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Prenatal exposure to dental amalgam and risk of symptoms of attention-deficit and hyperactivity disorder (ADHD)

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Abstract

Background—ADHD is multifactorial, including both genetic and environmental factors. The safety of amalgam used in dental treatment has been discussed due to its content of mercury and potential risks for negative neurodevelopmental consequences in the offspring. The aim of the study is to investigate possible associations between symptoms related to ADHD in children of three and five years of age and prenatal exposure to mercury from mothers' amalgam fillings.

Methods—Data from the Norwegian Mother and Child Cohort Study (MoBa) was used. Data was collected by questionnaires sent to participating women in week 17 (Q1) and 30 (Q3) of pregnancy and when the child was three (Q6) and five years of age (Q7). Information about exposure to amalgam during pregnancy was obtained from Q3. Information about symptoms related to ADHD was obtained from Q6 and Q7. Valid data was obtained for 42 163 children at three years of age and 23 392 children at five years of age. Logistic regression models, including mothers' age, education, body mass index, parity, smoking and alcohol consumption during pregnancy, were used to estimate the association between ADHD symptoms and prenatal exposure to amalgam fillings.

Results—No significant associations between number of teeth with amalgam filling, amalgam fillings placed or removed during pregnancy, and symptoms related to ADHD in children of three and five years of age were found.

Conclusions—In a large, prospective cohort study, we found no indication of increased risk for ADHD related symptoms in children prenatally exposed to mother's amalgam fillings.

Keywords

MoBa; dental amalgam; mercury; symptoms related to ADHD

INTRODUCTION

Attention Deficit and Hyperactivity Disorder (ADHD) is one of the most common childhood psychiatric disorders,¹ and is characterized by inattention, hyperactivity and impulsiveness.² For the majority, the disorder is diagnosed after school entry, but many have ADHD-like symptoms in preschool years.^{3, 4} There has been a growing recognition that origins of ADHD are multifactorial and complex in nature, including both genetic and environmental factors.⁵ Identifying environmental factors that might influence the development of ADHD represents a possible route for prevention and treatment of this debilitating disorder and may provide new insights in the etiological mechanisms involved. Studies indicate that prenatal exposure to toxic chemicals, together with genetic predispositions, can cause permanent brain injury even at low levels of exposure.⁶ Epidemiological studies have indicated that exposure to a number of neurotoxic agents may be associated with the loss of cognitive skills and behavioural difficulties.⁷ Animal studies have reported that metallic mercury exposure caused behavioural changes, including hyperactivity and learning difficulties in rats after pre- or postnatal exposure.^{8, 9} However, a recent study by Po-Yen et al (2018) investigated the effect of treatment with amalgam fillings during childhood and the relation to ADHD, but found no statistical significant association between exposure to amalgam fillings and attention-deficit/hyperactivity disorder after adjustment for age of the children.¹⁰

Other studies, focused on mercury exposure from fish consumption during pregnancy and neurodevelopment, are inconclusive.^{11–15} However, results from studies on mercury exposure from diet are not directly comparable to the results from studies on mercury exposure from amalgam fillings, because of the differences in toxicological properties.¹⁶

The safety of amalgam used in dental treatment of young women is discussed due to its mercury content¹⁷ and the potential risks for the foetus from prenatal exposure to mercury from mothers' amalgam fillings.^{18, 19} Studies have focused especially on possible effects on neurodevelopment in children due to prenatal exposure from mothers' amalgam fillings.^{18, 20} Dental amalgam comprises about 50% mercury by weight, mixed with a powder of silver, tin and copper.²¹ It is known that low levels of mercury vapour are released from the amalgam fillings into the oral cavity.²² Mercury and silver particles are also released into the oral cavity from the filling through wear or corrosion.²³ The amount of mercury released from the amalgam fillings is correlated to the number of amalgam fillings.^{24, 25} Mercury vapour is inhaled, absorbed and distributed to different body tissues²⁶ and is also released during setting and removing of amalgam fillings.²⁷

Mercury is transferred from the mother to the foetus via placenta.²⁸ Studies have shown that mercury concentrations in babies' hair, liver and kidneys were correlated with the mothers' amalgam fillings.^{29, 30} Therefore, a possible association between mothers' exposure to dental amalgam and the health of the developing foetus has been a matter of concern. As a consequence, several European countries have recommended women to avoid extensive restorative treatments during pregnancy.^{21, 31}

The aim of this study is to investigate possible associations between symptoms related to ADHD in children of three and five years of age and the extent of prenatal exposure to

amalgam, as measured by their mothers' number of amalgam-filled teeth and dental treatment with setting and removing of amalgam fillings during pregnancy. The Norwegian Mother and Child Cohort Study (MoBa) provides a unique opportunity to study possible associations between prenatal amalgam exposure in utero and early indicators of ADHD in the child.

