

Longitudinal analysis of the effect of prenatal nicotine exposure on subsequent smoking behavior of offspring

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We explored the influence of maternal smoking during pregnancy on the likelihood of smoking among offspring in adolescence and adulthood using data from two similar British birth cohort surveys, the 1958 National Child Development Study and the 1970 British Birth Survey. Similar information was available in each cohort on maternal age at delivery, offspring sex, maternal smoking during pregnancy, parental and offspring socioeconomic status, and parental smoking at the time offspring smoking was assessed at age 16 years. Offspring smoking at 16 years and at 30/33 years were the primary outcomes of interest. Our data support an association between maternal smoking during pregnancy and an increased risk of offspring smoking later in life among female offspring but not among male offspring. Female offspring of mothers who smoked during pregnancy were more likely to smoke at 16 years than were their male counterparts. Moreover, in this same subgroup, female offspring smoking at 16 years was associated with an increased likelihood of smoking at 30/33 years. Further investigation in larger studies with greater detail of factors shaping smoking in childhood and adulthood and biochemically verified outcome measures would be desirable to clarify the relationship.

Introduction

Identifying the causes underlying the development of smoking behaviors is of considerable public health importance. Contemporary accounts acknowledge a range of determinants, with recent literature suggesting a link between fetal exposures, in particular to nicotine, and the development of smoking behaviors

in later life. Given that 19% of women in the United Kingdom smoke throughout pregnancy (U.K. Department of Health, 2000), this potential association may have far-reaching consequences for the offspring in addition to the effects on the women's own health. Moreover, the effect could reverberate across generations as female offspring go on to become pregnant themselves.

Smoking during pregnancy contributes to a variety of short- and long-term effects on the growth in utero and neurodevelopment of offspring (Bell & Lau, 1995; Butler & Goldstein, 1974; DiFranza & Lew, 1995; Dunn & McBurney, 1977; Fried & Watkinson, 1988; Fried, Watkinson, & Siegel, 1997; Naeye, 1978; Olds, Henderson, & Tatelbaum, 1994). Also, a growing body of evidence suggests that maternal tobacco consumption during pregnancy may have specific, negative effects on a range of behavioral outcomes expressed in childhood and adolescence, including smoking (Brook, Brook, & Whiteman, 2000; Cornelius, Leech, Goldschmidt, & Day, 2000; Day, Richardson, Goldschmidt, & Cornelius, 2000;

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Fergusson, Horwood, & Lynskey, 1993; Fergusson, Woodward & Horwood, 1998; Griesler, Kandel, & Davies, 1988; Kandel, Wu & Davies, 1994).

Animal studies have suggested an association between prenatal nicotine exposure and subsequent offspring sensitivity to nicotine. Abreau-Villaça, Seidler, Tate, Cousins, and Slotkin (2004) reported that prenatal nicotine exposure is associated with subsequent offspring response to nicotine in adolescence in rats, and they suggested that this effect may be mediated by alterations in cell development that persist into adolescence (Abreau-Villaça, Seidler, & Slotkin, 2004). Studies among humans have been somewhat conflicting, however, with a case-control study and a cohort study each reporting a positive association between smoking during pregnancy and subsequent offspring smoking behavior (Buka, Shenassa, & Niaura, 2003; Kardia, Pomerleau, Rosek, & Marks, 2002), whereas another longitudinal study found no association between prenatal maternal levels of cotinine, the primary metabolite of nicotine, and daughters' subsequent smoking at age 23 years (Kandel & Udry, 1999). In this case, higher levels of testosterone in pregnant smokers were associated with increased likelihood of their daughters smoking in later life. Moreover, although studies of smoking during pregnancy and offspring smoking in childhood and adolescence offer some support for an association between maternal smoking during pregnancy and early initiation and vulnerability, they do not provide information directly relating to maintenance or dependence.

