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ADHD symptoms and body composition changes in childhood: a longitudinal study evaluating directionality of associations

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Summary

Background: Attention-deficit/hyperactivity disorder (ADHD) is linked to increased risk of overweight/obesity among children and adults. Studies have also implicated obesity as a risk factor for ADHD. However, no studies have evaluated bidirectional, longitudinal associations between childhood fat mass and ADHD symptom severity.

Objectives: We investigate bidirectional associations between ADHD symptoms and measures of body composition between ages 1.5 and 9. We further examine effects of specific eating patterns linked to ADHD on associations between symptom severity and body composition.

Methods: The study utilized data from children (N = 3903) participating in the Generation R cohort (Netherlands). Children were enrolled at birth and retained regardless of ADHD symptoms over time. Cross-lagged and change models examined bidirectional associations between body composition (body mass index/dual-energy X-ray absorptiometry) and ADHD symptoms at four time points in childhood.

Results: A child with a clinically concerning ADHD symptom z-score two standard deviations above the mean at age 6 would be expected to experience about 0.22 kg greater fat mass gain measured via dual-energy x-ray absorptiometry between ages 6 and 9, even if they displayed healthy eating patterns (95% CI: 0.11 - 0.28, $p < 0.001$). Conversely, fat mass at any age did not predict worse ADHD symptoms later.

Conclusions: Beginning in early childhood, more ADHD symptoms predict higher fat mass at later ages. We did not find evidence of a reverse association. Based on these and prior findings, lifestyle counselling during treatment for children with a diagnosis of ADHD should be considered, even if they are diagnosed in early childhood and do not yet have a body mass index of clinical concern.

Keywords: ADHD symptoms, adiposity, childhood, dietary patterns.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is linked to an increased risk of overweight/obesity in children, adolescents and adults (1,2). However, the majority of studies have been cross-sectional in nature or were conducted after childhood (1). A variety of mechanisms have been proposed for how ADHD may cause obesity, including disordered eating patterns caused by heightened impulsivity (3), neurotransmitter dysregulation (4), unintended effects of psychopharmacology (5,6) and fetal metabolic programming (7). In particular, disordered eating patterns including emotional overeating and impulsive eating have been linked to higher consumption of snack foods and sugar sweetened beverages (SSB), which have in turn been linked to higher adipose tissue (fat mass) in older children and adolescents (8,9). However, it is also important to note that some have hypothesized that a reverse association also exists, by which obesity exacerbates ADHD symptom severity via endocrine changes associated with increased adipose tissue (10).

Potential confounders and mediating factors complicate understanding of this relationship, including biological factors such as maternal adiposity and birthweight, social inequalities and comorbid mental health issues. For example, one study found that the association between ADHD and obesity disappeared when controlling for the diagnosis of oppositional defiant disorder (ODD) (11). Also, because the association between obesity and ADHD strengthens with age (1), elevated risks of overweight/obesity in adolescent/adult populations with ADHD could be due to lifestyle risk factors associated with the underlying health disparities experienced by individuals at higher risk for ADHD diagnosis (12,13). Methodological challenges also exist that may bias associations as well. Body mass index (BMI) – the most commonly used body composition measure – is an imperfect measure of body composition, particularly in children (14). Changes in BMI trajectories are particularly difficult to interpret in childhood/adolescence, when natural changes in growth rates occur and vary significantly (15). For example, given the strong association between low birth weight and ADHD development (16,17), increased BMI trajectory during pre-adolescence among children with ADHD may be due to delayed maturation and associated 'catch-up' in lean body mass during this time period instead of fat tissue gain. But if these increases in BMI trajectory *are* due to fat tissue gains, this is concerning, because small increases in BMI trajectory, particularly in pre-adolescence, can be important predictors of overweight/obesity later in the lifecourse (18).

