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ORIGINAL CONTRIBUTION

Maternal body mass index before pregnancy as a risk factor for ADHD and autism in children

Christina Hebsgaard Andersen[1] · Per Hove Thomsen[1] · Ellen Aagaard Nohr[2] · Sanne Lemcke[1]

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Abstract The risk of attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) may be influenced by environmental factors such as maternal obesity before pregnancy. Previous studies investigating those associations have found divergent results. We aim to investigate in a large birth cohort this association further in children with ADHD, ASD and comorbid ADHD and ASD. Our study population consisted of 81,892 mother–child pairs participating in the Danish National Birth Cohort (DNBC). Information about pre-pregnancy weight and height was collected in week 16 of pregnancy; the analysis was divided into groups based on BMI. Children with a clinical diagnosis of ADHD and/or ASD were identified in the Danish health registries at an average age of 13.3 years. Hazard ratios (HRs) were estimated using time-to-event analysis. Compared to normal weight mothers, the risk of having a child with ADHD was significantly increased if the mother was overweight (HR = 1.28 [95% CI 1.15;1.48]), obese (HR = 1.47 [95% CI 1.26;1.71]) or severely obese (HR = 1.95 [95% CI 1.58;2.40]). The same pattern was seen for the combined ADHD and ASD group. Regarding ASD, an increased risk was observed in underweight (HR = 1.30 [95% CI 1.01;1.69]) and obese (HR = 1.39 [95% CI 1.11;1.75]) mothers. Subgroup analysis revealed that the association in the ADHD group could mostly be attributable to the hyperactive group. Maternal obesity before pregnancy is a risk factor for ADHD in children. Maternal obesity as well as underweight may also be associated with an increased risk for ASD.

Keywords Body mass index · ADHD · Autism spectrum disorder · Hyperkinetic disorder · Longitudinal study · Birth cohort

Attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) are neurodevelopmental disorders with serious consequences for the affected children and their families. The prevalence of ADHD is estimated to be about 5% in children and adolescents, and symptoms related to ADHD seem to persist from childhood into adulthood in a majority of cases [1–3]. In a review from 2012, the prevalence of ASD is estimated to be 0.62% [4]. However, a study from 2015 found a prevalence of 1.1% in Danish children born in 1999–2001 and followed until 10 years of age [5]. The ASD diagnosis is considered to be rather stable throughout life [6]. In general, the prevalence of both ADHD and ASD has been increasing over the years [5].

The etiology of ADHD and ASD is assumed to be multifactorial and both heritable and environmental [7, 8]. Some risk factors are shared by ADHD and ASD, including low birth weight, premature birth and gender [9–11], while maternal smoking and socioeconomic status are only proven to be a risk factor for ADHD [10]. Likewise, high parental age and parental psychiatric disorders are risk factors for ASD in children [12–14].

Among environmental risk factors, maternal overweight/obesity in relation to pregnancy might also be important, and studies have investigated the association between maternal weight and ADHD or ASD in the offspring. With regard

✉ Sanne Lemcke
sanne.lemcke@ps.rm.dk

[1] Center for Child and Adolescent Psychiatry, Aarhus University Hospital, Risskov, Denmark

[2] Research Unit for Gynaecology and Obstetrics, Institute of Clinical Research, University of Southern Denmark, Odense, Denmark

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to ADHD, there seems to be a trend toward a higher risk of ADHD or symptoms related to ADHD in children whose mothers had a pre-pregnancy BMI higher than 25 [15–19], and a Swedish study suggests that the association may be ascribed to unmeasured familial confounding [20]. However, one study found little consistent evidence of intrauterine effects of maternal pre-pregnancy overweight on child cognition and behavior [21].

Also, the risk of having a child with ASD if the mother is overweight has been investigated in several studies, and the results are more divergent. Some studies found an increased risk of ASD if the mother was overweight [22–25] or had a large weight gain during pregnancy [22, 26]. Other studies found no direct association [27, 28] and in one study the association disappeared when siblings were used as controls in the analyses [29].