To explore the association between maternal smoking during pregnancy and subsequent offspring smoking, while controlling for other risk factors associated with likelihood of smoking, such as parental smoking after birth, we examined the association between maternal smoking during pregnancy and smoking in adolescence and adulthood in a pooled analysis of two British cohorts.

Method

Procedure

Data were drawn from the 1958 National Child Development Study (NCDS) and the 1970 British Birth Survey (BCS70), which are available for secondary analysis from the Data Archive at the University of Essex, United Kingdom. These studies are ongoing multidisciplinary investigations of two nationally representative cohorts of the British population born March 3–9, 1958, and April 5–11 1970, respectively. The cohorts have been followed from birth into adulthood, with data collection on all study participants attempted at several follow-up

“sweeps” by questionnaire, examination, or interview at varying ages.

Sample

NCDS cohort. Information was obtained on 17,414 births, with follow-up sweeps of survivors at ages 7, 11, 16, 23, and 33 years. Follow-up sweeps reached between 10,000 and 12,000 of the original cohort, with each sweep varying slightly in sample composition because of variable response rates. The cohort provides offspring smoking data at ages 16 and 33 years on a subset of 8,579 participants, representing 49% of the original study cohort that were eligible for inclusion in this study.

BCS70 cohort. Information was obtained on 17,196 births, with follow-up sweeps of survivors at ages 5, 10, 16, 26, and 30 years. Follow-up sweeps again varied slightly in sample composition because of variable response rates. The cohort provides offspring smoking data at ages 16 and 30 years on a subset of 4,873 participants, representing 28% of the original study cohort that were eligible for inclusion in this study.

Measures

Maternal smoking during pregnancy. Data on maternal smoking during pregnancy was ascertained from unverified maternal self-report by questionnaire administered at the end of pregnancy. In the NCDS cohort, smoking specifically after the fourth month of pregnancy was reported, whereas in the BCS70 cohort, smoking across pregnancy was reported. For the present analysis, smoking behavior was categorized as a dichotomous outcome (smoker vs. nonsmoker, where smoking was defined as at least 1 cigarette/day).

Maternal and paternal smoking at 16-year follow-up. Maternal and paternal smoking at 16-year follow-up was ascertained from unverified maternal self-report by questionnaire. Smoking behavior was dichotomized in the same way as maternal smoking during pregnancy.

Offspring smoking at 16-year and 30/33-year follow-up. Offspring smoking in adolescence (16-year follow-up) and adulthood (30/33-year follow-up) was ascertained from unverified offspring self-report by questionnaire. Smoking status at 16-year follow-up was categorized as smoker (at least 1 cigarette/week) versus nonsmoker (less than 1 cigarette/week). Smoking status at 30/33-year follow-up was categorized as a dichotomous outcome (smoker vs.

nonsmoker, where smoking was defined as at least 1 cigarette/day), in the same way as for maternal and paternal smoking at 16-year follow-up.

Data analyses

To test the effect of maternal smoking during pregnancy on offspring smoking in adolescence and adulthood, we conducted multivariable logistic regression analysis in two stages, first with offspring smoking at 16-year follow-up as the binary dependent variable, and second with offspring smoking at 30/33-year follow-up as the dependent variable. Covariates included offspring sex, birth cohort, maternal age at offspring birth, paternal social class at offspring birth, maternal smoking at 16-year follow-up, and paternal smoking at 16-year follow-up.

To test the interaction of maternal smoking during pregnancy with other predictors of offspring smoking behavior in adolescence and adulthood, we conducted a multigroup analysis, stratified by maternal smoking during pregnancy. To reduce the effects of data loss, we used all available data, with pairwise deletion (Muthén & Muthén, 2004). The multigroup model in this analysis tests for differences in the direct and indirect effects of covariates on smoking at 16-year and 30/33-year follow-up for mothers who did and did not report smoking during pregnancy. Interaction effects were tested using chi-square difference testing, with a weighted least-squares estimation method.