Because of BMI's limitations, body composition is ideally determined by dual-energy X-ray absorptiometry (DXA) (18); however, this assessment approach is rarely employed longitudinally for large numbers of children due to expense. Further complicating observational studies is the fact that ADHD is usually reported only as a dichotomous diagnosis, which often does not occur until after children are in the later years of primary school (19). As a result, prior studies have not been able to elucidate early relationships between ADHD symptom severity and fat mass.

Given the high prevalence of both ADHD diagnosis (5–7%) (20) and overweight/obesity (12–24%) (21–23) in children worldwide, it is imperative to better understand their interrelationship beginning in early childhood. Thus, this study uses early and long-term longitudinal data on ADHD symptom severity and multiple measures of body composition in children living in the Netherlands to address these gaps in knowledge. We do not focus on ADHD diagnosis as an exposure and clinical obesity as an outcome as previous research has, in large part because these classifications culminate from early childhood developmental trajectories; as a result, they tend not to be diagnosed until later childhood, adolescence or even adulthood. Instead, our aim is to elucidate bidirectional relationships during the evolution of early life ADHD symptoms and body composition changes that may heighten risk of overweight and obesity in later life.

First, to better understand how relationships between ADHD symptom severity and body composition evolve in early childhood (Aim 1), we examine bidirectional associations between measures of body composition and ADHD symptoms at four time points in childhood (18 months, 3 years, 6 years, 9 years). We then model ADHD symptoms in early childhood as a predictor of changes in total fat mass and lean mass measured via DXA scan at 6 and 9 years old (Aim 2), controlling for emotional eating score and SSB intake at 4 years of age. Finally, we reverse the analysis to examine how body composition at 6 years old is associated with subsequent changes in ADHD symptom severity (Aim 3).

Methods

Design

This study uses data from Generation R, an ongoing population-based birth cohort which recently completed follow-up with children at 9 years old. Study design and retention rates have been extensively written about elsewhere (24). Pregnant women who resided in Rotterdam, Netherlands and had an expected delivery date between April 2002 and January 2006 were invited to participate (participation rate: 61%). Information was obtained during clinical visits and via self-report questionnaires. Informed consent was obtained from all participants. The study was reviewed and approved by the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam.

Participants

In mid-childhood, 8548 children who were all progeny from the original pregnant enrollees were invited to participate with their parents, of whom 5862 children participated in the visit at the research center when they were 9 years old. Of those, 5096 had DXA scans at 6 and 9 years old. We excluded children without ADHD assessed at 6 or 9 years (n = 1058), and those taking medication to treat ADHD at 9 years old (n = 135) because such medications may be associated with short-term changes in BMI (25). The final study population was composed of N = 3903.

Participant demographics are shown in Table 1. A comparison of included (n = 3903) and excluded children due to missing outcomes (n = 1765) indicated that data were more often missing for children of families with incomes less than €1200 per month and those of non-Western ethnicity (both $P < 0.001$). Mothers of excluded children also had a higher BMI at intake ($P < 0.001$). However, early-life ADHD symptom severity and BMI were not different between the two groups.

Measures

ADHD

The Child Behavior Checklist 1½–5 (CBCL/1½–5) was used to obtain a standardized rating of the child's problem behavior by parents at 18 months, 3 years and 6 years, while the CBCL/6–18 was completed by parents when children were 9 years. The CBCL/1½–5 contains 99 problem items, and the CBCL/6–18 contains 118 problem items. Both questionnaires include multiple DSM-oriented scales, including the DSM-oriented ADHD scale (7 items). Parents were asked to rate emotions and behaviours of their child based on the preceding 2 months on a 3-point scale: 0 = not true, 1 = somewhat or sometimes true and 2 = very true or often true. Reliability and validity of the Dutch translation have been demonstrated, and syndrome scales derived from CBCL had a good fit in studies across diverse societies (26).

