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SMOKING IN PREGNANCY AND **DISRUPTIVE BEHAVIOUR IN 3-YEAR OLD BOYS AND
GIRLS: AN ANALYSIS OF THE UK MILLENNIUM COHORT STUDY**

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Abstract

Background: Maternal smoking during pregnancy has been consistently associated with **disruptive** behaviour in male offspring, however results for girls are inconsistent and little is known about emergent patterns in young children. Additionally, it is unclear whether **maternal smoking** is independently associated **in offspring** with hyperactivity-inattention or only when it co-occurs with conduct problems. Further, few studies have controlled for a broad range of maternal psychosocial problems.

Methods: We analysed associations between self-reported smoking in pregnancy and **maternal** reports of **externalising** behaviour in more than 13,000 3-year old boys and girls in the UK Millennium Cohort Study. Conduct and hyperactivity-inattention problems were assessed using the Strength and Difficulties Questionnaire.

Results: Boys whose mothers persistently smoked throughout pregnancy were at significant risk of conduct and hyperactivity-inattention problems compared to sons of non-smokers: the effect was stronger for heavy smokers. **After excluding children with co-occurring problems, conduct-only problems remained a significant risk for sons of heavy smokers, OR(95%CI)= 1.92(1.29 to 2.86); and hyperactivity-inattention-only for sons of light or heavy smokers, OR(95%CI)= 1.79(1.27 to 2.51) and 1.64(1.10 to 2.46). Daughters of light or heavy smokers were at significant risk of conduct-only problems, OR(95%CI)= 1.73(1.14 to 2.61) and 1.73(1.06 to 2.83). Relative to non-smokers, daughters of pregnancy quitters had significantly reduced odds of having conduct 0.61(0.39 to 0.97) or co-occurring problems 0.26(0.08 to 0.82), although only 79 and 20 girls met these criteria, respectively. All findings were robust to controlling for key social and psychosocial factors.**

Conclusions: Associations between maternal smoking during pregnancy and disruptive behaviour in 3 year old children vary by sex, smoking status and whether or not conduct or hyperactivity problems occur together or separately.

Smoking during pregnancy increases the risk of ectopic pregnancy, miscarriage, perinatal death, preterm delivery and low birth-weight.¹ In addition, prenatal smoking has been consistently associated across different populations, study designs and outcome measures with externalising problem behaviour in male offspring, i.e. hyperactivity and conduct disorder.^{2,3} Evidence reviewed by Wakschlag et al³ suggests a developmental pathway for the latter association, characterised by oppositional disorders in young children, conduct disorders and delinquency in older children and adolescents.

Evidence supporting an exposure-related early developmental pathway includes findings that smoking during pregnancy is associated with child-onset, rather than adolescent-onset conduct problems,^{4,5} and evidence that the elevated risk of externalising problems remains constant during childhood.⁶ Exposure-related externalising problem behaviour has also been identified in pre-school children,^{7,8} and linked to escalations in physical aggression, a component of conduct disorder.^{9,10-12} Negativity and difficult temperament in infants may also be part of the developmental pathway.^{13,14}

Smoking during pregnancy has been consistently associated with conduct symptoms in male offspring of school age,^{4,15-21} but inconsistently in school-aged girls.^{4,16,17,5,15,19} Significant associations with physical aggression and/or defiance have been found in both pre-school boys and girls.^{7,10-12} However, many studies appear to have had insufficient power to systematically test for interactions with gender, or have only sampled boys.^{6,7,11}

16 18-21

Attention deficit hyperactivity disorder (ADHD) in offspring has been associated with smoking during pregnancy in some studies,^{2 22-26} but not others.^{5 19 20} It is possible that this association only exists because ADHD tends to co-occur with exposure related conduct or oppositional defiant symptoms. In the two studies that have assessed ADHD-only symptoms, exposure was not significantly associated with ADHD-only in pre-school children without physical aggression symptoms, nor in 7-19 year olds without oppositional defiant disorder symptoms.^{9 21} Therefore we hypothesized, in our study, that hyperactivity-inattention would not be independently associated with smoking during pregnancy but that indirect associations would be found when it co-occurred with conduct problems.