All statistical analyses were conducted using MPlus version 3.11. An alpha level of .05 was maintained throughout.

Results

Characteristics of offspring and parents

Complete data on offspring sex, birth cohort, maternal age at offspring birth, paternal social class at offspring birth, maternal smoking at 16-year follow-up, paternal smoking at 16-year follow-up, and offspring smoking at 16-year and 30/33-year follow-up were available for 4,014 of the NCDS cohort and 2,700 of the BCS70 cohort, representing 47% and 55% of those eligible for inclusion, and 23% and 16% of the original study cohorts, respectively.

Among the NCDS cohort, participants for whom complete data were available did not differ substantially from the remainder of the original study cohort in maternal age at birth ($M=27$ years vs. 27 years, respectively), paternal social class at birth ($M=61\%$ manual vs. 64% manual), maternal smoking during pregnancy ($M=26\%$ vs. 31%), or offspring sex ($M=48\%$ male vs. 50% male), but those with

incomplete data did differ somewhat from the rest of the original study cohort in maternal smoking at 16-year follow-up ($M=61\%$ vs. 52%).

Among the BCS70 cohort, participants for whom complete data were available did not differ substantially from the remainder of the original study cohort in maternal age at birth ($M=26$ years vs. 26 years, respectively) or offspring sex ($M=52\%$ male vs. 50% male), but they did differ somewhat in paternal social class at birth ($M=62\%$ manual vs. 72% manual), maternal smoking during pregnancy ($M=33\%$ vs. 43%), and maternal smoking at 16-year follow-up ($M=74\%$ vs. 60%).

Among participants for whom complete data were available, the birth cohorts (NCDS vs. BCS70) did not differ substantially in maternal age at birth ($M=27$ years vs. 26 years, respectively) or paternal social class at birth ($M=61\%$ manual vs. 62% manual), but they did differ somewhat in maternal smoking during pregnancy ($M=26\%$ vs. 33%), maternal smoking at 16-year follow-up ($M=38\%$ vs. 26%), and offspring sex ($M=48\%$ male vs. 40% male).

In the NCDS cohort, among participants for whom complete data were available, 26% of mothers reported smoking during pregnancy, whereas 38% of mothers and 52% of fathers reported smoking at least 1 cigarette/day at 16-year follow-up. Among offspring, 30% reported smoking at least 1 cigarette/week at 16-year follow-up, and 29% reported smoking at least 1 cigarette/day at 30/33-year follow-up.

In the BCS70 cohort, among participants for whom complete data were available, 33% of mothers reported smoking during pregnancy, whereas 26% of mothers and 32% of fathers reported smoking at least 1 cigarette/day at 16-year follow-up. Among offspring, 22% reported smoking at least 1 cigarette/week at 16-year follow-up, and 28% reported smoking at least 1 cigarette/day at 30/33-year follow-up.

Demographic and descriptive characteristics of offspring and parents are presented in Table 1.

Logistic regression analysis

Maternal smoking during pregnancy was associated with offspring smoking at 16-year follow-up ($\beta=.19$, $Z=3.32$, $p<.01$), but this effect disappeared when maternal smoking at 16-year follow-up was included in the model ($\beta=-.03$, $Z=0.39$, $p>.05$).

Maternal smoking during pregnancy was associated with offspring smoking at 30/33-year follow-up when offspring smoking at 16-year follow-up was controlled for ($\beta=.16$, $Z=2.35$, $p<.05$), but this effect again disappeared when maternal smoking at 16-year follow-up was included in the model ($\beta=.05$,

Table 1. Demographic and smoking characteristics for NCDS and BCS70 cohorts^a.