MATERIALS AND METHODS

The present study used data from the Norwegian Mother and Child Cohort Study (MoBa), a prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health.^{32, 33}

Study population

Participants were recruited among all pregnant women in Norway during the period 1999–2008. Postal invitations based on lists from the hospitals were sent to the pregnant women after they had signed up for routine ultrasound examination around 17 gestational weeks. The pregnancy was the unit of observation, and a woman could participate with more than one pregnancy. There were no exclusion criteria.^{32, 33}

The women consented to participation in 41% of the pregnancies. The cohort includes information about 114.700 children, 95.200 mothers and 75.200 fathers.³² All participants have given written informed consent.

Data collection

Data for the present project was obtained from questionnaires (Q) filled out by the participating women in week 17 (Q1) and week 30 (Q3) of pregnancy and when the child was three (Q6) and five years of age (Q7). Information about prenatal exposure to dental treatment with amalgam during pregnancy was obtained from Q3. The questionnaire included questions about the number of teeth with amalgam fillings. The participants were instructed to look in the mirror and count the number of teeth and the number of teeth with amalgam fillings.³⁴ The amalgam fillings were categorized in four groups (0,1–4, 5–8, and more than 8 teeth). In addition, the pregnant women were asked to report if they had received or removed amalgam fillings during the pregnancy.

Information about symptoms related to ADHD-like behaviour was obtained from Q6 and Q7 when the children were three (Table 1) and five years (Table 2) of age. Q6 includes six items from the Child Behaviour Checklist (CBCL)³⁵ about restlessness and inattention, and five selected items from the symptom list for Attention Deficit and Hyperactivity Disorder (ADHD) from the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR).³⁶ The answers were rated “Not true” = 0, “Somewhat or sometimes true” = 1 and “Very true or often true” = 2. Scores on this scale ranged from zero to a maximum of 22. Q7 includes 12 items from the Conners' Parent Rating Scale (CPRS) and the ADHD Index, giving information about behaviour related to symptoms of ADHD³⁷. The answers were rated “Not true” = 0, “Somewhat true” = 1, “True” = 2 and “Very true or often true” = 3. Sum of scores on this scale thus ranged from zero to 36.

Covariates

Information about mothers' age at delivery, number of former births, and infant's gender was obtained from the Medical Birth Registry of Norway (MBRN).³⁸

Information regarding additional relevant covariates including mothers' weight and height before pregnancy, education (12 years, 13–16 years, and 17 years), smoking habits (never, occasionally, daily), and alcohol consumption during pregnancy (never, less than once a week, once a week, more than once a week), was obtained from Q1 and Q3 (37). Body mass index (BMI) [weight (kg)/height² (m²)] was calculated from self-reported weight and height before pregnancy obtained from Q1.³⁹

Statistical analyses

Pregnancies with invalid values for amalgam fillings were excluded. Only singleton births and pregnancies with valid data on weight and height were included in the analyses (Figure 1). Boys and girls were analysed both separately and together.

ADHD symptom scores were summarized separately for the children when they were three and five years of age. A sum score of ADHD symptoms above the 90th percentile was defined as high level of symptoms. Using logistic regression analyses, odds ratios with 95% confidence intervals were calculated for having sum scores at the 90th percentile or higher by the level of amalgam exposure (both as a continuous variable and categorized as 0, 1–4, 5–8 and 9 teeth with amalgam fillings; 0 amalgam fillings was used as reference). Odds ratios with 95% confidence intervals were also calculated for having sum scores at the 90th percentile or above by new amalgam fillings placed or amalgam fillings removed (yes/no).