The differences in study results may be caused by variations in study designs. All studies examining maternal overweight as a risk factor for offspring ADHD had different outcome measures. Most of them used mother or teacher ratings [15–18, 21], and only one study used clinical ADHD diagnoses [20]. Most of the studies on ASD agree on the outcome measure as they generally used register-based diagnoses according to ICD-9, ICD-10 or DSM-4, depending on the country of origin [22, 23, 26, 28, 29]. However, these studies did not agree on exposure. Some used maternal weight in kilograms [22], while others used maternal BMI [23, 26–29] or weight gain during pregnancy [22, 26, 29]. Also, the number of participants included in the studies varied very much for both ADHD and ASD studies.

The increase in both the prevalence of ADHD and ASD [5] and pre-pregnant obesity among pregnant women [30] makes it interesting to further investigate the possibility of an association. The present study utilizes a large population-based birth cohort to explore a possible association between maternal pre-pregnancy BMI and the occurrence of ADHD or ASD in children. Information from the cohort makes it possible to use standardized pre-pregnancy BMI as exposure, and clinical diagnoses of ADHD and ASD from the comprehensive Danish registries as outcome. In addition, the large cohort makes it possible in the same study population to compare the associations with both disorders and to investigate the occurrence in subgroups. We hypothesized that mothers with a BMI >25 would have an increased risk of having a child with ADHD or ASD.

Methods

Study population

Between 1996 and 2002, more than 100,000 pregnant women were included in the Danish National Birth Cohort (DNBC) [31]. The women were recruited through their general practitioner (GP) at the first prenatal visit, which usually took place between weeks 6 and 10 of gestation. In Denmark, more than 99% of all pregnant women participate in the antenatal care program, which is free of charge, through their GP and midwife. During the study period, approximately 31% of all pregnant women in Denmark were enrolled in the DNBC [31]. The women in the DNBC differed from women in the source population by being more often of normal weight, nonsmokers or previous smokers. They had a lower rate of preterm deliveries of infants with very low Apgar scores and of infants born small for gestational age. But the effect of the differences on risk estimates has been shown to be small [32].

The women were interviewed several times, and for this study we used information from the first structured telephone interview (interview 1) when the average length of gestation was 16 weeks. Of the recruited women, 92% completed interview 1, which included questions about lifestyle habits, work, medication, and diseases [33].

At birth or immigration, all residents in Denmark are assigned a unique personal identification number (CPR number registered in the Civil Registration System) which is used for linkage between all public registries [34]. The study population includes live-born singletons from the birth cohort identified in the Danish Medical Birth Register [35].

Children who left Denmark during the follow-up time ($n = 2464$), died or were missing in the Civil Registration System ($n = 1302$) were excluded because of lack of information. Children with missing data on gestational age and birth weight ($n = 76$) and children of mothers who did not answer interview 1 ($n = 5555$) or had missing data on pre-pregnancy weight or height ($n = 1369$) were also excluded (Fig. 1).

Exposure

Maternal BMI (kilogram per meter squared) was constructed from self-reported pre-pregnancy weight and height from interview 1. BMI was categorized according to World Health Organization (WHO) criteria as underweight (BMI < 18.5), normal weight ($18.5 \leq$ BMI < 25), overweight ($25 \leq$ BMI < 30), obese ($30 \leq$ BMI < 35), and severely obese (BMI ≥ 35) [36].

Confounders

Potential confounders were chosen a priori based on previous research examining potential risk factors for ADHD and ASD. It included maternal and paternal age, maternal psychiatric disorders, maternal smoking, socio-occupational status, gender, gestational age and birth weight.