BMI

Children had BMI measured at ages 18 months and 3 years during routine clinical visits, and at 6 and 9 years at the study research centre. At each visit, children's height and weight were measured using standardized procedures and devices. Height was measured utilizing a Harpenden stadiometer (Holtain Limited) in standing position. Weight was obtained with children wearing lightweight clothes and without shoes using a mechanical scale (SECA). Both scales and stadiometers were calibrated on a regular basis. BMI was calculated as weight (kg)/height $(m)^2$. Standard deviation scores (z-scores) adjusted for

Table 1 Characteristics of the study population (n = 3903)

Child characteristics	*N*	Values
Sex (% Male)	1900	48.7
BMI z-score at 6 years	3903	0.2 ± 0.9
BMI z-score at 9 years	3903	0.2 ± 1.0
ADHD DSM-oriented scale score at 6 years	3903	2.9 ± 2.4
ADHD DSM-oriented scale score at 9 years	3903	2.5 ± 2.6
Maternal characteristics		
Income[a](%)		
Less than €1200/mo	313	9.9
€1200–2000/mo	508	16.0
More than €2000/mo	2353	74.1
BMI[a] in kg/m^2	3465	24.4 ± 4.1
Ethnicity (%)		
Dutch	2590	66.4
Other Western	341	8.7
Non-Western	972	24.9
Marital status (has partner)[a](%)	3389	87.9
Smoking[a] (%)		
Never smoked	2702	78.1
Smoked till pregnancy	312	9.0
Continued during pregnancy	445	12.9
Parity (first child) (%)	2288	60.6
		394
Breastfeeding (yes)[a] (%)	3053	92.4

[a]Some data were missing for income (n = 729), maternal BMI (n = 438), marital status (n = 48), smoking (n = 444), parity (n = 124) and breastfeeding (n = 599). Means presented are unimputed; imputed means were similar for all variables.

age and gender were calculated based on Dutch reference growth curves using the Growth Analyser program (Growth Analyser 3.0, Dutch Growth Research Foundation, Rotterdam, The Netherlands.) (27).

Body composition

DXA scans (iDXA; General Electric, Madison, WI) were used to obtain percent fat and lean mass of the children at both 6 and 9 years. Children were scanned while lying down and positioned according to standard protocols, with feet together in a neutral position and hands flat by their sides (28). All DXA scans were performed by trained and certified staff using the same device and software (enCORE2010). The DXA scans provided measures of bone and soft tissue for the total body, including bone mineral content (g), fat mass (g) and lean mass (g). Percent fat and lean mass were calculated as 100% × [total body fat or lean mass(g)total body mass (fat mass + lean mass + bone mass of total body)(g)].

Covariates

Several potential confounders were identified in prior literature and theoretical causal models (1,7,10,15,16,29); maternal/family level factors were measured via questionnaire and included income (9), race/ethnicity (6), mother's BMI at intake (6), marital status (9), mother's global psychopathology symptoms (13) (assessed with the Brief Symptom Inventory) (30), parity, breastfeeding, and smoking status during pregnancy (12). Child level variables included sex (7), birthweight (12), gestational age (12) and baseline BMI or ADHD scale score. More detailed information on data collection procedures in the Generation R study is reported elsewhere (24). For standard regression models (Aims 2 and 3), baseline BMI is considered 6 years old. Due to a previous study's finding that the association between ADHD diagnosis and obesity/overweight may be attributable to comorbid ODD (11), we also conducted exploratory models controlling for both ODD symptoms at 5 and 9 years of age, as well as ODD diagnosis by 9 years of age.

Finally, two dietary pattern variables were included as potential explanatory variables in extended models. These were reported at 4 years old (by parents). The first was SSB intake, which – as a single dietary factor – has been strongly linked to fat mass gain in children (31). The second was emotional overeating score, which may increase concurrently with ADHD symptoms of impulsiveness and disinhibition (3).

