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Research paper

Prenatal alcohol exposure and risk of attention deficit hyperactivity disorder in offspring: A retrospective analysis of the millennium cohort study

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ABSTRACT

Objective: To investigate the relationship between prenatal maternal alcohol consumption and the risk of attention deficit hyperactivity disorder (ADHD), the strengths and difficulties questionnaire (SDQ) score and abnormal hyperactivity score in seven-year-old children.

Methods: This study is a retrospective analysis of the Millennium Cohort Study (MCS). Questionnaires were used to gather data on gestational alcohol consumption when children were 9 months old and neurodevelopmental outcomes in offspring at 7 years of age (N = 13,004). Alcohol consumption was classified into never, light, moderate and heavy. Crude and adjusted logistic regression models were used for data analysis.

Results: The total number of women who reported drinking alcohol in pregnancy (the light, moderate and heavy drinking group) was 3916 (30.1%). No significant association was found between light, moderate or heavy gestational alcohol consumption and ADHD (adjusted odds ratio [aOR] for light = 0.80, 95% confidence interval [CI] = [0.53,1.22], aOR for moderate = 0.83, [0.40, 1.74]; aOR for heavy = 1.27, [0.54, 2.98]); for abnormal SDQ score (aOR for light = 0.94, [0.78,1.13], aOR for moderate = 0.70, [0.49,1.00]; aOR for heavy = 1.08, [0.70, 1.66]); for abnormal Hyperactivity score (aOR for light = 1.02, [0.89,1.17]; aOR for moderate = 1.05, [0.82, 1.34]; aOR for heavy = 0.90, [0.62, 1.32]), in offspring.

Conclusion: Light, moderate or heavy antenatal alcohol consumption was not associated with an increased susceptibility to ADHD or behavioural outcomes in this study. However, due to the limited number of cases we cannot rule out an increased risk of ADHD in relation to heavy alcohol consumption.

1. Introduction

Existing literature links prenatal alcohol exposure to numerous adverse neurodevelopmental outcomes in offspring (Carmichael Olson et al., 1997; Banerjee et al., 2007; Jones et al., 1973). Long-term neurobehavioral deficits, including hyperactivity, even at low doses of prenatal alcohol exposure have been demonstrated in animal literature (Riley, 1990; Sood et al., 2001).

Conversely, there is conflicting evidence cited in the literature suggesting that low levels of maternal alcohol consumption in pregnancy (MACP) may not be associated with adverse neurodevelopmental and health outcomes in early childhood (Kelly et al., 2009; Kelly et al., 2012; Robinson et al., 2010; O'Leary et al., 2010; Alati et al., 2008; Eriksen et al., 2012; Testa et al., 2003; Gallagher et al., 2018). Attention deficit hyperactivity disorder (ADHD) is a childhood-onset neurodevelopmental disorder characterised by developmentally inappropriate and impairing inattention, impulsivity and/or overactivity (Thapar and Cooper, 2016). ADHD is the most common cognitive and behavioural disorder diagnosed among school children, with an estimated worldwide prevalence of 3.4% (Polanczyk et al., 2015) ADHD incurs a significant economic burden and is associated with subpar social, academic, adaptive and occupational functioning (Barkley, 2002; Banerjee et al., 2007; Gupte-Singh et al., 2017; Polanczyk et al. 2015). The aetiology of the disorder remains unclear, however a number of genetic and environmental factors have been proposed as increasing susceptibility to the condition, one of which being prenatal substance

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exposure (Froehlich et al., 2011).

This study aims to investigate the relationship between prenatal alcohol exposure and unfavourable developmental outcomes namely ADHD, abnormal Strengths and Difficulties Questionnaire (SDQ) scores and abnormal hyperactivity score in seven year old children and to elucidate whether there is a dose-response effect.

2. Methods

2.1. Millennium cohort study

We performed a retrospective analysis of data from the UK Millennium Cohort Study (MCS), a nationally representative observational cohort study of children born in the United Kingdom (UK) between 2000 and 2002. A detailed description of methods used in the UK Millennium Cohort Study has been previously published (Connelly and Platt, 2014). The first four sweeps of surveys involved home visits by interviewers when cohort members were aged 9 months, 3, 5 and 7 years. Parents were asked about drinking in pregnancy, socio-economic circumstances, demographic characteristics, psychosocial environment and cohort members' behaviour.