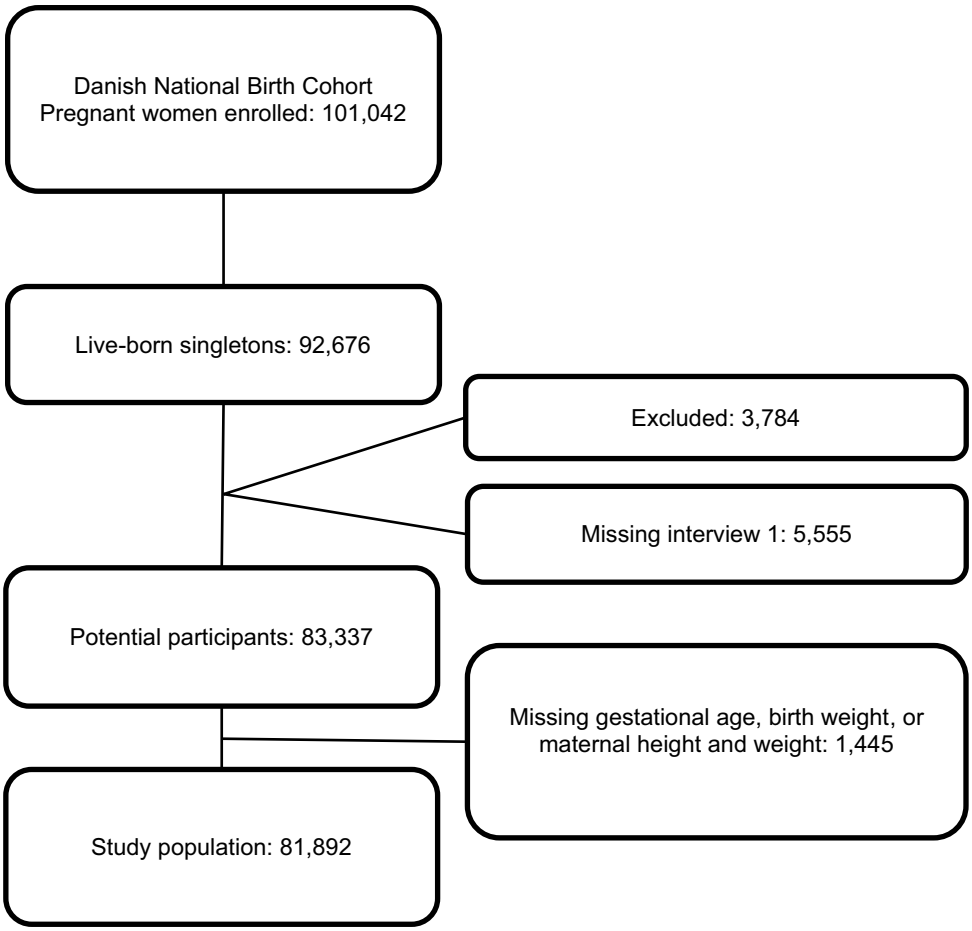

Fig. 1 Flowchart of the study population

Gestational age and birth weight were included in a polynomial regression equation [37] to calculate a relative weight to take the interaction between those factors into account. Information from interview 1 on current or most recent occupation and education was used as indicators of socio-occupational status [38]. We dichotomized maternal psychiatric disorders into "yes" or "no" based on answers to the questions: "Have you ever suffered any mental disorder or neurosis?" and: "Did you see a doctor or psychologist?" If a mother answered "yes" to both questions, she was categorized as "yes". This was done to exclude minor and self-diagnosed psychiatric disorders. Smoking was divided into three categories: (1) non-smoker, (2) quit smoking in pregnancy or smoked less daily, (3) daily smoker.

Outcome

In Denmark, ICD-10 is used to diagnose hyperkinetic disorder (HKD). The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) applies the term ADHD. There is a significant overlap between HKD and ADHD, although ADHD includes a broader group of children than HKD. The main difference is that ADHD permits symptoms of inattention in the absence of hyperactivity.

In the present study, ADHD case definitions were based on ICD-10 criteria for "disturbance of activity and attention (F90.0)", "hyperkinetic conduct disorder (F90.1)", "other specified behavioral and emotional disorder with onset usually occurring in childhood and adolescence (F98.8)" and without a diagnosis of ASD. In Denmark, the diagnosis F98.8 is commonly used to classify children with symptoms of inattention and no hyperactivity. Also, children who received at least one prescription for ADHD medication (methylphenidate or atomoxetine) were defined as ADHD cases.