Statistical analyses

Analyses used standardized z-scores for the DSM-oriented ADHD scale score, BMI, total fat mass and total lean mass. For Aim 1, we used two cross-lagged structural equation models to examine bidirectional associations between early childhood ADHD symptoms, BMI and DXA measures of total fat and lean tissue mass. The first model utilizes four waves of BMI and CBCL DSM-oriented ADHD scale measurements at 18 months, 3 years, 6 years and 9 years old, controlling for potential confounders. The second model decomposes these associations by examining the two waves of fat and lean mass DXA measurements at 6 and 9 years old and their cross-sectional and bidirectional associations with ADHD symptom score at 6 and 9 years old. The models followed established guidelines for error covariance, and model fit was tested using comparative fit index (CFI) and root mean squared error of approximation (RMSEA) following the use of Full Information Maximum Likelihood method to impute missing values (32).

For Aim 2, ADHD score at 6 years old was utilized in separate linear regressions to predict changes in fat and lean mass between 6 and 9 years old. To achieve Aim 3, total fat mass and total lean mass at age 6 years were used in separate models as independent predictors of ADHD symptom severity change scores (score at 9 years minus score at 6 years). For each of the regressions for Aim 2 and Aim 3, two models are presented; the first is adjusted for potential confounders (see table footnotes for all variables included), and the second is additionally adjusted for eating and dietary patterns which might explain any observed associations. Multiple imputation using chained equations was used to account for missing values in covariates. Imputations were based on available information on all variables included in the study, as well as additional baseline demographic variables and CBCL total scores at each wave. Twenty imputations were used based on the available fraction of missing information. Analyses were performed using STATA version 14.

Results

The demographic characteristics of the children and families are shown in Table 1, including descriptors of important potential confounders. The majority were Dutch (66.4%), two-parent households (87.9%) with more than €2000 per month income (74.1%). The majority of participating children were first-borns (60.6%), and average maternal pre-pregnancy BMI was 24.5 ± 4.1 kg/m^2. Please see supplemental materials for a comparison of unadjusted BMI, fat mass and lean mass from 1.5 to 9 years of age among children with and without ADHD diagnoses at age 9.

Aim 1: Bidirectional associations between ADHD symptoms and body composition

Results for Aim 1 are shown in Fig. 1. In the first (BMI-ADHD) model, higher BMI z-score at 18 months old significantly predicted lower ADHD symptom z-score at 3 years, even after controlling for birthweight ($\beta = -0.03$, $p < 0.05$). By 3 years old, BMI z-score was not predictive of ADHD symptom z-score at 6 years old ($\beta = 0.01$, $p > 0.05$). However, by 6 years old, higher BMI z-score once again significantly predicted lower ADHD symptom z-score at 9 years old ($\beta = -0.04$, $p < 0.01$).