Women who smoke during pregnancy are more likely to live in more difficult circumstances, to have low socio-economic status, lower social support, and experience more stressful life events.^{27 28} These psychosocial factors are also risk factors for disruptive behaviour problems in children.³ Additionally, poor adaptive functioning increases with increased prenatal smoking.²⁹ Nevertheless, only one previous study of smoking in pregnancy and disruptive behaviour has controlled for this.¹²

To our knowledge no studies of pre-school children have previously compared offspring of persistent smokers and those who quit, neither is it possible to distinguish between heavy and light smokers in many studies. In addition to identifying dose-response relationships, the potential importance of correctly classifying exposure was shown in a study which found that quitters were less likely to have temperamentally difficult infants compared to both persistent smokers and non-smokers.¹⁴ Since smoking patterns vary

across pregnancy,^{30 31} retrospective assessment of exposure, such as that used in the Millennium Cohort Study (MCS), can potentially identify exposure better than infrequent or untimely prospective questioning or biochemical analysis.³²

In this study we capitalize on the large sample size of the MCS with substantial numbers of persistent smokers (23%), and the ability to categorise smoking patterns during pregnancy. We aim to build on existing research by (a) examining sex differences in relationships between categories of smoking in pregnancy (quitting, light and heavy persistent smoking) and behaviour problems at 3 years of age; (b) testing robustness to potential confounding from key psychosocial domains empirically established as risk factors for persistent pregnancy smoking; and (c) investigating whether smoking exposure effects are specific to conduct problems, hyperactivity problems or their co-occurrence.

METHODS

Study population and sample

This research used pre-gathered data from The Millennium Cohort Study, a large, prospective, population-based study of children born in 2000 and 2001, selected from the whole UK Child Benefit Register^{33 34} The cohort was initiated to monitor the effects of new policies and structures on child development and families. To this end families from areas with high levels of child poverty, and from areas with high proportions of ethnic minority residents, were over-sampled. The response rate for the first wave of data collection was 72%; non-respondents were more likely to be without fixed residence, living in ethnic minority areas in England, or living in disadvantaged areas. The first

wave of data collection, which took place when infants were aged 9 months on average, included 18,819 infants in 18,552 families; of these 14,898 (80%) families participated in the second wave when children were 3 years old. Data was gathered in the family home by computer assisted interview.

For our study, we excluded families with multiple births (n=202 families), those lacking pregnancy smoking information (n=8) and non-natural mother (n=334), giving an eligible sample of 14,354 mother-child pairs. Further exclusions were made if insufficient information was provided for the Strength and Difficulties Questions (SDQ),³⁵ producing analytical samples of 13,788 and 13,654 families for the conduct and hyperactivity scales respectively.

Measurement of maternal smoking during pregnancy

Mothers were asked how many cigarettes they smoked per day before pregnancy and the number smoked before and after any change. Information was collected on average 9 months after birth. Mothers were classified into the following smoking categories: (1) Never smoked during pregnancy; (2) Quit smoking during pregnancy; (3) Continuous light smoker during pregnancy (less than 10 cigarettes per day); (4) Continuous heavy smoker during pregnancy (10+ cigarettes per day).

Measurement of child behaviour

Mothers rated their child's behaviour at age 3 using questions from the SDQ, widely used to assess 3-16 year olds. It consists of 25 items divided into 5 sub-scales of 5 items each,

using 4-point Likert scales.³⁵ In this study we examine the 2 disruptive behaviour sub-scales: conduct problems and hyperactivity-inattention problems.

The structure of questioning was “*What is your child like?*” followed by a statement e.g.: “*Often argumentative with adults*”. Respondents were asked to indicate the appropriate answer: “Not true” (scoring 0) “Somewhat true” (scoring 1), “Certainly true” (scoring 2) or “Can’t say” (scored as missing).

