (marijuana/hashish and cocaine) during pregnancy; and whether the mother was residing with a spouse or partner. The short form of the home-observation portion of the environment scale\textsuperscript{25} was used as an index of the quality of caregiving of the parent(s); specifically, the cognitive-stimulation and emotional-support subscales were used. Maternal education was the highest grade completed by the mother by the time of the birth of the index child. The measure of household poverty was based on whether the total household income was below the poverty threshold for the year of the birth of the index child.

**Statistical Analyses**

Linking the data from the NLSY79 with the child and young adult sample results in a data set that contains \( \geq 1 \) IQ assessment for each offspring and \( \geq 1 \) offspring per mother. This can be viewed as a hierarchical structure, with assessments nested within offspring and offspring nested within mothers. The multiple assessments made on each child are unlikely to be statistically independent, as are the data for siblings. To accommodate this lack of independence we used random-effects models, which have the additional advantage of being able to use all available assessments for each child and all children regardless of whether they are siblings. The statistical background for the use of random-effects models for repeated-measures data\textsuperscript{26} and for multilevel (hierarchical)\textsuperscript{27} data are provided elsewhere. To aid the comparison of results, all cognitive test outcomes are standardized to IQ-type scores, with a mean of 100 and SD of 15. Continuous predictors are standardized to zero mean and unit SD.

We began the statistical analyses by assessing the association between each of the potential confounding factors and maternal cigarette smoking during pregnancy. We then proceeded to examine the relation between maternal smoking and offspring IQ in an unadjusted analysis. Finally, we produced effect estimates after adjusting for individual covariates and, lastly, from a multiply adjusted analysis.

**RESULTS**

Table 1 presents the numbers of study participants (mothers and offspring) for which full data were available. There were \( \sim 3000 \) mothers in the data set, a number that varied slightly according to the PIAT subtest because of some missing data. The numbers of assessments of IQ in the offspring exceeded that of the number of mothers, because some mothers had \( \geq 1 \) child in the study. Depending on age at entry to the study, a child could have taken the PIAT test on \( \geq 1 \) occasion. On average, each child had 3 such assessments.

The relations between maternal smoking during pregnancy and covariates are reported in Table 2. For covariates that are continuous, the mean score (SD) is presented, whereas for categorical covariates, the percentage is shown. With the exception of offspring gender and gestational age, maternal smoking was related to each of the study covariates, although not all incrementally. In comparison to nonsmokers, mothers who smoked during pregnancy were younger, had a lower IQ test score, reported fewer years in education, and were more likely to be in a lower-income household. Smoking was also related to other behaviors by the mother, with smokers more likely to report illicit drug use and alcohol consumption during pregnancy. Postnatally, mothers who smoked during pregnancy were also less likely to breastfeed their offspring. Children of mothers who smoked had a lower birth weight and apparently less favorable home environments for care provision in terms of both emotional support and cognitive stimulation. Mothers who smoked were also less likely to be living with a partner or spouse. In this cohort, approximately one quarter of the mothers (28.71\%) reported smoking during pregnancy: 21.21\% consumed \( < 1 \) pack (1–19 cigarettes) per day, and 7.5\% consumed \( \geq 1 \) pack (\( \geq 20 \) cigarettes) per day.

Table 3 presents the associations between maternal smoking during pregnancy and offspring cognitive ability as indexed using the PIAT total score. The results presented are the mean difference in IQ score in each maternal-smoking category relative to the nonsmoking group. A negative number indicates a decrement in IQ score. In each row the effect estimates for smoking in relation to offspring IQ are adjusted separately for the named covariate. To judge the impact of controlling for each factor, comparison should be made between the effect estimates in each row and those from the unadjusted (crude) analyses; we express this difference in percentage terms.