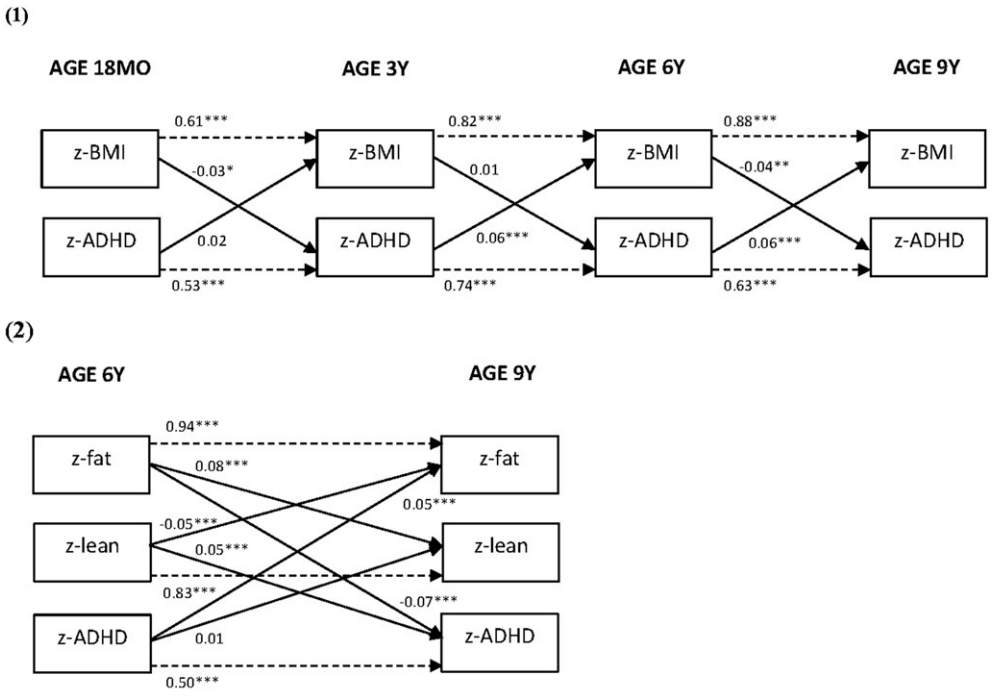
Conversely, ADHD symptom score at 18 months old did not significantly predict BMI z-score at 3 years old ($\beta = 0.02$, $p > 0.05$), but by 3 years, higher ADHD symptoms scores predicted higher BMI z-score at 6 years of age ($\beta = 0.06$, $p < 0.001$). More severe ADHD symptom scores at 6 years old continued to predict significantly higher BMI at 9 years old ($\beta = 0.06$, $p < 0.001$).

In the second model (DXA-ADHD), more severe ADHD symptoms at 6 years old are not predictive of greater lean mass at 9 years old ($\beta = 0.0$, $p > 0.05$), but do predict greater fat mass at 9 years old ($\beta = 0.05$, $p < 0.001$). Meanwhile, greater lean mass at 6 years old predicts higher ADHD symptom severity at 9 years old ($\beta = 0.05$, $p < 0.001$), while greater fat mass at 6 years old actually predicts lower ADHD symptom severity at 9 years old ($\beta = -0.07$, $p < 0.001$).

Goodness-of-fit indexes from exogenous modelling indicated a good model fit for both models (BMI model CFI = 0.997, RMSEA = 0.026; DXA model CFI = 1.0, RMSEA<0.01).

Aim 2: Early childhood ADHD symptoms predicting later body composition change

Results from linear regression models addressing Aim 2 are shown in Table 2. Consistent with the bidirectional model, in the confounder adjusted model



[1]Adjusted for baseline family income, race/ethnicity, maternal BMI, marital status, psychopathology symptoms, parity, breastfeeding, and smoking status, child sex, birthweight, and gestational age. Goodness-of-fit indexes from exogenous modeling indicate a good model fit (BMI Model: CFI=0.997, RMSEA=0.026), (DXA Model: CFI=1.0, RMSEA=0.0).
*P<0.05; **P<0.01; ***P<0.001.

Figure 1 Cross-lagged models of (1) associations between BMI and ADHD DSM score, and (2) DXA body composition measures and ADHD DSM score (all standardized z-scores, $n = 3903$). Values represent β's derived from structural equation modelling (linear regression analyses) (1).

Table 2 Results of linear regression analyses between DSM-oriented ADHD score and body composition at 6 and 9 years of age

Exposure	Outcome	
ADHD score 6 years[a]	Change in fat mass 6–9 years[a]	Change in lean mass 6–9 years[a]
	β (95% confidence interval)	
Model 1: Confounder adjusted[b]	0.04 (0.02, 0.05)***	0.01 (−0.01, 0.03)
Model 2: Dietary Pattern adjusted[c]	0.04 (0.02, 0.05)***	0.01 (−0.01, 0.03)
	Change in ADHD score 6–9 years[a]	
Fat mass 6 years[a]	*β, 95% confidence interval*	
Model 1: Confounder adjusted[b]	−0.02 (−0.06, 0.02)	
Model 2: Dietary pattern adjusted[c]	−0.02 (−0.06, 0.02)	
Lean mass 6 years[a]		
Model 1: Confounder adjusted[b]	0.00 (−0.03, 0.04)	
Model 2: Dietary pattern adjusted[c]	0.00 (−0.03, 0.04)	