Characteristic	Cohort ^a	
	NCDS 1958 (N=4,014)	BCS70 (N=2,700)
Maternal smoking (pregnancy)	1,061 (26.4)	903 (33.4)
Maternal smoking (16-year) ^b	1,545 (38.5)	703 (26.0)
Paternal smoking (16-year) ^b	2,072 (51.6)	865 (32.0)
Offspring smoking (16-year) ^c	1,183 (29.5)	589 (21.8)
Offspring smoking (30/33-year) ^b	1,164 (29.0)	756 (28.0)
Paternal social class (birth): manual	2,456 (61.2)	1,674 (62.0)
Offspring sex: male	1,929 (48.1)	1,077 (39.9)
Maternal age, in years (birth)	Mean (SD)=27.3 (5.4)	Mean (SD)=26.3 (5.1)

^aAll values are numbers of subjects (%), unless otherwise noted.

^bSmoking regularly (≥ 1 cigarette/day).

^cSmoking regularly (≥ 1 cigarette/week).

$Z=0.63$, $p>.05$). The results of the full multivariate logistic regression analyses are presented in Table 2.

Maternal age at birth was positively associated with offspring smoking at 16-year follow-up ($p<.05$). Maternal smoking at 16-year follow-up was associated with offspring smoking at 16-year and 30/33-year follow-up ($p<.001$ and $p<.05$, respectively), as was paternal smoking at 16-year follow-up ($p<.0001$ and $p<.05$). Manual social class was associated with increased likelihood of offspring smoking at 16-year and 30/33-year follow-up ($p<.001$ and $p<.01$), compared with nonmanual social class. Offspring in the 1970 birth cohort were 33% more likely to be nonsmokers at 16-year follow-up than were those in the 1958 birth cohort ($OR=1.33$, 95% $CI=1.19-1.49$). However, at 30/33-year follow-up, offspring in the 1970 birth cohort were 22% more likely to be smokers than were those in the 1958 birth cohort ($OR=1.22$, 95% $CI=1.06-1.40$).

Multigroup analysis

Multigroup analysis indicated a significant difference in the indirect effects of offspring sex ($\chi^2=8.67$, $df=1$,

$p<.005$) and maternal age at birth ($\chi^2=6.44$, $df=1$, $p<.05$) between mothers who did and did not smoke during pregnancy.

The total indirect effect of offspring sex was significant for offspring whose mothers smoked during pregnancy ($\beta=-.10$, $Z=2.49$, $p<.05$) but not for offspring of mothers who did not smoke during pregnancy ($p>.05$). Among offspring whose mothers smoked during pregnancy, therefore, female offspring were 15% more likely than male offspring to be smoking at 16-year follow-up ($OR=1.15$, 95% $CI=1.03-1.28$). In addition, among this subgroup of female offspring, smoking at 16-year follow-up doubled the likelihood of smoking at 30/33-year follow-up ($OR=2.05$, 95% $CI=1.96-2.14$).

The total indirect effect of maternal age at birth was significant for offspring whose mothers smoked during pregnancy ($\beta=.01$, $Z=3.33$, $p<.05$) but not for offspring of mothers who did not smoke during pregnancy ($p>.05$). Among offspring whose mother smoked during pregnancy, each additional year of maternal age at birth increased the likelihood of offspring smoking at 16-year follow-up by 2% ($OR=1.02$, 95% $CI=1.01-1.03$).

Table 2. Multivariate logistic regression analysis (N=6,714).