The conduct problem statements were: “*Often has temper tantrums or hot tempers*”; “*Generally obedient, usually does what adults request*”; “*Often fights with other children or bullies them*”; “*Often argumentative with adults*”; “*Can be spiteful to others*”. (Note: the last two statements replaced “Often lies or cheats” and “Steals from home, school or elsewhere” used in the SDQ for school aged children.) The hyperactivity-inattention problem statements were: “*Restless, overactive, cannot stay still for long*”; “*Constantly fidgeting or squirming*”; “*Easily distracted, concentration wanders*”; “*Can stop and think things out before acting*”; “*Sees tasks through to the end, good attention span*”.

If a mother answered two or fewer questions out of a total of 5 in each sub-scale then the sub-scale score for this child was counted as missing. The mean sub-scale scores for the remaining children were prorated to 5 items if at least 3 out of 5 items were completed (www.sdqinfo.com).³⁵ Scores were dichotomised into normal and abnormal behaviour, using the nearest whole number mean score as a cut-off point, to classify approximately the top 10% of the weighted sample as having abnormal behaviour (www.sdqinfo.com).³⁵

These dichotomised categories were used to test the hypothesis that smoking during pregnancy increases the risk of behaviour problems in children.

Potential confounding factors

Potential confounders were examined and grouped into 5 domains as listed in table 1. Unless otherwise specified, socio-demographic variables were measured at wave1 (W1) and variables for the other domains were measured at wave 2 (W2). All measures were self-reported by mothers. Additional details and references relating to variables in the domains below can be found in a related study of the psychosocial context of pregnancy smoking in this cohort.²⁹

Socio-demographic factors: mother's age (years) at index child's birth; number of children in the household at wave 2; mother's ethnicity; family stability based on change of partner or change of single parent status between waves. Three measures of socio-economic status were household poverty (household income below 60% of the median); low maternal education (less than GCSE A-C or no UK qualifications at wave 2); working class (routine or semi-routine occupation), using the highest of the mother's and/or father's social class (NS-SEC).

Problematic relationships as listed in table 1 included problematic relationships with the mother's family of origin; problematic relationships with peers; and those with partner.

Problematic parenting examined smacking child daily or weekly; strict parenting style; and lacking discipline. We also examined two proxy measures of mothers' conformity to

societal norms: having no wish to instil obedience or respect for authority or elders; having no wish to instil religious values in their children.

Poor adaptive functioning measured poor daily functioning as having no phone; having no bank account; having difficulty managing finances; having a very disorganised household; ever being homeless since the birth of the child. Poor general functioning variables were: feeling a lack of control over life; low self-esteem; low satisfaction with life.

Poor maternal and infant health and health-related behaviour variables included those relating to current psychological distress (measured using 6 items from the Psychological Distress Scale³⁶); history of depression; alcohol or drug problems; plus poor pre-natal and post-natal health behaviours as listed in table 1.

Statistical analysis

All analyses were weighted using Stata SE version 10 survey commands to correct for over-sampling of disadvantaged areas to produce UK representative results. All counts reported in tables are un-weighted and percentages are weighted. Characteristics of mothers and infants by smoking status were described using means and proportions, differences were tested by Wald tests and chi-square tests, respectively.

Unadjusted odds ratios were estimated separately for boys and girls for associations between pregnancy smoking status and behaviour. Our approach to adjustment was designed to produce parsimonious models. We first estimated domain-specific multiple

logistic regression models, including all potential confounding factors within that domain for each sex-behaviour association. Backwards stepwise elimination produced restricted models for each of the five domains. These reduced sets of confounders were then included in final multiple logistic regression models for each sex-behaviour association. We also tested the statistical significance of a sex-exposure interaction in models including both boys and girls.