In the unadjusted analysis, as anticipated, there was an inverse association between maternal smoking during pregnancy and offspring PIAT-based IQ test score, with lower scores seen in the children of mothers who smoked. There was also evidence of a dose-response
BATTY et al reported smoking in IQ test score in children born to mothers who smoke. This association: in comparison to the nonsmokers, the decrement in IQ test score in children born to mothers who reported smoking ≥1 pack per day during pregnancy (2.87-IQ-point decrement) was greater than that in those reporting ≤1 pack (1.73-IQ-point decrement). With the exception of adjustment for maternal alcohol consumption during pregnancy and ethnicity, which resulted in a marked increase in the magnitude of the relation of maternal smoking with offspring IQ, the separate addition of other covariates to the multivariable model led to some attenuation. The percentage attenuation can be broadly classified into 3 strata. One group of potential covariates had a very modest effect on the smoking-IQ gradient: gender of offspring, cognitive and emotional stimulation, gestational age, birth weight, birth order, illicit drug use by the mother, and both parents being present in the home. Another group of covariates resulted in some partial attenuation: mothers age, being breastfed, and household poverty. By far, the greatest attenuation of the inverse smoking-evidence.
ing-IQ gradient was evident when the mothers’ IQ and, particularly, education were added to the statistical models. The attenuating effect of maternal education was stronger than that for maternal IQ. We provide an illustration of these results in Fig 1. In this graph, the inverse maternal-smoking–IQ gradient apparent in unadjusted analyses is heavily attenuated after controlling for maternal IQ. However, the association is essentially lost when separate adjustment is made for maternal education. Controlling for further covariates had essentially no additional impact in comparison to that apparent for education alone.

When PIAT sub-scores of reading comprehension and reading recognition were the outcomes of interest, we found essentially the same pattern of association with maternal smoking (results are not shown but are available from the authors on request). The attenuation after individual and multiple adjustment for covariates was also very similar. We do, however, present results for PIAT mathematics subtest scores in relation to maternal smoking in pregnancy (Table 4), because these gradients differed somewhat from those evident in the aforementioned analyses. Whereas a similar maternal-smoking–IQ relation was apparent in unadjusted analyses when PIAT mathematics subtest scores were the outcome of interest, the association with maternal smoking was completely attenuated by separate control for maternal IQ (for other childhood mental ability outcomes, it was only partially attenuated). Again, adjustment for maternal educational level essentially eliminated this relation.

Given the birth weight–lowering effect of maternal smoking and the link between birth weight and IQ, birth weight has been advanced as a mediator in the maternal-smoking–offspring-IQ relation. Although statistical control for birth weight can be used to identify the "independent" effect of maternal smoking, data restriction is an alternative approach. When we restricted our analyses to offspring born at >34 completed weeks’ gestation and those weighing >2500 g (88 oz), the results were essentially the same as those reported above (results not shown).

**DISCUSSION**

In the present study we used a large, general population-based sample to examine the impact of controlling for maternal IQ and other potential covariates on the association between maternal smoking and offspring IQ. There was an inverse relation between maternal smoking during pregnancy and offspring IQ in unadjusted analysis, such that lower PIAT test results were apparent in the children of mothers who smoked. Although this effect was partially attenuated after separate adjustment for behavioral and social covariates, controlling for maternal education and, in some analyses, maternal IQ effectively eliminated this association. The mothers’ educational attainment was associated with cigarette smoking during pregnancy in a stepwise manner, whereas with IQ the same gradient with smoking was not evident. It is plausible that maternal education is more strongly related to knowledge and attitudes about the potentially harmful effects of smoking during pregnancy than maternal mental ability.

The first warning about the deleterious effects of ma-
ternal smoking during pregnancy were issued in the US in 1964 with the publication of the first Surgeon General’s report on the health consequences of this behavior. With increased awareness after the release of such information, particularly in better-educated/higher-IQ–scoring mothers, one would surmise that the magnitude of the maternal-smoking–offspring-IQ effect, if confounded by the aforementioned factors, would increase over time. This does not seem to be the case, however, with effect estimates across relevant studies generally stable over the intervening period. In fact, the strength of the smoking-IQ relation in our study, based on a relatively contemporaneous cohort, was somewhat weaker than most, if not all, reports. That maternal cigarette smoking was self-reported up to 2 years prior to delivery may result in an underestimation of effect introduced if a significant proportion of the heavy smokers tended to underreport their habit. However, retrospective recall of smoking levels even 30 years postpregnancy demonstrates high levels of sensitivity and specificity with archived maternal smoking histories. In addition, given the size of the study (one of the largest to examine this relation), the effect estimates reported may well be closer to the true value than those found in smaller-scale investigations.