In Denmark, only child and adolescent psychiatrists are allowed to initiate medical treatment for ADHD in children and adolescents (Danish National Board of Health 2013), and according to Danish guidelines medical treatment is only recommended if the child has a clinical diagnosis of ADHD and non-pharmacological treatment is ineffectual. Children diagnosed with narcolepsy ($n = 18$) were excluded from the study because they might get the same medical treatment as children with ADHD.

ASD case definitions were based on ICD-10 criteria for "childhood autism (F84.0)", "atypical autism (F84.1)", "Asperger syndrome (F84.5)", "other pervasive developmental disorder (F84.8)", pervasive developmental disorder, unspecified (F84.9)" and without a diagnosis of ADHD.

There is an ongoing discussion about whether ADHD and ASD are two manifestations of the same disorder [39–41], and many children are assigned both diagnoses. For analytical purposes, a group of children who had both ADHD and ASD diagnosis was identified as ADHD + ASD (either F90.0, F90.1, or F98.8 plus either F84.0, F84.1, F84.5, F84.8, or F84.9). Additional analyses were made separately for the hyperactive group (F90.0 + F90.1), the inattentive group (F98.8) and the group of children with childhood autism (F84.0). All diagnostic groups were compared to the cohort, which included all children.

Data on childhood diagnoses were obtained when the children were 13.3 years on average. Data came from the Danish National Psychiatric Register (DNP) [42] and the Danish National Patient Register (NPR) [43]. DNP and NPR include data on clinical diagnoses and dates of admission to and discharge from all hospitals. Treatment in public hospitals is free of charge, which ensures that the majority of patients seek public hospitals and will be registered in either one or the other register. Reporting to the hospital registers is mandatory and performed as standard procedure in the hospitals. Since 2000, the NPR has formed the basis for payment (by the state and not by the patients) to public hospitals. All sales of prescription medicine are reported to the Danish National Prescription Register (DNPR), which makes it possible to identify children with ADHD being medicated by private doctors [44]. Linking DNP, NPR, and DNPR via the CPR numbers with the DNBC makes it possible to identify children diagnosed with ADHD and/or ASD in the cohort.

Statistical analyses

This is a longitudinal cohort study with varying follow-up time for the children, which implies different risks. Therefore, time-to-event analysis was used to quantify the association between maternal weight and the children's diagnoses. Follow-up time ended at the first date of the reported diagnosis or on December 31, 2013, whichever came first. Cox proportional hazards regression analysis was performed with the age of the child as time scale. The effect measure was hazard ratio (HR) with 95% confidence interval. The proportional hazards assumption was evaluated by assessing log-minus-log survival plots. Clustering of outcomes within a family was adjusted for by robust variance estimates. HR can be interpreted as relative risk. All data management and analyses were performed with Stata 13.1 (StataCorp, College Station, TX, USA).

This study was registered with the Danish Data Protection Agency and approved by the Danish National Board of Health. The steering committee for the DNBC gave permission to use data for this project. On enrollment in the DNBC, all mothers gave consent to the use of data for research purposes.

Results

Our study population consisted of 81,892 children of whom 2417 (3.0%) had an ADHD diagnosis, and 1118 (1.4%) had an ASD diagnosis while 606 children (0.7%) had both disorders.

Four percent of all mothers were categorized as underweight, 68% as normal weight, 20% as overweight, 7% as obese, and 2% as severely obese. Mothers who were of normal weight before pregnancy had the highest socio-occupational status, and severely obese mothers had the lowest. The underweight women smoked more, had more psychiatric disorders, and gave birth to children with the lowest birth weight (Table 1).