The effects were adjusted for the mother's age, maternal education, smoking during pregnancy, alcohol consumption during pregnancy, parity, and BMI before pregnancy (as a continuous variable). Pregnancies with missing information for maternal education (n=1899 and n=1057 for three and five years, respectively), smoking habits (n=345 and n=213 for three and five years, respectively) and alcohol consumption during pregnancy (n=4758 and n=2585 for three and five years, respectively) were included in the analyses as a separate category within the variable.

P-values < 0.05 were considered statistically significant. Statistical analyses were carried out using SPSS (version 22, IBM corp. Armonk, NY, USA).

The MoBa cohort study has obtained a license from the Norwegian Data Inspectorate, and this research project has been approved by the Regional Ethics Committee for Medical Research (REC south-east D, number 2011/727-1).

RESULTS

Symptoms associated with ADHD at child age three years

Valid data on the number of teeth with amalgam fillings was obtained from 69 652 pregnancies (Figure 1). Data on 42 163 children at three years of age was obtained from Q6, and 77.3% of their mothers had amalgam fillings, and 14.8% had more than eight amalgam

fillings (Q3). The mean number of teeth with amalgam fillings was 4.3 (SD 3.9). For the mothers with amalgam fillings (n=33 651), the mean number was 5.5 (SD 3.6).

The mothers of 16 722 children (39.7%) reported that they had consulted a dentist during pregnancy, 270 (0.64%) mothers had new amalgam fillings placed and 1268 (3.0%) had amalgam fillings removed (Table 3). Of the mothers who had amalgam fillings removed during pregnancy, 49 (0.52%) had no amalgam fillings left after removal (Table 3). Mothers with the highest number of teeth with amalgam fillings before pregnancy were more likely to have amalgam fillings placed or removed during pregnancy compared to mothers with few amalgam fillings. The 90th percentile for sum score of ADHD symptoms was at 11 for both girls and boys (Table 4).

No increased risk was found (crude or adjusted) between having an ADHD symptom sum score at the 90th percentile or above and the number of teeth with amalgam fillings (both grouped and as continuous variable), neither when analysing the girls and boys separately nor together (Table 5) (results from analyses of amalgam as continuous variable not shown).

No statistically significant associations were found between having an ADHD symptom sum score at or above the 90th percentile and one or more amalgam fillings placed or removed during pregnancy at three years of age (Table 5).

Symptoms associated with ADHD at child age five years

Information about symptoms associated with ADHD in children at five years of age was obtained from Q7 (n= 23 302), and 78.8% of the children's mothers reported that they had amalgam fillings, while 13.1% reported that they had more than eight amalgam fillings. The mean number of teeth with amalgam fillings was 4.1 (SD 3.8), and 5.3 (SD 3.5) for the mothers with amalgam fillings (n=18 236).

Dentist consultation was reported by 9105 mothers (39.1%), and 111 (0.48%) mothers had one or more new amalgam fillings placed and 658 (2.8%) had one or more amalgam fillings removed. Of the mothers who had amalgam fillings removed, 28 (0.52%) had no amalgam fillings left after removal.

The 90th percentile for the sum score of ADHD symptoms was 10 (11 for boys and 9 for girls) (Table 3).

No statistically significant associations were found (crude or adjusted) between having an ADHD sum score at the 90th percentile or above (sum score 10) and the number of teeth with amalgam fillings neither when analysing the girls and boys separately nor together (Table 5), or when using the separate 90th percentiles for girls (sum score 9) and boys (sum score 11).

No statistically significant associations between an ADHD sum score at or above the 90th percentile (sum score 10) and amalgam fillings placed or removed were found when analysing girls and boys separately and together (Table 6), or when using the separate 90th percentiles.

For those with valid data both in child aged three and five years (n=19 220) (Table 4), the mean sum score of symptoms associated with ADHD at five years was 4.2 (SD 4.5). The mean sum score for girls was 3.6 (SD 3.9) and for boys 4.8 (SD 4.9). In this group, 813 children had an ADHD symptom sum score at or above the 90th percentile at both three and five years of age. We found no increased risk (crude or adjusted) between having a high ADHD symptom score at two time points and the number of teeth with amalgam fillings (both grouped and as continuous variable) in this group, neither when analysing girls and boys separately nor together (Table 5). No statistically significant associations between the sum score at or above the 90th percentile and amalgam fillings placed or removed during pregnancy were found when analysing boys and girls separately and together (Table 6).