Multinomial logistic regression was performed to test sex-specific associations between smoking and conduct-only, hyperactivity-inattention-only, and co-occurring conduct and hyperactivity-inattention problems. To determine specific behavioural effects of smoking exposure, children with each abnormal behaviour type were compared to children who had neither conduct nor hyperactivity-inattention problems.

Results

Almost 10% of women reported smoking heavily throughout pregnancy, 12.5% were light smokers, and 12.4% quit during pregnancy. Of those who quit 92% stopped during 1st trimester and 7% in 2nd trimester. Maternal smoking status was significantly associated with all socio-demographic characteristics and also with the majority of maternal problems; less favourable characteristics being significantly associated with more persistent and heavier smoking (table 1).

Table 1 Characteristics of mothers and infants by maternal smoking status during pregnancy

	Never smoked	Quit smoking	Light smoker	Heavy smoker
	N=9,401 65.5%	N=1,787 12.4%	N=1,795 12.5%	N=1,371 9.6%
Socio-demographic	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)
Maternal age (years) at birth *	30.6(0.12)	27.2(0.19)	26.7(0.18)	27.1(0.17)
Children in Household W2 *	2.2(0.01)	1.9(0.02)	2.1(0.03)	2.5(0.04)
	% of smoke cat.			
Family stability between waves*:				
Same Partner, married	76.6%	52.4%	38.4%	32.4%
Same Partner, cohabiting	13.6%	21.9%	27.7%	29.6%
Change of partner	0.7%	1.2%	1.2%	2.3%
Split from partner, now single	3.5%	7.1%	8.7%	8.7%
Previously single, now partnered	1.3%	4.1%	5.4%	7.1%
Single mother at both waves	4.3%	13.3%	18.6%	19.9%
Below 60% median poverty *	17.3%	26.3%	44.5%	56.8%
Less than GCSE A-C, or no UK qualifications W2*	18.5%	24.4%	40.7%	54.8%
Working class family *	13.5%	24.4%	36.2%	49.3%
	% of ethnic grp.			
Maternal ethnic group*:				
White	65.3%	13.7%	12.1%	8.9%
Mixed	60.3%	13.8%	17.3%	8.6%
Indian	92.8%	5.7%	0.7%	0.8%
Pakistani/Bangladeshi	95.5%	1.3%	2.5%	0.7%
Black/Black British	78.8%	10.1%	9.0%	2.1%
Other	85.6%	7.5%	4.5%	2.4%
Problematic relationships	% of smoke cat.			
Lived away from home pre 17 *	10.3%	17.7%	23.0%	29.9%
Spent any time in care as child*	0.6%	1.5%	2.1%	5.5%
Maternal parents separated *	23.8%	38.0%	42.0%	48.6%
Never sees mother if alive*	1.6%	2.1%	2.2%	3.8%
Never sees father if alive*	5.6%	7.9%	9.9%	13.2%
No time with friends #	18.2%	15.5%	16.8%	20.0%
No-one to share feelings *	4.8%	7.8%	9.0%	14.0%
No visits to/by other parents *	6.4%	7.3%	8.0%	13.6%
Poor child-mother relationship *	8.6%	12.2%	16.7%	24.5%
Low partner satisfaction *	14.8%	22.6%	24.1%	31.7%
Partner perpetrated violence *	3.0%	5.4%	7.2%	8.9%
Ever lived with more than one partner *	26.7%	38.3%	43.0%	48.1%
Problematic Parenting	% of smoke cat.			
Lacking parenting competence *	2.5%	3.8%	3.6%	5.5%
Smacking daily or weekly #	9.1%	8.0%	10.1%	11.7%
Lack of discipline *	13.3%	12.5%	17.0%	18.1%
Don't instil either obedience or respect	9.2%	13.6%	16.1%	15.7%
Don't instil religious values *	35.6%	51.3%	62.0%	66.2%
Poor adaptive functioning	% of smoke cat.			
Low sense of control W1*	10.4%	18.0%	23.3%	30.9%
Low satisfaction with life *	6.8%	11.8%	16.8%	22.1%
Low self esteem W1*	8.35%	9.9%	12.3%	17.5%
Ever homeless (since the birth) *	1.3%	3.1%	3.5%	4.6%
No phone W1*	1.6%	3.8%	5.2%	7.3%
Difficulty managing Finances *	6.9%	10.1%	13.6%	15.8%