Unadjusted analyses

The overall crude risk of having a child with ADHD was elevated for mothers having a BMI lower or higher than the normal weight. The higher the BMI, the higher is the risk of ADHD. HR for underweight mothers was 1.26 [95% CI 1.04;1.52] and for overweight mothers 1.34 [95% CI 1.22;1.48]. Obese and severely obese mothers had HRs of 1.57 [95% CI 1.35;1.82] and 2.19 [95% CI 1.79;2.68] respectively. The overall risk of having a child with both ADHD and ASD was elevated for obese and severely obese mothers, and the risk of ASD alone was elevated for underweight and obese mothers (Table 2). Analyses of the ADHD subgroups revealed that the increased risk of ADHD was associated with the hyperactive subgroup, F90.0 + F90.1, and not the inattentive group, F98.8. There was no association with childhood autism (Table 3).

Adjusted analyses

After adjusting for potential confounding factors, the HRs for all outcomes were slightly attenuated (Table 2). According to ADHD, HR for overweight mothers was 1.28 [95% CI 1.15;1.41], for obese 1.47 [95% CI 1.26;1.71], and for severely obese 1.95 [95% CI 1.58;2.40]. The risk of having a child with both ADHD and ASD was still significantly elevated for obese (HR = 1.42 [95% CI 1.05;1.92]) and severely obese mothers (HR = 2.08 [95% CI 1.40;3.08]),

Table 1 Participant characteristics by maternal BMI before pregnancy

	BMI < 18.5	18.5 ≤ BMI < 25	25 ≤ BMI < 30	30 ≤ BMI < 35	BMI > 35	Study population
n (%)	3662 (4.5)	55,305 (67.5)	16,064 (19.6)	4967 (6.1)	1894 (2.3)	81,892
Child characteristics						
Mean age at follow-up, years (min/max/SD)	13.3 (10.6/16.2/1.39)	13.3 (10.5/16.1/1.38)	13.2 (10.6/16.1/1.36)	13.1 (10.6/16.2/1.37)	13.1 (10.6/16.2/1.39)	13.3 (10.5/16.2/1.38)
Gender: male (%)	1887 (51.5)	28,322 (51.2)	8259 (51.4)	2512 (50.6)	971 (51.3)	41,951 (51.2)
Mean birth weight (g)	3360	3566	3662	3680	3748	3584
Mean gestational age (days)	278.1	280.0	280.3	280.1	280.3	280.0
Parental characteristics						
Mean maternal age (years)	29.2	30.1	29.8	29.5	29.5	29.9
Mean paternal age (years)	31.7	32.3	32.1	32.0	32.2	32.2
Socio-occupational status (%)						
Group 1 (%)	1635 (47.5)	30,328 (57.0)	7139 (46.7)	1777 (38.2)	579 (33.0)	41,458 (52.9)
Group 2	1364 (39.7)	18,825 (35.4)	6571 (42.9)	2212 (47.5)	840 (47.9)	29,812 (38,0)
Group 3	440 (12.8)	4060 (7.6)	1593 (10.4)	668 (14.3)	336 (19.2)	7097 (9.1)
Maternal smoking (%)						
Non-smoker	2301 (62.9)	41,127 (74.4)	11,953 (74.4)	3698 (74.5)	1424 (75.2)	60,503 (73.9)
Non-daily or quit smoking	414 (11.3)	6309 (11.4)	1604 (10.0)	440 (8.86)	162 (8.6)	8929 (10.9)
Daily smoker	946 (25.8)	7847 (14.2)	2502 (15.6)	829 (16.7)	308 (16.3)	12,432 (15.2)
Maternal psychiatric disorder (%)	410 (11.2)	4165 (7.5)	1224 (7.6)	399 (8.0)	198 (10.5)	6396 (7.8)

and for ASD alone for underweight (HR = 1.30 [95% CI 1.01;1.69]) and obese (HR = 1.39 [95% CI 1.11;1.75]) mothers. Subgroup analyses showed that overweight, obese, and severely obese mothers had a significantly elevated risk of having a child with hyperactivity (F90.0 + F90.1), but not with inattention (F98.8) or childhood autism (Table 3).