[a]All standardized z-scores.
[b]Adjusted for baseline family income, race/ethnicity, maternal BMI, marital status, psychopathology symptoms, parity, breastfeeding, and smoking status, child sex, birthweight, gestational age and baseline BMI.
[c]Adjusted for sugar sweetened beverage consumption and emotional overeating sub-score in addition to variables included in Model 2.
*$P < 0.05$,
**$P < 0.01$,
***$P < 0.001$.

(model 2), each standard deviation higher ADHD symptom score at age 6 was associated with a 0.04 standard deviation greater fat mass change from 6 to 9 years old ($p < 0.001$). Neither ODD symptom score nor ODD diagnosis by age 9 attenuated the association between ADHD symptom score and later body composition change. Additionally, adjusting for potential explanatory dietary patterns (model 3) also did not attenuate that relationship. Also consistent with bidirectional model results, ADHD score at 6 years old did not predict lean mass change in either of the adjusted models.

Aim 3: Early childhood body composition predicting later ADHD symptom changes

Results for Aim 3 are shown in Table 2. In contrast with the cross-lagged models in Aim 1, neither fat nor lean mass at 6 years old predicted change in ADHD symptom between 6 to 9 years old.

Discussion

This study used longitudinal data on ADHD symptom severity in medication naïve children living in the Netherlands, in order to investigate associations with changes in three measures of body composition from 18 months to 9 years old. Excluding children who may be using stimulants eliminates potential confounding of the association between ADHD symptoms and body composition changes, while the use of DXA scanning allows the differentiation of associations between ADHD symptoms and lean versus fat mass changes over time.

Our research finds that by 3 years old ADHD symptom severity begins to predict higher fat mass at later ages. This relationship was not explained by comorbid ODD, in contrast to one study's previous findings (11). Even after adjusting for potential confounders and earlier dietary behaviours, more severe ADHD symptoms by age 6 predicted an increased gain in fat mass between 6 and 9; a child with a clinically concerning ADHD symptom z-score of two standard deviations above the mean would be expected to experience an approximately 0.08 greater fat mass gain z-score (0.22 kg or 0.48 lb) during this time period, even if they displayed healthy eating patterns. While this reflects a relatively small effect size for overall fat mass gain, its occurrence during a critical body composition programming period makes it of clinical concern (33). Although research into ADHD and early life endocrine function is scarce, this finding could potentially be due to underlying associations between ADHD symptoms and endocrine dysregulation, such as underproduction of adiponectin (34). However, it could also still be explained by eating patterns, such as impulsive and emotional overeating, that were not well captured by our measures.

Adipose tissue acts as an endocrine organ (35,36). Pro-inflammatory effects could conceivably extend to neurological changes, including alterations in neurotransmitter secretion (36). This has led some researchers to hypothesize that increased fat mass in childhood could cause the exacerbation of ADHD

symptoms and may worsen risk of diagnosis into adulthood (10). While our results cannot be causally interpreted, clearly they do not appear to support this hypothesis. However, it is important to note that given the youth of our population, effects of excess fat mass on ADHD symptoms may yet emerge in adolescence and adulthood. Also, as the cohort ages, children will continue to be screened for ADHD and eventually significant numbers will be formally diagnosed with the disorder; these diagnoses will be captured in future rounds of planned data collection. Therefore, future research should examine fat mass and lifestyle differences specifically among those diagnosed.