DISCUSSION

The aim of this study is to investigate possible associations between symptoms related to ADHD in children at three and five years of age and prenatal exposure to dental amalgam, measured by mothers' number of teeth with amalgam fillings and treatment with new amalgam fillings or removal of amalgam fillings during pregnancy. The study was based on data of about 42 163 children at age three years and 23 302 children when they were five years of age, and their mothers' amalgam exposure obtained from questionnaires at the 17th and 30th weeks of pregnancy.

No evidence was found to indicate that mothers' number of amalgam fillings or amalgam fillings placed or removed during pregnancy increased the risk for symptoms related to ADHD in children at three or five years of age. Separate analyses for boys and girls showed generally the same results as for boys and girls analysed together. Our findings are consistent with the results from the Seychelles Child Development Study that found no evidence that the number of amalgam surfaces was associated with adverse neurodevelopmental outcomes in children at 30 months and at 5 years of age.^{20, 40}

The mean sum score of symptoms related to ADHD at child age five years was higher in boys compared to girls. This is in accordance with the results from other studies.^{41, 42}

The present study is based on questionnaire data, and the information about exposure to amalgam fillings is based on the women's registrations of number of teeth with amalgam fillings and amalgam fillings placed or removed at a given time during the pregnancy.³⁴ Various methods of registration of amalgam fillings during pregnancy have been used in different studies.^{18, 19, 40} It could be questioned if a biological marker for inorganic mercury exposure (e.g. concentration of inorganic mercury in blood or total mercury in urine) would give other results. However, the number of teeth with amalgam fillings, number of amalgam surfaces and 'amalgam points' are found to be significantly correlated with the concentration of inorganic mercury in blood.²⁶ Thus, the number of teeth with amalgam fillings could be a useful indicator of mercury exposure from amalgam fillings.²⁸

Studies on the effects of prenatal exposure to dental amalgam have a retrospective design.^{20, 28} We assume that the prospective design of our study will give more reliable data about amalgam exposures.

The information about symptoms related to ADHD is based on maternal report only. The validity of the information may be questioned. The respondents may have different understanding of the meaning of the questions, and both over- and underreporting of the children's problems could occur. Studies have shown differences in the rating of the symptoms between parents and teachers^{42, 43}, both when boys and girls are analysed separately and together. It is important to note that parental reports on the presence of symptoms are not sufficient to diagnose ADHD. Furthermore, we included information about symptoms in preschool children only, although the normative range for behaviour, characterized as inattentive, restless and impulsive is wide at that age and most children receive a diagnosis in school age. Although, high levels of ADHD symptoms in preschool age are not an unambiguous predictor of deviating neurodevelopment or a later ADHD diagnosis, it has been shown that high scores in ADHD symptoms in preschool age are predictive of later symptoms of ADHD⁴⁴ and of an ADHD diagnosis.⁴⁵

CONCLUSION

In the present study, which includes a large number of participants, we found no increased risk for symptoms related to attention deficit and hyperactivity disorder (ADHD) in children prenatally exposed to mother's dental amalgam fillings.

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Figure 1.
Flowchart showing number of participants included in the study and the groups available for analysis.

Questions included in MoBa questionnaire Q6 completed at child age 3 years, source of questions and rating scale.

TABLE 1

Questionnaire at child age 3 years (Q6)			
Source	Questions	MoBa question number	Rating scale
CBCL	<i>Can't concentrate, can't pay attention for long</i>	28: 2	0-2
CBCL	<i>Can't sit still, restless or hyperactive</i>	28: 3	0-2
CBCL	<i>Can't stand waiting, wants everything now</i>	28: 4	0-2
CBCL	<i>Demands must be met immediately</i>	28: 8	0-2
CBCL	<i>Gets into everything</i>	28: 15	0-2
CBCL	<i>Quickly shifts from one activity to another</i>	28: 20	0-2
DSM-IV	<i>Becomes distracted or diverted by outside stimuli</i>	29: 1	0-2
DSM-IV	<i>Finds it difficult waiting his/her turn</i>	29: 2	0-2
DSM-IV	<i>Has problems keeping focused on tasks or activities</i>	29: 3	0-2
DSM-IV	<i>Is excessively talkative</i>	29: 4	0-2
DSM-IV	<i>Doesn't seem to listen when he/she is being spoken to</i>	29: 7	0-2

CBCL: Child Behavior Checklist²⁶

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders IV-TR²⁷.