Discussion

This study investigated whether maternal pre-pregnancy BMI was associated with ADHD and/or ASD in children in a large birth cohort. An association was found between maternal overweight and increased risk of ADHD in the children, especially for the hyperactive subgroup. The results are similar to the results of previous studies that have also shown an association between maternal BMI higher than 25 and ADHD or ADHD symptoms in the offspring [15–19]. With regard to ASD, this study found an elevated risk of ASD in children with underweight or obese mothers. Previous studies of the association between maternal pre-pregnancy BMI and ASD in the offspring have reported diverse results [25]. However, the findings in this study are in accordance with the results from another large population-based study by Getz et al., who also found that the extremes in maternal BMI were associated with increased risk of ASD in children [25].

The relationship between ADHD and obesity has been investigated in a meta-analysis by Cortese et al. [45], who found evidence of a significant association between obesity/overweight and ADHD. Also, Martinez de Velasco et al. found a significantly higher prevalence of ADHD in obese patients than in normal weight controls in a review [46]. However, Nigh et al. concluded in their review that the association between ADHD and obesity was small, but significantly larger in adults and adolescents than in children [47]. It is suggested that impulsivity as a permanent trait could maintain high-calorie intake and cause obesity [48]. Thus, some of the overweight and obese mothers in this study might have undiagnosed ADHD and their

Table 2 Crude and adjusted risk of ADHD, ASD, and ADHD + ASD according to maternal pre-pregnancy BMI

Crude risk	ADHD			ASD			ADHD + ASD			Study population
	N (%)	HR (95% CI)	*P* value	*N* (%)	HR (95% CI)	*P* value	*N* (%)	HR (95% CI)	*P* value	*N* (%)
BMI < 18.5	120 (5.0)	1.26 (1.04;1.52)	0.016	66 (5.9)	1.40 (1.09;1.80)	0.009	32 (5.3)	1.25 (0.87;1.80)	0.220	3662 (4.5)
18.5 ≤ BMI < 25	1440 (59.6)	Ref. group		710 (63.5)	Ref. group		383 (63.2)	Ref. group		55,305 (67.5)
25 ≤ BMI < 30	555 (23.0)	1.34 (1.22;1.48)	<0.001	223 (19.9)	1.10 (0.94;1.27)	0.232	116 (19.1)	1.05 (0.85;1.29)	0.642	16,064 (19.6)
30 ≤ BMI < 35	198 (8.2)	1.57 (1.35;1.82)	<0.001	87 (7.8)	1.41 (1.12;1.76)	0.003	48 (7.9)	1.43 (1.06;1.92)	0.021	4967 (6.1)
BMI ≥ 35	104 (4.3)	2.19 (1.79;2.68)	<0.001	32 (2.9)	1.37 (0.96;1.95)	0.080	27 (4.5)	2.11 (1.43;3.13)	<0.001	1894 (2.3)
Adjusted risk	ADHD			ASD			ADHD + ASD			Study population
	N (%)	HR (95% CI)	*P* value	*N* (%)	HR (95% CI)	*P* value	*N* (%)	HR (95% CI)	*P* value	*N* (%)
BMI < 18.5	120 (5.0)	1.05 (0.87;1.28)	0.593	66 (5.9)	1.30 (1.01;1.69)	0.043	32 (5.3)	1.09 (0.75;1.58)	0.667	3662 (4.5)
18.5 ≤ BMI < 25	1440 (59.6)	Ref. group		710 (63.5)	Ref. group		383 (63.2)	Ref. group		55,305 (67.5)
25 ≤ BMI < 30	555 (23.0)	1.28 (1.15;1.41)	<0.001	223 (19.9)	1.09 (0.94;1.27)	0.267	116 (19.1)	1.03 (0.83;1.27)	0.807	16,064 (19.6)
30 ≤ BMI < 35	198 (8.2)	1.47 (1.26;1.71)	<0.001	87 (7.8)	1.39 (1.11;1.75)	0.005	48 (7.9)	1.42 (1.05;1.92)	0.024	4967 (6.1)
BMI ≥ 35	104 (4.3)	1.95 (1.58;2.40)	<0.001	32 (2.9)	1.38 (0.97;1.97)	0.074	27 (4.5)	2.08 (1.40;3.08)	<0.001	1894 (2.3)

Adjusted for socioeconomic status, maternal smoking, maternal psychiatric diagnoses, parental age, gestational age and birth weight

children are at risk of inheriting the ADHD traits in which case the disorder is not caused by exposure to maternal overweight/obesity per se. Buss et al. further investigated the association between maternal pre-pregnancy BMI and ADHD symptoms in children in a cohort of 174 children followed from early gestation through childhood and concluded that children's executive functions mediated this association [49].