Cross-lagged modelling showed that lower BMI z-scores at 18 months old predicted higher ADHD symptom severity at 3 years old, even after controlling for birthweight. This is in keeping with residual early-life growth delays found among children with ADHD in previous studies (16,37). However, by age 3, BMI z-score no longer predicts later ADHD symptoms at 6 years old. This indicates that, while low birthweights and early growth delays may be associated with ADHD risk, children with higher ADHD symptoms 'catch up' in their BMI between 18 months and 6 years old. Although this study did not obtain DXA measurements until 6 years old, this growth 'catch-up' seems to be occurring in lean mass (bone and muscle) rather than adipose tissue, because by 6 years old, greater lean mass becomes predictive of more severe ADHD symptoms, while greater amounts of fat at 6 years old predict the occurrence of fewer ADHD symptoms at a later age.

Cross-lagged models depict associations between measures controlling for all previous waves of measurement. Because ADHD symptom severity is relatively stable for most children in this age range, while BMI is increasing, it is helpful to look at unidirectional predictors of change in order to clarify specific explanatory mechanisms. And in fact, linear regression models using body composition to predict changes in ADHD symptom severity found that neither fat nor lean tissue mass predicted any change in ADHD symptoms between 6 and 9 years old. Thus, fat mass does not appear to have a protective *or* a harmful effect on ADHD risk. This was the case even after accounting for early life dietary patterns which might moderate later associations between body composition and ADHD symptoms.

While utilizing a large population-based cohort, our sample is not representative of the general population, having a greater proportion of ethnic minorities and higher median income. Thus, generalizability may be limited. Also, due to the large sample size and relatively small effect size, we cannot dismiss the possibility that the observed association is spurious. However, it is consistent with prior studies that have found an association between ADHD diagnosis and risk of obesity and overweight that strengthens with age (1). Future studies could utilize spline function analysis to better elucidate the relationship between ADHD symptom severity and fat mass across the life course, particularly as more longitudinal data become available (38).

An important limitation of our cross-lagged modelling approach is the lack of lifestyle measures captured between 6 and 9 years old. Thus, our model does not assess potential mediation by dietary intake patterns or physical activity levels. ADHD symptoms were not clinically assessed but measured via parental report on the CBCL. Also, no DXA measurements were taken prior to 6 years old, so bidirectional relationships at early ages are subject to the limitations associated with BMI discussed in the introduction.

Although multiple imputation was used to account for missing data, observations with missing outcomes were deleted following best practice guidelines (39). This approach subjects the study to limitations imposed by selective follow-up. However, early-life ADHD symptom severity and BMI were not different between those with and without outcome measurements, making it unlikely that point estimates of associations would be significantly affected.

This study indicates that an important area for future research is exploring relationships between ADHD symptoms, dietary intake, feeding and eating patterns, and physical activity levels in early childhood. Future research could also focus on exploring potential associations between ADHD symptoms and endocrine dysregulation.

Taken in context of previous research that has consistently found higher risk of obesity and overweight among individuals diagnosed with ADHD, our results support the clinical practice of lifestyle counselling during treatment for children with a diagnosis of ADHD, even if they are diagnosed in early childhood and do not yet have a BMI of clinical concern. Given heightened risk of overweight/obesity, community organizations and schools should also consider the needs of children with behavioural health diagnoses such as ADHD when developing physical activity and nutrition programming, in order to expand accessibility/engagement among these populations.

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Dr Bowling conceived the original research questions, conducted the primary analyses and drafted the manuscript. Dr Jansen refined the specific aims and study design, oversaw the development of the analytical plan and conducted extensive editing of the manuscript. Dr Tiemeier is a Principal Investigator of the Generation R study, oversees data collection and provided significant input into the specific aims, analytical design, and provided feedback on the manuscript. Dr Jaddoe is a Principal Investigator of the Generation R study, oversees data collection and provided expertise on BMI trajectory and adiposity measures. Dr Barker provided expertise regarding psychiatric measures and extensive feedback during manuscript development.

Conflict of interest statement

No conflict of interest was declared.

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Supporting information

Additional Supporting Information may be found online in the supporting information tab for this article.

Supplemental Table A. Comparison of unadjusted BMI, fat mass and lean mass from 1.5 to 9 years of age among children with and without ADHD diagnoses at age 9.