No bank account W1*	4.5%	7.5%	16.3%	24.5%
Very disorganised household *	1.5%	2.0%	2.8%	4.6%
Health related Behaviours	% of smoke cat.			
Current psychological distress *	7.7%	11.6%	16.2%	23.0%
History of Depression *	22.6%	35.5%	40.0%	47.4%
Drink Problem *	3.3%	7.2%	6.4%	8.1%
Drug Problem *	1.3%	7.23%	9.15%	11.3%
Limiting long term illness *	19.8%	20.7%	23.1%	30.9%
Unplanned pregnancy W1 *	31.5%	50.0%	57.5%	63.0%
Late entry to antenatal care W1 *	19.8%	23.0%	25.9%	24.7%
Not attempted breast feeding W1*	20.2%	28.0%	42.4%	51.6%
Incomplete immunisations E*	3.5%	4.7%	6.0%	9.4%
Postnatal smoking near child E*	11.0%	20.3%	41.4%	64.9%
Drinking during pregnancyW1	34.0%	37.2%	34.0%	34.2%
Low birth weight (<2500g)W1*	4.8%	5.0%	8.9%	10.1%
Preterm delivery(<37 wks)W1#	6.4%	6.1%	8.7%	8.9%

Differences statistically significant at * = $p < 0.001$, ^ = $p < 0.01$, # = $p < 0.05$

W1= recorded at wave 1, about 9 months after birth

W2 = recorded at wave 2, about 3 years after birth

E = recorded at either wave

The unadjusted analyses show statistically significant associations between risks of problem behaviour and both light and heavy smoking. Dose-response relationships were significant for conduct symptoms in boys and were apparent but non-significant for the other relationships (Table 2). Although an unadjusted statistically significant interaction was found between heavy smoking and sex in relation to conduct scored as a continuous variable, no individual interaction term was significant when conduct or hyperactivity-impulsivity were used as dichotomous outcomes in logistic regression models. Nevertheless, based on previous literature we proceeded to perform adjusted stratified analyses.

Table 2 shows that for boys, after adjustment for all socio-demographic, psychosocial and parenting domains, significant associations for individual exposure categories remained and non-significant dose-response relationships remained between persistent smoking in pregnancy and conduct problems (light smoking OR = 1.44, 95% CI: 1.01-2.06, $p=0.044$; heavy smoking OR= 1.80, 95% CI: 1.28-2.54, $p=0.001$), and also hyperactivity-

inattention problems (light smoking OR = 1.56, 95% CI:1.12-2.15, p=0.016; heavy smoking OR= 1.62, 95% CI: 1.13-2.33, p=0.009 respectively). Daughters of mothers who quit smoking during pregnancy had reduced risks of conduct problems compared to daughters of non-smokers which only became significant after adjusting for all social and psychosocial domains (OR = 0.61, 95% CI: 0.39-0.97, p=0.035).

Table 2 Odds ratios for behaviour problems at age 3 by maternal smoking in pregnancy