2.2. Study population

Stratified cluster sampling was used to select the participants for the Millennium Cohort Study. Sampling was stratified by region and electoral ward. Information on population size, socioeconomic status and ethnic characteristics of wards was collected (Connelly and Platt, 2014). For this study, data were obtained from the first wave (infants aged 9 months) and fourth wave (children aged 7 years old). A total of 18,552 families participated in the wave 1 of the Millennium Cohort Study. 13,857 families participated in wave 4 (Hansen et al., 2014). After the exclusion of those who did not answer the questions on MACP and ADHD, the total sample size of the current study cohort was 13,004 children.

2.3. Maternal drinking patterns

When the cohort members were 9 months old, mothers were asked whether they drank alcohol during pregnancy. If they answered yes, they were asked to quantify how much, namely; every day, 5–6, 3–4, 1–2 days per week; 1–2 times per month; less than once per month; or never. If the mother drank at least once or twice per week, she was asked: 'In an average week, how many units of alcohol did you drink?'. If she answered yes to consuming alcohol once or twice per month or less than once per month, she was then asked: 'On the days when you did drink alcohol, on average how many units did you drink in a day?'. A unit was defined as half a pint of beer, a glass of wine or a single measure of spirit or liqueur'. Methods employed have previously been published elsewhere (Gallagher et al., 2018). During each sweep of surveys, mothers were asked if they currently drank alcohol. This information was combined with the aforementioned data collected on drinking during pregnancy to identify those mothers who never drank alcohol during pregnancy or quit drinking during pregnancy; 'never' drinkers, 'light' drinkers, 'moderate' drinkers and 'heavy' drinking group.

Women who reported 'never' drinking included those women who never drink alcohol at all and those who decided to quit drinking during pregnancy. The never drinking group was used as the reference group.

There are no widely standardised definitions for 'light', 'moderate' and 'heavy' drinking in pregnancy. We adopted the definitions as outlined by the National Institute on Alcohol Abuse and Alcoholism. 'Light' drinking was defined as not drinking more than 3 to 7 units per week, 'moderate' drinking as not more than 8 to 14 units per week and 'heavy' drinking as consuming more than 14 units per week or per occasion (Abel et al., 1998).

2.4. Outcomes measures

During the fourth sweep of surveys, when the children were 7 years old, parents were asked whether or not their child had received a diagnosis of ADHD from a doctor or other healthcare professional ("Has a doctor or healthcare professional ever told you that your child had any of the following problems?"). If parents answered "yes", then the child was reported to have ADHD in this study (Kelly et al., 2013).

Behavioural difficulties were assessed via the Strength and Difficulties Questionnaire (SDQ). This is a validated 25-item broad-band behavioural assessment tool for children aged between 4 and 15 years old and comprises five domains: hyperactivity, emotional symptoms, conduct problems, peer problems and prosocial behaviour. The SDQ score is the sum of the main care givers responses to a series of items that describe child's emotional (internalising) and behavioural (externalising) problems. The SDQ is classified into 3 categories; normal (score is between 0–13), borderline (score is between 14–16) and abnormal (score is between 17–40). A "borderline/abnormal" score suggests that the child has behavioural difficulties (Goodman et al., 2004). The SDQ includes a hyperactivity-inattention sub-domain which has been shown to be an effective surrogate marker for ADHD (Overgaard et al., 2018). An abnormal hyperactivity score of 7 or higher was taken as the third outcome measure in this study. A cutoff of 7/10 has been used in important epidemiological research (Dopfner et al., 2008) (Cuffe et al., 2009) See the Web site (http://www.sdqinfo.org/) for further details.

2.5. Statistical analysis

Descriptive analysis was carried out to describe the socio-demographic characteristics of the study population. The association between prenatal alcohol exposure and each of the three outcome measures, namely; ADHD, abnormal total SDQ scores and abnormal hyperactivity score were analysed using crude and adjusted logistic regression. Univariate logistic regression was employed to estimate the odds ratio of the association between MACP and each of the three outcome measures. Potential confounding factors were controlled for in adjusted models, namely; gender, gestational age at delivery, parity, paternal age, maternal age, maternal smoking status, maternal pre-pregnancy BMI, household income, maternal education, ethnicity and marital status. The potential confounders were included in the models as categorical variables as presented in Table 2. The adjusted odds ratio and the crude odds ratio were compared to assess if there were changes in these associations due to confounding. Separate models were used for each of the three outcomes. The analysis was repeated with data stratified by gender (Appendix A 1, Table 1). ADHD was not used as an outcome measure in the stratified analysis due to the limited number of exposed cases especially for the moderate and heavy alcohol consumption categories. All analyses were performed using the statistical software package SPSS (IBM v 0.26).