TABLE 2

Questions included in MoBa questionnaire Q7 completed at child age 5 years, source of questions and rating scale.

Questionnaire at child age 5 years (Q7)			
Source	Questions	MoBa question number	Rating scale
CPRS	<i>Inattentive, easily distracted</i>	35: 1	0–3
CPRS	<i>Cannot keep your attention</i>	35: 2	0–3
CPRS	<i>Fidgets with hands and feet, squirms in his/her chair</i>	35: 3	0–3
CPRS	<i>Messy or disorganized at home or in kindergarten</i>	35: 4	0–3
CPRS	<i>Participates only in what he/she is very interested in</i>	35: 5	0–3
CPRS	<i>Problems with concentration or attention</i>	35: 6	0–3
CPRS	<i>Avoids, expresses reluctance or have difficulty engaging in something that requires endurance (for example activities in kindergarten or to help at home)</i>	35: 7	0–3
CPRS	<i>Becomes distracted when he/she is asked to do something</i>	35: 8	0–3
CPRS	<i>Concentration problems in kindergarten</i>	35: 9	0–3
CPRS	<i>Leaving his place in the group in kindergarten or in other situations where it is expected to sit quietly</i>	35: 10	0–3
CPRS	<i>Not keeping up when things are explained and does not finish tasks in kindergarten or duties at home (not because of unwillingness or difficulty understanding what to do)</i>	35: 11	0–3
CPRS	<i>Become easily frustrated by efforts</i>	35: 12	0–3

CPRS: Conner's Parent Rating Scale²⁸

Characteristics of the pregnant women related to the number of teeth with amalgam fillings (% within amalgam dose category). Information from mothers with completed questionnaire at child aged 3 years (Q6) (n=42 163).

TABLE 3

Characteristics of the pregnant women	0 amalgam	1–4 amalgam	5–8 amalgam	9 amalgam	Total
Mean age (SD)	28.6 (4.1)	30.1 (4.1)	31.5 (4.2)	32.7 (4.3)	30.5 (4.4)
Parity					
First pregnancy	5649 (59.1)	7662 (49.8)	4636 (42.3)	2193 (35.1)	20 140 (47.8)
Second pregnancy or more	3914 (40.9)	7734 (50.2)	6325 (57.7)	4050 (64.9)	22 023 (52.2)
Consulted dentist during pregnancy					
Yes	3533 (36.9)	6044 (39.3)	4471 (40.8)	2674 (42.8)	16 722 (39.7)
No	6030 (63.1)	9635 (60.7)	6490 (59.2)	3569 (57.2)	25 441 (60.3)
Amalgam fillings placed					
Yes	0 (0.00)	54 (0.35)	93 (0.85)	123 (2.0)	270 (0.64)
No	9563 (100)	15 342 (99.6)	10 868 (99.2)	6120 (98)	41 893 (99.4)
Amalgam fillings removed					
Yes	49 (0.52)	396 (2.6)	465 (4.2)	358 (5.7)	1268 (3.0)
No	9514 (99.5)	15 000 (97.4)	10 496 (95.8)	5885 (94.3)	40 895 (97)
Maternal education					
12 years	2394 (25.0)	3907 (25.4)	3232 (29.5)	2246 (36.0)	11 779 (27.9)
13–16 years	4016 (42.0)	6677 (43.4)	4704 (42.9)	2581 (41.3)	17 978 (42.6)
17 years	2644 (27.6)	4116 (26.7)	2568 (23.4)	1179 (18.9)	10 507 (24.9)
Missing information	509 (5.3)	696 (4.5)	457 (4.2)	237 (3.8)	1899 (4.5)
Body Mass Index (BMI) ^a Mean (SD)	23.4 (3.8)	23.7 (4.0)	24.2 (4.2)	25.0 (4.5)	24.0 (4.1)
Smoking during pregnancy					
Never	9127 (95.4)	14532 (94.4)	10 168 (92.8)	5645 (90.4)	39 472 (93.6)
Occasionally	128 (1.3)	268 (1.7)	199 (1.8)	162 (2.6)	757 (1.8)
Daily	233 (2.4)	470 (3.1)	502 (4.6)	384 (6.2)	1589 (3.8)
Missing information	75 (0.78)	126 (0.82)	92 (0.84)	52 (0.83)	345 (0.83)
Alcohol during pregnancy					
Never	7685 (80.4)	11 922 (77.4)	8305 (75.8)	4582 (73.4)	32494 (77.1)
Less than once a week	821 (8.6)	1599 (10.4)	1372 (12.5)	891 (14.3)	4683 (11.1)