Potential Explanations
At least 3 explanations exist for our observation that controlling for maternal IQ and education eliminated the association between maternal smoking and reduced offspring IQ. In the first explanation, IQ and/or education lie on the pathway linking maternal smoking with offspring IQ. In this scenario, maternal smoking would have an IQ-lowering effect on the mother, thus rendering her less able to perform optimally educationally and provide a cognitively stimulating environment for her offspring. Although this is plausible, we believe it is very unlikely. A second suggestion is that it is instead maternal smoking that lies on the pathway between the mother’s IQ and offspring IQ. If this is correct, the maternal-smoking–offspring-IQ association would, in fact, be causal, and successful smoking–offspring-IQ gradient was apparent in a small cohort of socioeconomically disadvantaged women. It is likely that such a group would have a narrower-than-normal range of maternal IQ scores, which would effectively have led to some statistical control of this covariate via data restriction. In this study, the maternal-smoking–offspring-IQ score association held after adjustment for the mothers’ mental ability for some, if not all, measures of childhood cognition. By contrast, the findings of a much larger cohort drawn from the Michigan area more clearly reflect those of our own (ie, controlling for the IQ and educational level of the mother effectively eliminated the deleterious effect of maternal smoking on offspring IQ).

Table 4
Relation of Maternal Smoking During Pregnancy With Offspring’s Cognition (PIAT Mathematics; N = 6026)

<table>
<thead>
<tr>
<th>Smoking Consumption</th>
<th>Nonsmoker (4323)</th>
<th>&lt;1 Pack per d (1217)</th>
<th>≥1 Pack per d (486)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B %</td>
<td>B %</td>
<td>B %</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>0 (ref) –</td>
<td>–1.483 –</td>
<td>–2.130 –</td>
</tr>
<tr>
<td>Mother’s age</td>
<td>0 –</td>
<td>–1.021 –31</td>
<td>–1.756 –18</td>
</tr>
<tr>
<td>Male</td>
<td>0 –</td>
<td>–1.484 0</td>
<td>–2.132 0</td>
</tr>
<tr>
<td>Low-income family</td>
<td>0 –</td>
<td>–1.163 –22</td>
<td>–1.239 –42</td>
</tr>
<tr>
<td>Mother’s education</td>
<td>0 –</td>
<td>0.261 –118</td>
<td>0.582 –127</td>
</tr>
<tr>
<td>Mother’s IQ score</td>
<td>0 –</td>
<td>–0.153 –90</td>
<td>–0.657 –69</td>
</tr>
<tr>
<td>HOME (cognitive stimulation)</td>
<td>0 –</td>
<td>–1.249 –16</td>
<td>–1.590 –25</td>
</tr>
<tr>
<td>HOME (emotional support)</td>
<td>0 –</td>
<td>–1.410 –5</td>
<td>–1.973 –7</td>
</tr>
<tr>
<td>First born</td>
<td>0 –</td>
<td>–1.491 –1</td>
<td>–1.938 –9</td>
</tr>
<tr>
<td>Birth weight</td>
<td>0 –</td>
<td>–1.140 –23</td>
<td>–1.627 –24</td>
</tr>
<tr>
<td>Gestational age</td>
<td>0 –</td>
<td>–1.503 –1</td>
<td>–2.134 0</td>
</tr>
<tr>
<td>Mother consumed alcohol in pregnancy</td>
<td>0 –</td>
<td>–2.090 41</td>
<td>–2.613 23</td>
</tr>
<tr>
<td>Breastfed</td>
<td>0 –</td>
<td>–1.059 –29</td>
<td>–1.389 –35</td>
</tr>
<tr>
<td>Illicit drug use by mother</td>
<td>0 –</td>
<td>–1.495 –1</td>
<td>–2.142 –1</td>
</tr>
<tr>
<td>Both parents present</td>
<td>0 –</td>
<td>–1.029 –31</td>
<td>–1.574 –26</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>0 –</td>
<td>–2.121 43</td>
<td>–3.845 81</td>
</tr>
<tr>
<td>Multiple adjustment</td>
<td>0 –</td>
<td>0.2481 –117</td>
<td>0.2372 –111</td>
</tr>
</tbody>
</table>