Table 1
Alcohol categories in pregnancy as defined in the National Institute on Alcohol Abuse and Alcoholism.

None: subdivided into	Never drinks alcohol (teetotal) Drink alcohol but not during pregnancy
Light	Not more than 3–7 units per week
Moderate	Not more 8–14 units per week
Heavy	14 or more units per week or per occasion

3. Results

3.1. Descriptive analysis

69.9% (N = 9088) of women reported 'never' drinking (never drinking alcohol at all or decided to quit drinking during pregnancy). 23.11% (N = 3001) of women reported 'light' drinking during pregnancy. 5.1% (N = 657) of women reported 'moderate' alcohol consumption during pregnancy. 2.0% (N = 258) of women reported 'heavy' alcohol consumption during pregnancy. 16.9% (n = 611) of mothers who consumed alcohol in pregnancy also smoked cigarettes during pregnancy compared to 15.7% (n = 1335) of those who never drank alcohol or who quit drinking alcohol during their pregnancy. 65.3% (n = 1480) of mothers who consumed alcohol in pregnancy were primiparuos women. 20.9% (n = 38) of women belonging to families in the lowest annual income category (£0-£3099) reported MACP. 53.2% (n = 367) of women belonging to families in the highest annual income category (£52,000 or more) reported drinking alcohol in pregnancy. Mothers whose highest educational qualification was in tertiary education had the highest proportion of women who reported gestational alcohol consumption (45.9%, n = 221 reported MACP) compared to other levels of academic qualification (see Tables 2 and 3).

96.3% (n = 13,004) participants answered the question about ADHD status in the fourth wave of surveys. 1.3% (n = 167) mothers reported that their child had received a diagnosis of ADHD from a healthcare professional. 1.0% (n = 29), 1.2% (n = 8) and 2.3% (n = 6) of women belonging to the light, moderate and heavy drinking categories respectively had children reported to have ADHD. amongst our study population; SDQ and hyperactivity scores were obtained for 97% (n = 12,618) of children and 97.5% (n = 12,675) of children respectively in the fourth wave survey. 7.3% (n = 919) of children had an abnormal SDQ score. 12.6% (n = 1599) of children had an abnormal hyperactivity score. amongst the group with the abnormal SDQ score; 18.1% (n = 166), 3.9% (n = 36) and 2.8% (n = 26) of the mothers belonged to the light, moderate and heavy drinking categories respectively. 5.6% (n = 166), 5.6% (n = 36) and 10.2% (n = 26) of women belonging to the light, moderate and heavy drinking categories respectively had children with an abnormal SDQ score. 11.2% (n = 332), 13,3% (n = 86) and 13.6% (n = 35) of women belonging to the light, moderate and heavy drinking categories respectively had children with an abnormal hyperactivity score (see Table 3.

3.2. Logistic regression

Results of the logistic regression analyses on the association between maternal alcohol consumption and ADHD, abnormal SDQ score and abnormal hyperactivity scores are displayed in Table 4. No significant association was noted between MACP consumption and ADHD, compared to never drinking [OR= 0.48, 95% confidence interval [CI] = [0.61 1.26]. Similarly, results suggest that light, moderate or heavy maternal alcohol consumption was not significantly associated with ADHD, compared to never drinking (OR for light = 0.80, 95% CI = [0.53,1.22], OR for moderate = 0.83, 95% CI = [0.40, 1.74]; OR for heavy = 1.27, 95% CI = [0.54, 2.98]). MACP was not noted to be associated with abnormal SDQ score [OR = 0.11, 95% CI = [0.75,1.03]. No significant association was observed between light, moderate or heavy MACP and abnormal SDQ scores (OR for light = 0.94, 95% CI = [0.78,1.13], OR for moderate =0.70, 95% CI = [0.49,1.00]; OR for heavy = 1.08, 95% CI = [0.70, 1.66]). Finally, results suggest that MACP was not significantly associated with abnormal hyperactivity scores [OR = 0.85, 95% CI = [0.90, 1.14] Furthermore, light, moderate or heavy alcohol consumption was not significantly associated with abnormal hyperactivity scores (OR for light = 1.02, 95% CI = [0.89,1.17], OR for moderate = 1.05, 95% CI = [0.82, 1.34]; OR for heavy = 0.90, 95% CI = [0.62, 1.32]).