Characteristics of the pregnant women	0 amalgam	1–4 amalgam	5–8 amalgam	9 amalgam	Total
Once a week	36 (0.38)	60 (0.39)	52 (0.47)	39 (0.62)	187(0.44)
More than once a week	2 (0.02)	15 (0.10)	13 (0.12)	11 (0.18)	41 (0.78)
Missing information	1019 (10.7)	1800 (11.7)	1219 (11.1)	720 (11.5)	4758 (11.3)

^a BMI = weight (kg)/height² (m²)

TABLE 4

ADHD symptoms at child aged 3 years (n=42,163), at child aged 5 years (n=23 302) and a subgroup with information about ADHD-like behaviour at both age 3 and 5 years (n=19,220) related to the number of teeth with amalgam fillings in mothers. (% within amalgam dose category)

ADHD symptoms	0 amalgam	1–4 amalgam	5–8 amalgam	9 amalgam	Total
Child aged 3 years					
ADHD sum score. Mean (SD)					
All	6.4 (3.6)	6.4 (3.6)	6.5 (3.6)	6.5 (3.6)	6.5 (3.6)
Boys	6.6 (3.7)	6.5 (3.7)	6.5 (3.6)	6.7 (3.7)	6.6 (3.7)
Girls	6.3 (3.6)	6.3 (3.6)	6.4 (3.6)	6.4 (3.6)	6.3 (3.6)
^a Frequency of ADHD sum score at or above 90 th percentile (%)					
All	1338 (14.0)	2067 (13.4)	1491 (13.6)	843 (13.5)	5739 (13.6)
Boys	720 (14.8)	1099 (13.8)	772 (13.9)	468 (14.8)	3059 (14.2)
Girls	618 (13.2)	968 (13.0)	719 (13.3)	375 (12.2)	2680 (13.0)
Child aged 5 years					
ADHD sum score. Mean (SD)					
All	4.4 (4.5)	4.2 (4.5)	4.1 (4.3)	4.2 (4.5)	4.2 (4.5)
Boys	5.0 (4.8)	4.8 (4.9)	4.6 (4.7)	4.8 (4.8)	4.8 (4.8)
Girls	3.7 (4.1)	3.7 (3.9)	3.6 (3.8)	3.6 (4.1)	3.7 (3.9)
^b Frequency of ADHD sum score at or above 90 th percentile (%)					
All	629 (11.6)	999 (11.3)	599 (10.0)	344 (11.3)	2571 (11.0)
Boys	409 (14.8)	640 (14.1)	370 (12.4)	209 (13.6)	1628 (13.8)
Girls	220 (8.3)	359 (8.3)	229 (7.6)	135 (8.9)	943 (8.2)
Subgroup with information about symptoms related to ADHD at both child aged 3 and 5 years:					
ADHD sum score at child aged 5 years. Mean (SD)					
All	4.3 (4.5)	4.3 (4.5)	4.1 (4.4)	4.2 (4.5)	4.2 (4.5)
Boys	5.0 (4.9)	4.8 (4.9)	4.7 (4.8)	4.8 (4.9)	4.8 (4.9)
Girls	3.6 (4.0)	3.7 (3.9)	3.6 (3.9)	3.6 (4.0)	3.6 (3.9)
Frequency of ADHD sum score at or above 90 th percentile at both child aged 3 and 5 years (%)					
All	218 (4.8)	295 (4.1)	195 (3.9)	105 (4.2)	813 (4.2)
Boys	144 (6.3)	190 (5.1)	117 (4.7)	59 (4.7)	510 (5.2)
Girls	74 (3.4)	105 (3.0)	78 (3.1)	46 (3.7)	303 (3.2)