Sample size refers to the number of children with complete data for maternal smoking, PIAT (total), and other covariates. Results are mean difference in IQ score relative to the “nonsmoker” category (ref). Percent change is for comparison with the unadjusted value. Each row represents the separate (not cumulative) adjustment for each covariate.
cessation interventions targeted at pregnant mothers would exert IQ-boosting effects. A final, noncausal possibility is that, as described earlier, maternal IQ may be a confounding variable in the maternal-smoking–offspring-IQ relation. As such, differences in maternal IQ and/or educational attainment across the smoking groups may be generating this gradient rather than maternal smoking itself.

Study Strengths and Limitations
The strengths of this study lie in the size (resulting in high statistical power), the nationally representative nature of the cohort (resulting in high generalizability, although some sectors of the population were oversampled), and the range of covariate data gathered on the mother, the rearing environment, and the child (resulting in comprehensive control for potential confounding/mediating variables). There are, of course, some shortcomings also. First, there were, inevitably, missing data for some of the variables, including the IQ test results. For this to have led to selection bias, however, the directions of the associations we report here would have to be opposite and unfeasibly large to those in persons with missing data. Second, the IQ tests were administered to the offspring between the ages of 5 and 14 years. Future studies should examine if the pattern of association observed herein is the same in persons who have an IQ assessment later in childhood, when scores will more closely resemble lifetime cognitive ability and the influence of between-family effects (shared environment) is lower.

CONCLUSIONS
In our study, adjustment for maternal IQ and, to a greater extent, educational attainment effectively eliminated the association of mothers’ smoking with offspring IQ. This could suggest that, rather than tobacco smoking in the mother leading to declines in offspring IQ, this effect might be explained by low levels of maternal education and cognitive ability. On the basis of this evidence, previous studies may have overestimated the influence of maternal smoking consumption on offspring IQ by not controlling for appropriate covariates. These results notwithstanding, there are many other reasons for mothers to abstain from smoking during pregnancy, not the least of which are the apparent influence on perinatal and postnatal growth and the financial burden incurred by continuing the habit. Clearly, then, the findings of our study should not be taken to lessen the imperative to refrain from tobacco smoking during pregnancy.

ACKNOWLEDGMENTS
Dr Batty is a Wellcome Fellow, and Prof Deary is the recipient of a Royal Society-Wolfson Research Merit Award.

We thank 2 anonymous referees for their helpful comments.

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19. Center for Human Resource Research. NLSY79 Child and Young Adult Data Users Guide. Columbus, OH: Ohio State University; 2002
MAKING BABIES

“In his 2004 book, ‘The Empty Cradle: How Falling Birthrates Threaten World Prosperity and What to Do About It,’ Phillip Longman exploded one of the planet’s most enduring modern myths. He demonstrated that population growth is not the threat that it has been made out to be and that population decline is the real challenge ahead of us. By the time of the book’s publication, many developed nations were already struggling to address the obvious result of falling fertility: What to do when so few babies are being born that eventually there won’t be enough workers to sustain your country’s economy, let alone support the elderly? One of the most recent answers comes from Portugal, where the birthrate has fallen to 1.7—below the replacement rate of 2.1 children per couple. The government there has come up with a plan to give tax breaks to people who have more than two children and to levy higher taxes on those who have fewer than two. Singapore, France, Sweden and many other states already employ various incentives to encourage parenthood. . . . What a change from only a few decades ago, when conventional wisdom had it that the only route to prosperity was smaller families.”

Noted by JFL, MD

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DOI: 10.1542/peds.2006-0168