Behaviour Problems	Never smoked	Quit smoking OR (95% CI)	Light smoker OR (95% CI)	Heavy smoker OR (95% CI)
BOYS				
unadjusted				
Conduct	Ref	1.54 (1.16 to 2.04)^	2.66 (2.07 to 3.42)*	4.50 (3.60 to 5.65)*
Hyperactivity-inattention	Ref	1.09 (0.86 to 1.39)	1.64 (1.35 to 2.02)*	2.21 (1.74 to 2.79)*
Fully adjusted				
Conduct	Ref	1.21 (0.83 to 1.78)	1.44 (1.01 to 2.06)#	1.80(1.28 to 2.54)^
Hyperactivity-inattention	Ref	0.94 (0.67 to 1.32)	1.56 (1.12 to 2.15)^	1.62 (1.13 to 2.33)^
GIRLS				
unadjusted				
Conduct	Ref	1.14 (0.83 to 1.55)	2.28 (1.70 to 3.07)*	3.45 (2.69 to 4.44)*
Hyperactivity-inattention	Ref	1.31 (0.98 to 1.73)	1.80 (1.36 to 2.38)*	2.28 (1.71 to 3.04)*
Fully adjusted				
Conduct	Ref	0.61 (0.39 to 0.97)#	1.06 (0.70 to 1.63)	1.34 (0.88 to 2.03)
Hyperactivity-inattention	Ref	0.96 (0.66 to 1.41)	1.28 (0.90 to 1.81)	1.17 (0.79 to 1.72)

Differences statistically significant at * = p<0.001, ^ = p<0.01, # = p<0.05

Conduct problems = scores of 6 or above out of 10 (top 10.3% male, 8.7% female)

Hyperactivity-inattention problems = scores of 7 or above (top 14.9% male, 9.2% female)

Co-occurring and non-co-occurring behaviour problems

When comparing the risk of having a single type of behaviour problem (either conduct or hyperactivity-inattention) with having neither behaviour problem, and after adjusting for all covariates, associations with heavy smoking in pregnancy were statistically significant (Table 3) for conduct-only problems (OR = 1.92, 95% CI: 1.29-2.86, p=0.001), hyperactivity-inattention-only problems (OR = 1.64, 95% CI: 1.10-2.46, p=0.016), and co-occurring problems in boys (OR = 1.76, 95% CI: 1.05-2.94, p=0.032).

Statistically significant associations were also found between light smoking and hyperactivity-inattention-only problems (OR = 1.79, 95% CI: 1.27-2.51, p=0.001). For

girls, light and heavy smoking in pregnancy were significantly associated with conduct-only problems (Light smoking OR = 1.73, 95% CI: 1.14 to 2.61, p=0.009; heavy smoking OR = 1.73, 95% CI: 1.06 to 2.83, p= 0.028). Additionally, girls whose mothers quit smoking in pregnancy were significantly less likely to have co-occurring problems than girls whose mothers never smoked (OR = 0.26, 95% CI: 0.08 to 0.82, p= 0.022). Table 4 shows that conduct-only symptoms are as prevalent in girls as they are in boys at 3 years old.

Table 3 Adjusted odds ratios of conduct-only, hyperactivity-inattention-only and co-occurring problems by maternal smoking status, with children having neither problem behaviour as reference group.

	Never smoked	Quit smoking OR (95% CI)	Light smoker OR (95% CI)	Heavy smoker OR (95% CI)
BOYS				
Conduct-only	Ref	1.14 (0.71 to 1.85)	1.44 (0.92 to 2.26)	1.92 (1.29 to 2.86) [^]
Hyperactivity-only	Ref	0.89 (0.62 to 1.26)	1.79 (1.27 to 2.51) [^]	1.64 (1.10 to 2.46) [#]
Co-occurring	Ref	1.07 (0.67 to 1.71)	1.32 (0.84 to 2.07)	1.76 (1.05 to 2.94) [#]
GIRLS				
Conduct-only	Ref	0.89 (0.53 to 1.51)	1.73 (1.14 to 2.61) [^]	1.73 (1.06 to 2.83) [#]
Hyperactivity-only	Ref	1.23 (0.88 to 1.72)	1.35 (0.96 to 1.91)	1.39 (0.95 to 2.04)
Co-occurring	Ref	0.26 (0.08 to 0.82) [#]	0.69 (0.26 to 1.84)	1.05 (0.51 to 2.16)

Differences statistically significant at [^] = p<0.01, [#] = p<0.05

Table 4 Prevalence of behaviour problems: count (%)