11. The 90th percentile of ADHD sum score was p
10. The 90th percentile of ADHD sum score was p

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TABLE 5

Crude and adjusted odds ratios (OR) at child aged 3 years and 5 years for having sum score of ADHD symptoms at or above 90th percentile in the different amalgam groups compared to the group without amalgam fillings (Reference category: 0 teeth with amalgam fillings, OR=1) and odds ratios for having ADHD sum score at or above 90th percentile at both child aged 3 years and 5 years. Data analysed for girls and boys separately and together.

Children's sex and age	1-4 amalgam			5-8 amalgam			9 amalgam		
	OR	(95% CI)	p-value	OR	(95% CI)	p-value	OR	(95% CI)	p-value
<i>a</i> At child aged 3 years									
<i>All (n=42 163)</i>									
Crude	0.95	(0.89, 1.03)	0.21	0.97	(0.89, 1.05)	0.42	0.96	(0.88, 1.05)	0.38
Adjusted	0.99	(0.92, 1.11)	0.86	1.02	(0.94, 1.11)	0.63	1.02	(0.92, 1.12)	0.73
<i>Girls (n=20 615)</i>									
Crude	0.98	(0.88, 1.09)	0.73	1.01	(0.90, 1.13)	0.86	0.91	(0.80, 1.05)	0.19
Adjusted	1.01	(0.90, 1.12)	0.93	1.04	(0.93, 1.18)	0.50	0.94	(0.81, 1.09)	0.40
<i>Boys (n=21 548)</i>									
Crude	0.93	(0.84, 1.03)	0.15	0.93	(0.83, 1.04)	0.20	1.00	(0.88, 1.14)	0.97
Adjusted	0.98	(0.89, 1.10)	0.74	1.00	(0.89, 1.12)	0.97	1.09	(0.96, 1.25)	0.20
<i>b</i> At child aged 5 years									
<i>All (n=23 302)</i>									
Crude	0.97	(0.87, 1.08)	0.56	0.84	(0.75, 0.95)	0.005**	0.96	(0.84, 1.11)	0.61
Adjusted	1.04	(0.93, 1.16)	0.48	0.96	(0.85, 1.09)	0.45	1.11	(0.96, 1.30)	0.11
<i>Girls (n=11 472)</i>									
Crude	1.01	(0.84, 1.20)	0.96	0.91	(0.75, 1.11)	0.35	1.08	(0.86, 1.35)	0.52
Adjusted	1.08	(0.90, 1.29)	0.42	1.03	(0.84, 1.26)	0.79	1.27	(1.00, 1.62)	0.050
<i>Boys (n=11 830)</i>									
Crude	0.95	(0.83, 1.08)	0.41	0.81	(0.70, 0.94)	0.007**	0.91	(0.76, 1.09)	0.28
Adjusted	1.01	(0.88, 1.16)	0.84	0.92	(0.78, 1.08)	0.29	1.05	(0.86, 1.27)	0.63
Subgroup with information about symptoms related to ADHD at both child aged 3 and 5 years:									
<i>All (n=19220)</i>									
Crude	0.83	(0.70, 1.00)	0.045*	0.80	(0.66, 0.98)	0.030*	0.86	(0.68, 1.09)	0.22
Adjusted	0.90	(0.75, 1.09)	0.28	0.92	(0.75, 1.14)	0.45	1.03	(0.80, 1.33)	0.79
<i>Girls (n=9419)</i>									

Children's sex and age	1–4 amalgam			5–8 amalgam			9 amalgam		
	OR (95% CI)	p-value		OR (95% CI)	p-value		OR (95% CI)	p-value	
Crude	0.89 (0.66,1.20)	0.45		0.93 (0.68, 1.29)	0.68		1.10 (0.76, 21.60)	0.62	
Adjusted	0.95 (0.70,1.29)	0.73		1.04 (0.74, 1.46)	0.82		1.30 (0.87 ,1.95)	0.20	
<i>Boys (n=9801)</i>									
Crude	0.80 (0.64,1.00)	0.047*		0.74 (0.58, 0.95)	0.018*		0.74 (0.54, 1.01)	0.06	
Adjusted	0.87 (0.69,1.09)	0.22		0.86 (0.66, 1.12)	0.27		0.89 (0.64, 1.25)	0.51	

Odds ratios are adjusted for mothers age (19, 20–24, 25–29, 30–34, 35–39, 40+), education (12 years, 13–16 years, 17 years), smoking (never, occasionally, daily), alcohol consumption during pregnancy (never, less than once a week, once a week, more than once a week), parity (first, second or more births) and BMI (as continuous variable).