	β	Standard error	Z statistic	Odds ratio	95% Confidence interval
Offspring smoking at 16-year follow-up					
Maternal smoking (pregnancy)	-0.03	0.07	-0.39	0.97	0.85-1.12
Maternal age (birth)	0.01	0.01	2.34	1.01	1.00-1.02
Offspring sex	-0.01	0.05	-0.12	0.99	0.90-1.10
Paternal smoking (16-year)	0.42	0.06	7.41	1.52	1.36-1.70
Maternal smoking (16-year)	0.38	0.07	5.32	1.46	1.27-1.68
Paternal social class (birth)	-0.29	0.06	-5.03	0.75	0.67-0.84
Birth cohort	0.29	0.06	5.06	1.33	1.19-1.49
Offspring smoking at 30/33-year follow-up					
Maternal smoking (pregnancy)	0.05	0.08	0.63	1.05	0.90-1.24
Maternal age (birth)	0.01	0.01	1.58	1.01	1.00-1.02
Offspring sex	0.07	0.06	1.11	1.07	0.95-1.21
Paternal smoking (16-year)	0.17	0.07	2.47	1.18	1.04-1.35
Maternal smoking (16-year)	0.19	0.08	2.21	1.20	1.02-1.42
Offspring smoking (16-year)	2.11	0.06	33.38	8.28	7.31-9.37
Paternal social class (birth)	-0.17	0.07	-2.65	0.84	0.74-0.96
Birth cohort	-0.20	0.07	-3.08	0.82	0.72-0.93

Paternal smoking at 16-year follow-up had a significant indirect effect on offspring smoking at 16-year follow-up in both groups (i.e., offspring whose mothers did and did not smoke during pregnancy). Although the comparable effect for maternal smoking at 16-year follow-up was statistically significant only among offspring whose mothers did not smoke during pregnancy, the difference between the two groups was not significant. The results of the full multigroup analysis are presented in Table 3 and Figure 1.

Discussion

We used data from two British birth cohorts, recruited 12 years apart, to examine the association between maternal smoking during pregnancy and subsequent offspring smoking behavior. Although smoking behavior in the United Kingdom changed over the period of the two cohorts, parental and offspring smoking rates at each assessment were consistent with national survey data (U.K. Department of Health, 2003; Wald & Nicolaides-Bouman, 1991), suggesting that the two study cohorts sufficiently represented nationwide smoking behaviors at the time of assessment. Smoking rates in pregnancy appear to be somewhat resilient despite

changes in overall adult smoking behavior between 1958 and 1970.

Our data support an association between maternal smoking during pregnancy and an increased risk of offspring smoking later in life among female offspring but not among male offspring. After adjustment for selected demographic measures and independent smoking variables, multivariate logistic regression analyses indicated no significant association between maternal smoking during pregnancy and offspring smoking at either 16 years or 30/33 years. Multigroup analysis, however, indicated that maternal smoking during pregnancy interacted with other risk factors for offspring smoking. Female offspring of mothers who smoked during pregnancy were more likely to smoke at 16 years than were their male counterparts. Moreover, in this same subgroup, female offspring smoking at 16 years was associated with an increased likelihood of smoking at 30/33 years. In addition, among mothers who smoked during pregnancy, maternal age was associated with increased probability of offspring smoking at 16 years. Consistent with a number of previous studies of postnatal smoking history (Kardia et al., 2002; O'Loughlin, Paradis, Renaud, & Gomez, 1998; Osler, Clausen, Ibsen, & Jensen, 1995), concurrent paternal smoking at 16 years was significantly

Table 3. Multigroup analysis ($N=6,714$).