	Never smoked	Quit smoking	Light smoker	Heavy smoker	Total count (%)
BOYS					
Conduct-only	219 (4.2%)	52 (5.5%)	99 (10.6%)	97 (15.9%)	467 (6.1%)
Hyperactivity-only	447 (9.6%)	91 (8.5%)	109 (12.6%)	101 (13.6%)	748(10.1%)
Co-occurring	141 (2.7%)	46 (4.9%)	56 (6.0%)	62 (8.9%)	305 (3.9%)
Neither	3981 (83.6%)	685 (81.1%)	685 (70.8%)	458 (61.6%)	5809 (79.9%)
GIRLS					
Conduct-only	222 (4.6%)	59 (5.7%)	92 (10.7%)	101 (13.5%)	474 (6.1%)
Hyperactivity-only	250 (5.4%)	75 (7.7%)	70 (9.3%)	56 (8.7%)	451 (6.4%)
Co-occurring	95 (1.9%)	20 (1.8%)	31 (3.2%)	53 (6.1%)	199 (2.4%)
Neither	4046 (88.1%)	759 (84.9%)	653 (76.8%)	443 (71.7%)	5901 (85.1%)

Note: All counts reported in table are un-weighted and percentages are weighted to correct for over-sampling of poorer families.

DISCUSSION

Our study suggests that persistent light and heavy smoking during pregnancy may play an aetiological role in conduct and hyperactivity-inattention problems in 3 year old boys, consistent with previous research in older age groups.^{2 3} The association with hyperactivity-inattention problems was not confined to boys who had co-occurring conduct problems. Girls whose mothers quit smoking during pregnancy had a lower risk of conduct problems than those whose mothers never smoked and, after excluding co-occurring hyperactivity-inattention problems, persistent smoking was associated with conduct-only problems in girls.

A possible limitation of the study is that the child's behaviour was reported by their mother, potentially producing bias; if mothers who reported smoking were more likely to under-report poor behaviour then this would attenuate the association. Future research in this cohort using teacher assessments of behaviour at older ages is needed to rule this out. Furthermore, maternal psychopathology, beyond the psychosocial characteristics already measured, should be collected in future MCS waves and controlled for in similar analyses.

Another possible limitation is under-reporting or denial of smoking due to strong social pressure on women not to smoke. If women who are more willing to admit to smoking are also more likely to have unmeasured characteristics which are independently associated with child behaviour problems, then we may have over-estimated the effect of smoking. However, previous work suggests that pregnant women's self-reports are reasonably accurate measures of smoking (compared to repeated assays of the metabolic

by-products of smoking), particularly when interview based assessments of smoking patterns are used.³⁰ Retrospective recall of exposure 9 months after pregnancy may have created recall bias, nevertheless a recent study found that retrospective reporting (mean 14 years after birth) was excellent relative to prospective measures and more likely to identify heavy smokers or those who quit during the first trimester.³² Furthermore, despite potential problems with ascertainment of smoking status, the four categories: never smoking during pregnancy, quitting, light and heavy smoking were clearly differentiated; virtually all less-favourable maternal characteristics became more frequent with more persistent and heavier smoking.

In addition to using four smoking categories, our study has a novel combination of strengths in areas with little previous research: the large sample size allowed us to examine girls and boys separately as young as 3 years old; to analyse singular behaviour problems in addition to their co-occurrence; and to control for a very broad range of potential confounding factors, without which a biased overestimation of risk may occur.²⁹

We are unaware of other studies of exposure-related conduct and hyperactivity problems in children as young as 3 years old using the SDQ. Our results support other research suggesting that cigarette smoke is associated with precursors to disruptive behaviour in young children, including difficult temperament in infants aged 9 months,¹⁴ externalizing problems in toddlers aged 18 months,¹² and physical aggression and defiance in children aged 3 years and younger.⁹⁻¹¹ Two studies with much lower statistical power, report no significant associations between externalising behaviour of 3 year olds and smoking during pregnancy.^{37 38} Despite not reaching significance, the odds ratios for aggressive

and inattention/hyperactivity problems in one study were 1.40 and 1.78, respectively; similar to the present study.³⁷