^a₉₀th percentile at sum score 11.

^b₉₀th percentile at sum score 10.

Crude and adjusted odds ratios (OR) of having sum score of ADHD symptoms at or above 90th percentile in relation to having amalgam fillings placed or removed during the first 30 weeks of pregnancy, and odds ratios in the subgroup with sum score at or above 90th percentile at both child aged 3 and 5 years.

TABLE 6

Children's sex and age	Amalgam fillings placed		Amalgam fillings removed	
	OR (95%CI)	p-value	OR (95% CI)	p-value
<i>^a At child aged 3 years</i>				
<i>All (n=42 163)</i>				
Crude	1.17 (0.84, 1.63)	0.35	0.98 (0.83, 1.15)	0.77
Adjusted	1.07 (0.77, 1.50)	0.69	0.96 (0.82, 1.14)	0.66
<i>Girls (20 615)</i>				
Crude	1.45 (0.93, 2.26)	0.10	0.98 (0.83, 1.15)	0.77
Adjusted	1.31 (0.84, 2.04)	0.24	0.88 (0.69, 1.13)	0.33
<i>Boys (21 548)</i>				
Crude	0.93 (0.57, 1.53)	0.77	1.04 (0.83, 1.29)	0.76
Adjusted	0.87 (0.53, 1.43)	0.58	1.03 (0.83, 1.29)	0.77
<i>^b At child aged 5 years</i>				
<i>All (n=23 302)</i>				
Crude	1.36 (0.80, 2.31)	0.26	1.10 (0.87, 1.40)	0.42
Adjusted	1.24 (0.72, 2.11)	0.44	1.13 (0.89, 1.44)	0.32
<i>Girls (n=11 472)</i>				
Crude	1.16 (0.46, 2.93)	0.75	0.89 (0.58, 1.36)	0.59
Adjusted	1.04 (0.41, 2.65)	0.93	0.93 (0.61, 1.42)	0.72
<i>Boys (n=11 830)</i>				
Crude	1.47 (0.76, 2.84)	0.25	1.24 (0.93, 1.67)	0.15
Adjusted	1.36 (0.70, 2.64)	0.37	1.25 (0.93, 1.69)	0.14
Subgroup with information about symptoms related to ADHD at both child aged 3 and 5 years:				
<i>All (n=19220)</i>				
Crude	0.95 (0.35, 2.60)	0.93	1.17 (0.79, 1.75)	0.44
Adjusted	0.84 (0.31, 2.29)	0.73	0.83 (0.56, 1.25)	0.37

Children's sex and age	Amalgam fillings placed		Amalgam fillings removed	
	OR (95%CI)	p-value	OR (95% CI)	p-value
<i>Girls (n=9419)</i>				
Crude	0.64 (0.88, 4.65)	0.66	1.64 (0.93, 2.91)	0.088
Adjusted	0.52 (0.07, 3.82)	0.52	1.75 (0.99, 3.12)	0.056
<i>Boys (n=9801)</i>				
Crude	1.47 (0.76, 2.84)	0.25	0.90 (0.51, 1.58)	0.71
Adjusted	1.13 (0.35 ,3.68)	0.84	1.11 (0.62, 1.96)	0.73

Odds ratios are adjusted for mothers age (-19, 20–24, 25–29, 30–34, 35–39, 40+), education (12 years, 13–16 years, 17 years), smoking (never, occasionally, daily), alcohol consumption (never, less than once a week, once a week, more than once a week), parity (first, second or more), and BMI (as continuous variable).

^a90th percentile at sum of symptoms 11.

^b90th percentile at sum of symptoms