A number of studies focus on inflammation playing a role in the association between maternal overweight/obesity and ADHD/ASD in children. Leptin is a hormone released in accordance with the amount of adipose tissue and is suggested to have an inflammatory function [50, 51]. Obese pregnant women are known to have higher levels of circulating pro-inflammatory cytokines than their normal weight counterparts, and placental and intrauterine inflammation is associated with altered fetal cytokine expression, fetal neuronal damage, and changes in neonatal brain gene expression [52]. This predisposes the fetus to comorbid psychiatric and systemic pathologies, as ASD and ADHD are associated with increased level of inflammatory cytokines [51, 53–56]. The results of the present study clearly show how overweight, obese, and severely obese mothers have an increased risk of having a child with ADHD, but do not provide an answer to how this association is driven.

We also found that obese mothers had an increased risk of getting a child with ASD. ASD without ADHD symptoms might be relatively rare in population samples [40], and the association between obese mothers and ASD in children might be driven by undetected ADHD in the children with ASD. Furthermore, it is possible that the finding of an increased, but not significant risk of ASD in children of severely obese mothers is due to lack of statistical power. The association between maternal underweight and the risk of ASD in children might be explained by the connection between ASD and eating disorders found by others [57, 58]. We have no information about eating disorders among mothers in the study and cannot examine it further. However, it is also possible that maternal undernutrition itself affects the intrauterine environment and thereby increases the risk of having a child with ASD.

One of the strengths of the present study is the large population-based study cohort. Further, information in the DNBC was collected prospectively before the mothers were aware of their child's condition or development. ADHD and ASD were clinically diagnosed according to the ICD-10 classification system by child psychiatrists and reported to the Danish registers. Most previous studies have used parent- or teacher-reported information on diagnoses.

There are also limitations to address. As mentioned in "Methods", participants in the DNBC were healthier than mothers in the source population [32], but we have no reason to suspect that it affects the observed association

Table 3 Crude and adjusted risk of F90.0[a] + F90.1[b], F98.8[c], and F84.0[d] according to maternal pre-pregnancy BMI

Crude risk	F90.0[a] + F90.1[b]			F98.8[c]			F84.0[d]			Study population
	N (%)	HR (95% CI)	*P* value	*N* (%)	HR (95% CI)	*P* value	*N* (%)	HR (95% CI)	*P* value	*N* (%)
BMI < 18.5	75 (5.1)	1.29 (1.02;1.63)	0.035	10 (3.7)	0.87 (0.46;1.65)	0.671	20 (5.7)	1.33 (0.84;2.10)	0.224	3662 (4.5)
18.5 ≤ BMI < 25	878 (59.3)	Ref. group		172 (63.5)	Ref. group		227 (65.0)	Ref. group		55,305 (67.5)
25 ≤ BMI < 30	348 (23.5)	1.38 (1.22;1.56)	<0.001	60 (22.1)	1.22 (0.91;1.63)	0.194	69 (19.8)	1.05 (0.81;1.38)	0.697	16,064 (19.6)
30 ≤ BMI < 35	117 (7.9)	1.51 (1.25;1.83)	<0.001	20 (7.4)	1.34 (0.84;2.13)	0.220	23 (6.6)	1.15 (0.74;1.79)	0.544	4967 (6.1)
BMI ≥ 35	63 (4.3)	2.16 (1.67;2.79)	<0.001	9 (3.3)	1.59 (0.81;3.10)	0.177	10 (2.9)	1.31 (0.70;2.48)	0.392	1894 (2.3)
Adjusted risk	F90.0[a] + F90.1[b]			F98.8[c]			F84.0[d]			Study population
	N (%)	HR (95% CI)	*P* value	*N* (%)	HR (95% CI)	*P* value	*N* (%)	HR (95% CI)	*P* value	*N* (%)
BMI < 18.5	75 (5.1)	1.09 (0.86;1.39)	0.462	10 (3.7)	0.67 (0.33;1.37)	0.276	20 (5.7)	1.22 (0.77;1.93)	0.398	3662 (4.5)
18.5 ≤ BMI < 25	878 (59.3)	Ref. group		172 (63.5)	Ref. group		227 (65.0)	Ref. group		55,305 (67.5)
25 ≤ BMI < 30	348 (23.5)	1.29 (1.14;1.47)	<0.001	60 (22.1)	1.24 (0.92;1.67)	0.151	69 (19.8)	1.07 (0.81;1.41)	0.634	16,064 (19.6)
30 ≤ BMI < 35	117 (7.9)	1.40 (1.15;1.70)	0.001	20 (7.4)	1.33 (0.83;2.15)	0.237	23 (6.6)	1.19 (0.76;1.88)	0.439	4967 (6.1)
BMI ≥ 35	63 (4.3)	1.86 (1.42;2.42)	<0.001	9 (3.3)	1.63 (0.83;3.20)	0.154	10 (2.9)	1.38 (0.73;2.59)	0.324	1894 (2.3)