3.3. Analysis

In the stratified analysis for gender, no significant association between MACP and abnormal hyperactivity score was noted, while a negative association between moderate MACP and abnormal SDQ scores in male offspring was observed (OR = 0.61, 95% CI = [0.38,0.97]; see Appendix A 1, Table 1).

4. Discussion

4.1. Main findings

To summarise our findings, we found that there was no significant association between light, moderate or heavy gestational alcohol consumption and increased risk of ADHD, abnormal SDQ score or abnormal Hyperactivity score in offspring.

Our findings are congruent with a UK study, which reported no association between low doses of gestational alcohol consumption and unfavourable developmental consequences in offspring (Kelly et al., 2013) and to a cohort study which found no association between binge drinking or low levels of MACP and ADHD in offspring (Weile et al., 2020). Conversely, other studies have shown an association between symptoms of inattention and impulsivity with prenatal exposure to alcohol (Streissguth et al., 1994; Sampson et al., 1989). Similarly, a case-control study noted a 2.5 fold increased risk of ADHD associated with prenatal exposure to alcohol (Mick et al., 2002). Mick et al. assigned the diagnosis of ADHD on the basis of DSM-III-R diagnostic criteria and interviewers in the study had undergraduate degrees in psychology and κ coefficients of agreement were calculated between raters and experienced psychiatrists who listened to audiotaped interviews made by the raters. In contrast, our study based ADHD diagnosis on parental report. The study by Mick et al. also includes offspring aged between 6 and 17 years while our study examines behavioural outcomes in 7 year old children.

However, it is prudent to mention that retrospective assessment of prenatal alcohol exposure by parental report increases the potential of both recall and reporting bias. This is substantiated by a growing number of studies including a large Canadian study which suggests maternal self-report of gestational alcohol consumption is ten-fold lower than objective measure of maternal alcohol exposure via analysis of meconium fatty acid ethyl esters (Delano et al., 2019). However, under-reporting of alcohol consumption is unlikely to be related to ADHD diagnosis because MACP was measured at 9 months of age. It may be opportune to conduct a study using objective measures of gestational alcohol consumption to assess the true prevalence of MACP and to assess the relationship between this and ADHD in offspring.

4.2. Strengths

The present study has a number of strengths. The study population is part of a large, nationally representative cohort, which increases the likelihood that the findings are comparable to the general population. Furthermore, our large sample size and high response rates in the first and fourth wave of the Millennium Cohort Study reduces the likelihood of the study being affected by selection bias. A wide range of potential confounding factors were accounted for in this study, including socio-economic factors such as maternal age, maternal pre-pregnancy BMI, maternal academic qualifications, family income, and antenatal smoking. This is one of the few studies which examines different levels of MACP to elucidate if a dose-response relationship exists between MACP and ADHD, abnormal SDQ score and abnormal hyperactivity score.

4.3. Limitations

The design of this study is subject to some limitations. The diagnosis

Table 2
Maternal and offspring characteristics according to level of maternal alcohol consumption in pregnancy.