	Odds ratio	95% Confidence interval	99% Confidence interval
Mother smoked during pregnancy			
Offspring smoking at 16-year follow-up			
Maternal age (birth)*	1.02	1.01–1.03	1.00–1.03
Offspring sex*	0.87	0.78–0.97	0.75–1.01
Maternal smoking (16-year)	1.14	0.99–1.31	0.95–1.37
Paternal smoking (16-year)**	1.21	1.08–1.36	1.04–1.42
Paternal social class (birth)	0.88	0.78–1.00	0.75–1.04
Birth cohort**	1.18	1.05–1.32	1.02–1.37
Offspring smoking at 30/33-year follow-up			
Maternal age (birth)	1.00	0.99–1.01	0.99–1.02
Offspring sex	1.08	0.98–1.20	0.95–1.23
Maternal smoking (16-year)	1.09	0.95–1.24	0.91–1.29
Paternal smoking (16-year)	1.05	0.94–1.17	0.91–1.21
Paternal social class (birth)	0.99	0.89–1.12	0.86–1.16
Birth cohort**	0.77	0.70–0.85	0.68–0.88
Offspring smoking (16-year)**	2.05	1.96–2.14	1.93–2.17
Mother did not smoke during pregnancy			
Offspring smoking at 16-year follow-up			
Maternal age (pregnancy)	1.00	1.00–1.01	0.99–1.01
Offspring sex	1.06	0.99–1.14	0.96–1.17
Maternal smoking (16-year)**	1.33	1.21–1.47	1.17–1.52
Paternal smoking (16-year)**	1.31	1.21–1.42	1.18–1.46
Paternal social class (birth)**	0.83	0.77–0.90	0.75–0.92
Birth cohort**	1.19	1.09–1.29	1.07–1.32
Offspring smoking at 30/33-year follow-up			
Maternal age (pregnancy)	1.01	1.00–1.01	1.00–1.01
Offspring sex**	1.13	1.05–1.20	1.03–1.23
Maternal smoking (16-year)	1.01	0.92–1.11	0.90–1.14
Paternal smoking (16-year)**	1.11	1.03–1.20	1.01–1.23
Paternal social class (birth)	0.94	0.88–1.01	0.86–1.04
Birth cohort**	0.81	0.76–0.87	0.74–0.89
Offspring smoking (16-year)**	1.89	1.82–1.95	1.80–1.98

* $p < .05$ within group; ** $p < .05$ between groups.

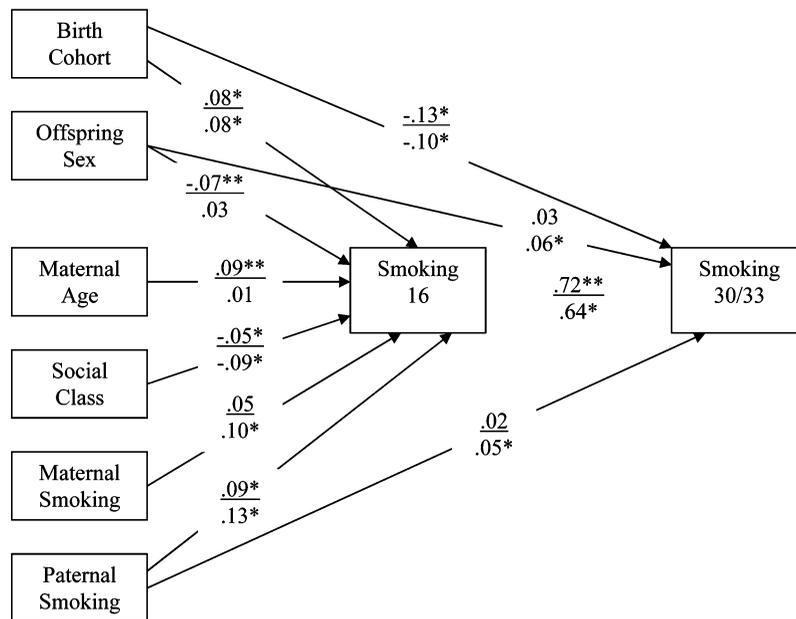


Figure 1. Multigroup path analysis model.

associated with offspring smoking at 16 years, whereas maternal smoking at 16 years was associated with offspring smoking only among mothers who did not smoke during pregnancy. Paternal smoking was significantly associated with offspring smoking at 30/33 years but only among offspring whose mothers did not smoke during pregnancy. Social class and cohort effects on offspring smoking also were observed. Manual paternal social class at birth was associated with increased likelihood of offspring smoking. In all cases, however, the magnitude of the effects observed, though statistically significant, was modest.