Pervious studies of sex differences in the association between smoking in pregnancy and conduct symptoms have found that associations are specific to boys, among children aged 4-18 years^{5 15 19} but are associated with both sexes in pre-school children.^{7 10-12} Small sample sizes in the studies of preschool children may have constrained their ability to detect sex differences – the largest being 1,745,¹⁰ compared to our sample of over 13,000. This study also found associations with hyperactivity for both boys and girls,¹⁰ in contrast to our research. These studies focused on physical aggression and defiance, whereas our study covers a wider range of behaviours including tantrums, bullying, argumentativeness and spitefulness, as well as disobedience and fighting.

The majority of studies reviewed by Linnet et al²⁴ and Button et al² report associations between maternal smoking and hyperactivity-inattention, but other studies have found no relationship.^{5 19 20} We had hypothesised effects for conduct-only problems and co-occurring problems, but not for inattention-hyperactivity-only problems.^{9 12} Nevertheless, we note that associations we found for hyperactivity-inattention-only problems did not exhibit a dose-response relationship, additionally there were no associations for girls.

The significant associations between quitting and reduced risk of conduct problem or co-occurring problems for daughters supports findings relating to decreased risks to distress to novelty and irregularity in infants of quitters in the MCS.¹⁴ **These results may be due to**

small numbers meeting the behaviour criteria. Nevertheless, the ability to quit may be an intergenerational characteristic of restraint and easy temperament.

Conversely, persistent and in particular heavy smoking throughout pregnancy may be a useful marker of families who need holistic support beyond pregnancy for a range of maternal psychosocial problems, parenting, and everyday difficulties which continue to characterize these family environments 3 years after birth. Such support, in addition to targeted smoking cessation interventions,²⁹ may minimise associated child behaviour problems.

Smoking during pregnancy may have direct effects on the development of behaviour problems, most plausibly via adverse teratological effects on the foetal development of brain structure and functioning, which is well-characterized in animal models.³⁹ If boys' foetal development is more sensitive to these insults, then this would indicate why sons of smokers were more likely to have behaviour problems than daughters of smokers.

Alternatively, smoking may be a marker for the intergenerational transmission of processes associated with both smoking during pregnancy and problems in offspring. If daughters of smokers are susceptible to genetic or family environmental influences linked to conduct problems but not to hyperactivity-inattention, then this may explain the significant risk of girls displaying conduct-only problems at this age. Rather than genes, exposure or environment being sole causes, the aetiology of disruptive behaviour disorders most likely involves gene-exposure-environment interactions.^{40 41} Further research is needed to elucidate the genetic factors and aspects of family environment that

increase the vulnerability of the child to any teratological insults resulting from exposure to cigarette smoke.

WHAT THIS PAPER ADDS

What is already known on this subject

- Smoking during pregnancy has been consistently associated with abnormal conduct problems and hyperactivity-inattention in school-aged boys.

What this study adds

- Boys as young as 3 years old are at significant risk of displaying exposure-related conduct symptoms as measured by the Strength and Difficulties Questionnaire, after adjustment for an extensive range of social and psychosocial confounding factors.
- Three year old boys are at significant risk of displaying exposure-related hyperactivity-inattention symptoms even when these do not co-occur with conduct symptoms.
- Girls born to prenatal smokers are at significant risk of displaying conduct-only symptoms at 3 years old. However, girls born to quitters have a reduced risk of co-occurring conduct and hyperactivity-inattention problems.

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Competing Interest statement

All authors declare that the answer to the questions on your competing interest form are all No and therefore have nothing to declare.

Contributors

All authors participated in the design and writing of the study. JH conducted the analyses and is guarantor for the paper

Ethics approval was not required for this secondary analysis of anonymized data.

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