	Never (n = 9088) (69.9%)	Any Alcohol Consumption (n = 3916) (30.1%)	Light (n = 3001) (23.1%)	Moderate (n = 657) (5.1%)	Heavy (n = 258) (2.0%)	Total (%) (n = 13,004) (100%)
Infant's Gender						
Male	4575(50.3%)	2007(51.3%)	1538(51.2%)	339(51.6%)	130(50.4%)	6582(49.4%)
Female	4513(49.7%)	1909(48.7%)	1463(48.8%)	318(48.4%)	128(49.6%)	6422(50.6%)
Total						13,004(100%)
Mother's age at the time of birth						
13 to 19	483(5.3%)	149 (3.8%)	93(3.1%)	31(4.7%)	25(9.7%)	632(4.9%)
20 to 29	4168(45.9%)	1325(33.8%)	982(32.7%)	231(35.2%)	112(43.4%)	5493(42.2%)
30 to 39	4157(45.7%)	2249(57.4%)	1781(59.3%)	361(54.9%)	107(41.5%)	6406(49.3%)
40 plus	279(3.1%)	193(4.9%)	145(4.8%)	34(5.2%)	14(5.4%)	472(3.6%)
Unknown						1(0.0%)
Total						13,004(100%)
Father's age at the time of birth						
13 to 19	59(0.8%)	24(0.7%)	14(0.5%)	6(1.1%)	4(2.1%)	83(0.8%)
20 to 29	2293(30.2%)	731(21.4%)	553(20.6%)	118(21.7%)	60(31.7%)	3024(27.4%)
30 to 39	4345(57.1%)	2162(63.2%)	1739(64.7%)	331(60.8%)	92(48.7%)	6507(59.0%)
40 plus	907(11.9%)	505(14.8%)	383(14.2%)	89(16.4%)	33(17.5%)	1412(12.8%)
Unknown						1978(15.2%)
Total	7604(100%)	2689(100%)	2689(100%)	544(100%)	189(100%)	13,004(100%)
Gestation at birth						
24 to 36 weeks	634(7.1%)	634(7.1%)	168(5.6%)	34(5.2%)	17(6.7%)	853(6.6%)
37 weeks	512(5.7%)	512(5.7%)	127(4.3%)	38(5.8%)	17(6.7%)	694(5.4%)
38 weeks	1249(13.9%)	1249(13.9%)	374(12.5%)	83(12.7%)	33(13.0%)	1739(13.5%)
39 weeks	1875(20.9%)	1875(20.9%)	682(22.9%)	121(18.6%)	56(22.0%)	2734(21.2%)
40 weeks	2575(28.6%)	2575(28.6%)	844(28.3%)	192(29.5%)	68(26.8%)	3679(28.6%)
41 weeks +	2143(23.8%)	2143(23.8%)	788(26.4%)	183(28.1%)	63(24.8%)	3177(24.7%)
Unknown						128(1.0%)
Total						13,004(100%)
Pre-pregnancy BMI						
Underweight (<18.5)	517(6.3%)	137(3.7%)	92(3.2%)	28(4.6%)	17(6.9%)	654(5.5%)
Normal (18.5 to 24.99)	5183(62.9%)	2593(70.1%)	2010(70.7%)	419(68.6%)	164(66.9%)	7776(65.1%)
Overweight (25 to 29.99)	1731(21.0%)	736(19.9%)	561(19.7%)	121(19.8%)	54(22.0%)	2467(20.7%)
Obese (≥ 30)	814(9.9%)	231(6.3%)	178(6.3%)	43(7.0%)	10(4.1%)	1045(8.8%)
Unknown						1062(8.2%)
Total	8245(100%)	3697(100%)	2841(100%)	611(100%)	245(100%)	13,004(100%)
Ethnicity						
White/Caucasian	7353(80.9%)	3765(96.1%)	2875(95.8%)	638(97.1%)	252(97.7%)	11,118(85.5%)
Afro-Caribbean	332(3.7%)	61(1.6%)	53(1.8%)	6(0.9%)	2(0.8%)	393(3.0%)
Asian	1221(13.4%)	34(0.9%)	30(1.0%)	3(0.5%)	1(0.4%)	1255(9.7%)
Other	182(2.0%)	56(1.4%)	43(1.4%)	10(1.5%)	3(1.2%)	238(1.8%)
Unknown						0(0.0%)
Total	9088(100%)	3916(100%)	3001(100%)	657(100%)	258(100%)	13,004(100%)
Smoking						
Non-smoker	5991(70.2%)	2330(64.4%)	1910(67.5%)	334(58.1%)	86(40.4%)	8321(68.5%)
Quit during/before pregnancy	1204(14.1%)	676(18.7%)	521(18.4%)	102(17.7%)	53(24.9%)	1880(15.5%)
Smoked during pregnancy	1335(15.7%)	611(16.9%)	398(14.1%)	139(24.2%)	74(34.7%)	1946(16.0%)
Unknown						857(6.6%)
Total	8530(100%)	3617 (100%)	2829(100%)	575(100%)	213(100%)	13,004(100%)
Parity						
1	3107(58.5%)	1480(65.3%)	1154(67.6%)	246(57.5%)	80(60.6%)	4587(60.5%)
2	1441(27.1%)	549(24.2%)	403(23.6%)	117(27.3%)	29(22.0%)	1990(26.3%)
3	520(9.8%)	175(7.7%)	111(6.5%)	52(12.1%)	12(9.1%)	695(9.2%)
4+	246(4.6%)	62(2.7%)	38(2.2%)	13(3.0%)	11(8.3%)	308(4.1%)
Unknown						5424(41.7%)
Total	5314(100%)	1706(100%)	1706(100%)	428(100%)	132(100%)	13,004(100%)
Family income						
£52,000 or more	323(3.8%)	367(9.8%)	294(10.3%)	60(9.6%)	13(5.3%)	690(5.6%)
£31,200 to £51,999	1155(13.5%)	789(21.1%)	649(22.7%)	111(17.7%)	29(11.7%)	1944(15.8%)
£20,800 to £31,199	1718(20.1%)	833(22.3%)	683(23.9%)	110(17.5%)	40(16.2%)	2551(20.8%)
£10,400 to £20,799	2876(33.7%)	1034(27.7%)	765(26.8%)	191(30.5%)	78(31.6%)	3910(31.9%)
£3100 to £10,399	2110(24.7%)	602(16.1%)	391(13.7%)	135(21.5%)	76(30.8%)	2712(22.1%)
£0 to £3099	144(1.7%)	38(1.0%)	28(1.0%)	3(0.5%)	7(2.8%)	182(1.5%)
Refused	217(2.5%)	69(1.8%)	48(1.7%)	17(2.7%)	4(1.6%)	286(2.3%)
Unknown						729(5.6%)
Total	8543(100%)	2858(100%)	2858(100%)	627(100%)	247(100%)	13,004(100%)
Marital status						
Single never married	2806(30.9%)	1212(30.9%)	818(27.3%)	249(37.9%)	145(56.2%)	4018(30.9%)
1st and only marriage	5270(58.0%)	2254(57.6%)	1841(61.3%)	328(49.9%)	85(32.9%)	7524(57.9%)
Legally separated	262(2.9%)	87(2.2%)	67(2.2%)	17(2.6%)	3(1.2%)	349(2.7%)
Divorced	346(3.8%)	178(4.5%)	130(4.3%)	35(5.3%)	13(5.0%)	524(4.0%)
Remarried	389(4.3%)	180(4.6%)	143(4.8%)	26(4.0%)	11(4.3%)	569(4.4%)