Our findings are consistent with those of Kandel et al. (1994), who found that maternal smoking during pregnancy selectively increased the probability that female adolescent children would smoke and would persist in smoking into adulthood. A recent retrospective, self-report study also reported that maternal smoking during pregnancy was associated with an increased likelihood of smoking initiation among female offspring only (Oncken, McKee, Krishnan-Sarin, O'Malley, & Mazure, 2004). Our results provide some support for behavioral modeling theories of smoking initiation, which emphasize the reciprocal interaction between individuals' behavior and their social environment, in particular parental smoking behavior (Conrad, Flay, & Hill, 1992). Parental smoking during offspring adolescence may be particularly salient in this respect. These results are consistent with a number of other studies demonstrating an association between socioeconomic status and smoking behavior status (e.g., U.K. Department of Health, 2003).

The effect of birth cohort is more complex and appears to be associated with different effects at

different time points. At 16 years, offspring in the NCDS cohort were more likely to be smokers than were those in the BCS70 cohort. This result is congruent with national smoking statistics, which show that smoking prevalence fell between 1974 and 1986 in those aged 16–19 years (U.K. Department of Health, 2003). At 30/33 years, however, offspring from the BCS70 cohort were more likely to smoke than were offspring in the NCDS cohort. These findings are more difficult to explain because national smoking prevalence rates for 24–35-year-olds in 1991 and 2000 are comparable (U.K. Department of Health, 2003).

The present study had a number of limitations that should be borne in mind when interpreting these results. First, because neither cohort study was set up to specifically examine smoking behavior, the smoking data are limited and not comparable across study cohorts or within cohorts at each follow-up in all cases. Similarly, we were unable to include a number of potential risk factors and confounders associated with offspring tobacco and other substance use, such as additional environmental and behavioral influences (e.g., peer group and sibling smoking). Second, most studies of the behavioral consequences of fetal exposure to nicotine are based on maternal and offspring self-reports without validation, and our study is no exception. Third, the proportion of participants for whom complete data were available was extremely modest, suggesting caution in generalizing these findings. This limitation is compounded by evidence that participants for whom complete data were available differed somewhat from the remainder of the original cohorts with respect to maternal smoking at 16-year follow-up (in both cohorts), and paternal social class at birth and

maternal smoking during pregnancy (in the BCS70 cohort). Fourth, the two birth cohorts differed with respect to maternal smoking during pregnancy, maternal smoking at 16-year follow-up, and offspring sex. Although birth cohort was included in our analysis model, the difference in maternal smoking during pregnancy is noteworthy, suggesting possible under-reporting of maternal smoking during pregnancy in the NCDS cohort.

In summary, the present findings support the hypothesis that prenatal exposure to nicotine is associated with smoking in later life but indicate that this association exists only for female offspring. We observed an indirect effect of maternal smoking during pregnancy through an interaction with other risk factors, namely offspring sex and maternal age at birth. Our findings also indicate that concurrent parental smoking behaviors are a risk factor for offspring smoking during late adolescence, possibly reflecting modeling processes, although shared genetic vulnerability is possible (Heath, Martin, Lynskey, Todorov, & Madden, 2002). Because a high proportion of those who begin smoking in adolescence will go on to become established smokers in adulthood, this finding has obvious public health implications. For instance, earlier onset of cigarette smoking provides more life-years to use tobacco and thereby increases the potential duration of use and the risk of a range of more serious health consequences. Although younger women are more likely to smoke than are older women, those that do usually do not smoke as heavily (Office for National Statistics, 1996, 2002). However, given that younger age at onset of smoking has been reported to be associated with increased likelihood of smoking during pregnancy (Cnattingius, Lindmark, & Meirik, 2001), smoking during pregnancy may increase in the future. These issues are important, and there remains a need for large studies designed with greater measurement detail in order to explore more fully the relative risks of parental smoking during pregnancy and childhood on subsequent offspring smoking behavior, because an independent effect on liability to smoking would be of importance, if demonstrated.

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