Adjusted for socioeconomic status, maternal smoking, maternal psychiatric diagnoses, parental age, gestational age, and birth weight

[a] Disturbance of activity and attention

[b] Hyperkinetic conduct disorder

[c] Other specified behavioral and emotional disorder with onset usually occurring in childhood and adolescence

[d] Childhood autism

between maternal BMI and ADHD or ASD in children. At the end of the follow-up, the youngest children in the cohort were 10 years old and the average age was 13 years. Atladottir et al. have shown that in Denmark, children with both ASD and ADHD can be undiagnosed until adolescence or early adulthood [5]. Thus, some children might not have been diagnosed at follow-up, and it can have minimized some of the differences between the diagnostic groups and the cohort and biased the results. The validity of diagnoses recorded in registers can be discussed. The validity of childhood autism diagnoses in the DNP has been investigated by Lauritsen et al., who found that 94% of the registered cases were true positive [59]. A Danish longitudinal study reported that 73.5% of children registered with an ADHD diagnosis in the Danish registers screened positive for ADHD on the Strengths and Difficulties Questionnaire at age 5–7 years [60], and another study showed an agreement percentage on the ADHD diagnosis in the registries of 83% [61]. Telephone interviews leave us with self-reported data on maternal weight and height before pregnancy, maternal psychiatric disorders, smoking habits, and socio-occupational status and thus risk of bias. Nohr validated the self-reported pre-pregnancy weight by comparing the DNBC information with information obtained in a clinical obstetric database on 5033 women. Results showed that BMI categories agreed in 91.4% of cases [38]. We have no specific information about maternal ADHD, ASD, or other psychiatric disorders. Surén et al. found that paternal obesity was an independent risk factor for ASD in children [28]. We have no information on paternal weight or psychiatric disorders, as well as no information on weight or executive function in the children, which might result in residual confounding. More research is needed to determine the underlying mechanisms in the association between maternal overweight and ADHD and/or ASD in children.

Maternal pre-pregnancy overweight is a risk factor for having a child with ADHD, especially with hyperactive disorder. Maternal obesity as well as maternal underweight is found to be a risk factor for ASD in the offspring, but despite these results we cannot say that maternal BMI is a causal risk factor. Awareness about the association between maternal obesity and ADHD in children can lead to an early assessment of children at risk and enhance the chances of early diagnosis and intervention.

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Compliance with ethical standards

Conflict of interest Per Hove Thomsen has received speaker's honoraria from Shire, Novartis, and HB-Pharma within the last 3 years. He is not a member of any advisory boards nor does he hold any stocks. The other authors have no conflicts of interests to declare.

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