(*continued on next page*)

Table 2 (*continued*)

	Never (n = 9088) (69.9%)	Any Alcohol Consumption (n = 3916) (30.1%)	Light (n = 3001) (23.1%)	Moderate (n = 657) (5.1%)	Heavy (n = 258) (2.0%)	Total (%) (n = 13,004) (100%)
Widowed	15(0.2%)	5(0.1%)	2(0.1%)	2(0.3%)	1(0.4%)	20(0.2%)
Unknown						0 (0%)
Total	9088(100%)	3916(100%)	3001(100%)	657(100%)	258(100%)	13,004(100%)
Maternal Education						
Secondary Education	5009(55.2%)	1982(50.6%)	1514(50.5%)	339(51.6%)	129(50.0%)	6991(53.8%)
Tertiary Education	2040(22.5%)	1467(37.5%)	1197(39.9%)	198(30.1%)	72(27.9%)	3507(27.0˙%)
Other	288(3.2%)	43(1.1%)	34(1.1%)	8(1.2%)	1(0.4%)	331(2.5%)
None of the above	1732(19.1%)	422(10.8%)	254(8.5%)	112(17.0%)	56(21.7%)	2154(16.6%)
Unknown						21(0.2%)
Total	9069(100%)	3914(100%)	2999(100%)	657(100%)	258(100%)	12,983(99.8%)

of ADHD was based on parental reporting rather than clinical notes. This may result in some children who do not have a formal diagnosis of ADHD being misclassified into this group. Of note, SDQ Questionnaire score is not based on a clinical diagnosis and is designed to be completed by parents or teachers. It is also possible that parents would be reluctant to report the true diagnosis due to social perception and stigma connected to ADHD or over-report if they feel their child has behavioural difficulties. As data were anonymized it was not possible to confirm this. The prevalence of ADHD in our study was 1.3% which is lower than the global estimation of 3.4% (Hansen et al., 2014; Polanczyk et al., 2015). This difference may be attributable to age at diagnosis (diagnosis at 7 years old vs. from 6 to18 years old respectively). Different diagnostic criteria such ICD or DSM classifications, cultural factors and different screening programmes in different countries may also affect the prevalence estimates.

A large nationally representative study carried out in Britain reported the prevalence of ADHD as defined in DSM-IV-TR to be 3.6% and 0.85% for boys and girls respectively(Ford et al., 2003). This study assessed 10,438 children aged 5–15 years old using a Development and Wellbeing Assessment. This was a strucutred interview with verbatim reports reviewed by clinicains. Of note, this study reported the prevalence of ADHD in 5–7 years old children as 1.9% which is marginally higher than our finding of 1.3% in 7 year old children.

Retrospective assessment of prenatal alcohol exposure by parental report increases the potential of both recall and reporting bias. This is substantiated by a growing number of studies including a large Canadian study which suggests maternal self-report of gestational alcohol consumption is ten-fold lower than objective measure of maternal alcohol exposure via analysis of meconium fatty acid ethyl esters (Delano et al., 2019). However, under-reporting of alcohol consumption is unlikely to be related to ADHD diagnosis because MACP was measured at 9 months of age. It may be opportune to conduct a study using objective measures of gestational alcohol consumption to assess the true prevalence of MACP and to assess the relationship between this and ADHD in offspring.. Studies have found that the amount

Table 4
The association between maternal alcohol consumption and ADHD, SDQ and hyperactivity in the offspring.

Alcohol Dose	Number	Crude OR [95% CI]	Adjusted OR[a] OR [95% CI]
ADHD results			
Never drinkers	124	Reference [1]	Reference [1]
Drinkers	43	0.22 [0.57,1.14]	0.48 [0.61 1.26]
Light drinkers	29	0.71 [0.47, 1.06]	0.80 [0.53, 1.22]
Moderate drinkers	8	0.89 [0.43, 1.83]	0.83 [0.40, 1.74]
Heavy drinkers	6	1.72 [0.75, 3.94]	1.27 [0.54, 2.98]
Abnormal SDQ Score results			
Never drinkers	691	Reference [1]	Reference [1]
Drinkers	228	0.00 [0.63, 0.85]	0.11 [0.75,1.03]
Light drinkers	166	0.69 [0.58, 0.82]	0.94 [0.78, 1.13]
Moderate drinkers	36	0.69 [0.49, 0.98]	0.70 [0.49, 1.00]
Heavy drinkers	26	1.32 [0.87, 1.99]	1.08 [0.70, 1.66]
Abnormal Hyperactivity Score results			
Never drinkers	1146	Reference [1]	Reference [1]
Drinkers	453	0.35 [0.79, 0.99]	0.85 [0.90, 1.14]
Light drinkers	332	0.84 [0.74, 0.95]	1.02 [0.89, 1.17]
Moderate drinkers	86	1.03 [0.81, 1.30]	1.05 [0.82, 1.34]
Heavy drinkers	35	1.05 [0.73, 1.51]	0.90 [0.62, 1.32]

Adjusted for; gender, gestational age at delivery, maternal age, paternal age, maternalsmoking, maternal pre-pregnancy BMI, household income, maternal education, ethnicity, marital status.

Table 3
Neurodevelopmental outcomes according to level of maternal alcohol consumption in pregnancy.

	Never (N = 9008)(69.9%)	Any Alcohol Consumption (n = 3916) (30.1%)	Light (N = 3001)(23.1%)	Moderate (N = 657)(5.1%)	Heavy (N = 258)(2.0%)	Total (N = 13,004)(100%)
	Children reported to have ADHD at wave 4					
Has ADHD	124 (1.4%)	43 (1.1%)	29 (1.0%)	8 (1.2%)	6 (2.3%)	167 (1.3%)
No ADHD	8964 (98.6%)	3873(98.9%)	2972 (99.0%)	649 (98.8%)	252 (97.7%)	12,837 (98.7%)
Total	9088(100%)	3916(100%)	3001(100%)	657(100%)	258(100%)	13,004 (100%)
	SDQ scores at wave 4					
Abnormal score	691(7.9%)	228(5.9%)	166(5.6%)	36(5.6%)	26(10.2%)	919(7.3%)
Normal score	8061(92.1%)	3638(94.1%)	2803(94.4%)	605(94.4%)	230(89.8%)	11,699(92.7%)
Unknown						386(3.0%)
Total	8752(100%)	3866(100%)	2969(100%)	641(100%)	256(100%)	13,004(100%)
Hyperactivity scores at wave 4						
Abnormal score	1146 (13.0%)	453(11.7%)	332(11.2%)	86(13.3%)	35(13.6%)	1599(12.6%)
Normal score	7650(87.0%)	3426(88.3%)	2645(88.8%)	559(86.7%)	222(86.4%)	11,076(87.4%)
Unknown						329(2.5%)
Total	8796(100%)	3879(100%)	2977(100%)	645(100%)	257(100%)	13,004(100%)

Table A 1
. Results of stratified adjusted analysis by sex of offspring.

Alcohol Dose	Boys (n = 6582)	Girls (n = 6422)
Abnormal SDQ Score results		
Never drinkers	Reference [1]	Reference [1]
Drinkers	0.15 [0.70, 1.06]	0.46 [0.69, 1.18]
Light drinkers	0.94 [0.75, 1.19]	0.93 [0.69, 1.26]
Moderate drinkers	0.61 [0.38, 0.97]	0.87 [0.50, 1.50]
Heavy drinkers	0.95 [0.54, 1.67]	1.32 [0.69, 2.51]
Abnormal Hyperactivity Score results		
Never drinkers	Reference [1]	Reference [1]
Drinkers	0.98 [0.86,1.17]	0.88 [0.83, 1.24]
Light drinkers	1.04 [0.87, 1.23]	0.99 [0.79, 1.24]
Moderate drinkers	0.94 [0.69, 1.29]	1.23 [0.84, 1.80]
Heavy drinkers	1.02 [0.65, 1.61]	0.72 [0.37, 1.39]

of alcohol in a drink poured and consumed outside of licenced premises can vary significantly (Gill and Donaghy, 2004) (Wilson, 1981) The alcohol content of alcohol beverages was not documented in this study. The definition of 'light', 'moderate' and 'heavy' alcohol consumption used in this study was adopted from American guidelines, UK guidelines would have been more accuarate as American measures of alcohol differ from UK measures.

Data on a family history of ADHD is not available within the Millennium Cohort Study, therefore a genetic predisposition could not be accounted for in this study, making it difficult to rule out genetic confounding factors. Data on the timing of drinking during pregnancy is not available in the MCS cohort. Hence, it is not clear how many women stopped drinking prior to conception or during which trimesters of pregnancy they drank alcohol. It would be valuable to examine if the timing of alcohol consumption related to gestational age influences behavioural and health outcomes in offspring. Due to the limited number of cases, results were limited by statistical power and more research is warranted to investigate the relationship between heavy MACP and ADHD.

5. Conclusion

In conclusion, light, moderate or heavy MACP was not associated with an increased likelihood of developing ADHD, abnormal hyperactivity scores or abnormal SDQ scores in this study cohort. Prospective studies are needed to investigate the effects of antenatal drinking and the gestational timing of such episodes on development of ADHD. The use of objective methods of measuring fetal alcohol exposure to examine the relationship between MACP and ADHD may be more accurate and therefore may be more helpful in guiding clinical practice than self-report.

Contribution to authorship

FLJ and ASK planned the study. JM and GM carried out analysis and interpreted results, JM and FLJ drafted the manuscript and GM, FMC and ASK took part in drafting the article or revising it for critically important intellectual content and all gave final approval of the version to be published.

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Ethical approval

The Millennium Cohort Study attained full ethical approval from an NHS Research Ethnics Committee (MREC). Informed consent is obtained from parents and children. The London Multicentre Research Ethics Committee (MREC) granted ethical approval for the MCS surveys. The Clinical Research Ethics Committee of the Cork teaching hospitals (CREC) granted ethical approval for this secondary data analysis.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2020.03.027.

Appendix 1

Adjusted for; gender, gestational age at delivery, maternal age, paternal age, maternal smoking, maternal pre-pregnancy BMI, household income, maternal education, ethnicity, marital status.

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