**Longitudinal Associations Between Symptoms of ADHD and BMI from Late Childhood to Early Adulthood**

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**Short Title:** ADHD and BMI during adolescence

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**Abbreviation:** ADHD: Attention Deficit Hyperactivity Disorder; BMI: Body Mass Index; CFI: Comparative Fit Index; FIML: Full information maximum likelihood method; RI-CLPM: Random Intercept Cross-lagged Panel Model; RMSEA: Root Mean Square Error of Approximation; SD: Standard deviation; SES: Socioeconomic Status; SRMR: Standardized Root Mean Squared Residual; TFI: Tucker–Lewis Fit Index; TRAILS: Tracking Adolescents Lives Survey

**Article Summary**

The study examined the longitudinal relationships between ADHD symptoms and BMI from late childhood to early adulthood spanning five measurement waves and over 10 years.

**What’s Known on This Subject**

Children and adults with ADHD have a higher prevalence of obesity compared to those without ADHD. Mechanisms that explain the development of the co-occurrence of ADHD and obesity are unclear.

**What This Study Adds**

This prospective cohort study followed adolescents five times in over 10 years and found no direct effects such that ADHD symptoms increased BMI or vice versa. In this developmental period, the association between hyperactive/impulsive symptoms and BMI is stable.

**Contributors’ Statement**

Bezawit E. Kase, Nanda Rommelseand Catharina A. Hartman conceptualized and designed the study, acquired, and analyzed the data, and drafted the initial manuscript, and reviewed and revised the manuscript. Qi Chen, Lin Li, Anneli Andersson, Ebba Du Rietz, Melissa Vos, Samuele Cortese, and Henrik Larsson conceptualized and designed the study, provided expertise and oversight throughout the process and critically reviewed the draft of the manuscript. All the authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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**Abstract**

**Background and Objectives:** Attention-Deficit/Hyperactivity Disorder (ADHD) and obesity are two frequent conditions that co-occur, which has implications for the management of both conditions. We hypothesized that ADHD symptoms predict body mass index (BMI) and vice versa from late childhood (10-12 years) up to early adulthood (20-22 years).

**Method:** Participants were adolescents in the Netherlands (n=2773, 52.5% males, mean age=11 years at baseline, five waves up to mean age 22) from the Tracking Adolescents’ Individual Lives Survey cohort. We examined bi-directional relationship between ADHD symptoms (hyperactivity/impulsivity and inattention) and BMI using the Random Intercept Cross-lagged Panel model. Time varying covariates were pubertal status, stimulant use, depressive symptoms and family functioning and SES was a time invariant covariate.

**Results:** We found a time invariant association of BMI with hyperactivity/impulsivity, but not with inattention, which was slightly stronger in females (females: r=0.102; males: r=0.086, p < 0.05). No longitudinal direct effects were found between ADHD symptoms and BMI during this period.

**Conclusions:** Over the course of adolescence, the link between ADHD and BMI is stable and is predominantly with hyperactive/impulsive symptoms rather than inattention. There was no direct effect of ADHD symptoms on BMI increase nor of BMI on enhanced ADHD symptoms during this developmental period. The findings point to a shared genetic or familial background and/or potential causal effects established already earlier in childhood, thus suggesting that intervention/prevention programs targeting overweight/obesity in children with ADHD should be implemented in early childhood.

**Keywords:** ADHD; BMI, Obesity; Adolescence

**Introduction**

Attention-deficit/hyperactivity disorder (ADHD) is defined by developmentally inappropriate and impairing levels of inattention and/or hyperactivity/impulsivity.1 ADHD affects about 5-7% of school age children and 2.5% of adults, and is associated with considerable personal, financial, and societal burden.2 Among other comorbidities, meta-analytic evidence shows that ADHD is significantly associated with overweight/obesity, with the pooled prevalence of obesity being increased by nearly 40% in children with ADHD relative to those without ADHD.3 The co-occurrence of ADHD with overweight/obesity may have long-term negative health consequences. In addition to the double burden of these illnesses, the co-occurrence negatively influences treatment outcome.4 For instance, it was shown that the symptoms of ADHD can be barrier to successful weight loss during treatment intervention for individuals with obesity.4

Whilst the cross-sectional association between ADHD and overweight/obesity is well supported by meta-analytic evidence, the presence of a causal link and the direction of causality, if present, need further clarification. A number of mechanisms may explain the co-occurrence between these two conditions. First, the association between ADHD and overweight/obesity may be genetically driven. Indeed, the most recent genome-wide association study (GWAS) has shown shared genetic liability of ADHD with Body Mass Index (BMI), and childhood obesity, with estimates of genetic correlations of 0.26 and 0.22, respectively.5 However, genetic correlations can be found in the absence of causal relations. A study that examined biological mechanisms underlying the observed genetic association indicated that dopaminergic neurotransmission system partially explained this genetic overlap between ADHD and BMI.6 Different findings were reported in Mendelian Randomization studies (MR; i.e., robust genetic associations are used as instrumental variable for causal inference): both bidirectional causal relationships of ADHD with BMI6–8 and of higher BMI increasing the risk of ADHD but not vice versa.9 Longitudinal studies conducted during early childhood indicated that ADHD symptoms predicted higher fat mass gain later on but not the other way around (investigated in children between ages 1.5 and 9).10 Another longitudinal study between ages 8 and 16 showed consistent longitudinal associations from ADHD symptoms to BMI, although this study did not adjust for the presence of stable associations between these variables during this developmental period.8 Regardless, found longitudinal associations disappeared in twin difference analyses8, indicating they were due to environmental and genetic confounding, as indicated by other studies.12,13 It is also important to mention the use of stimulants when studying the association ADHD and BMI. Stimulants are the first-choice drugs in the pharmacological treatment of ADHD. Stimulant use is associated with lower BMI,14,15 by influencing reward processing, motivation, and executive functioning, as well as suppressing appetite.16 The effect of stimulants on weight reduction may, however, be temporary. A longitudinal study showed that children with ADHD and treated with stimulants are more likely to have slower early BMI growth in childhood but later faster growth in adolescence compared to children with no history of ADHD and stimulant use14,15 This illustrates that stimulant use is a potential confounder, although often not adjusted for in previous work (e.g., MR findings from GWASs, but also behavioral studies). In all, these incomplete and, at times conflicting, findings illustrate the need for further study, including comprehensive assessment in longitudinal designs and rigorous statistical methods examining the interrelated development of ADHD and overweight/obesity over time. Such rigor in longitudinal analysis is necessary, as associations can arise because of potential reverse causation and residual confounding. Evidence from such studies is crucial to implement management and preventive strategies for individuals who present with the double burden of ADHD and obesity.

The current study investigated if ADHD symptoms predict BMI and/or vice versa from late childhood up to early adulthood. In addition, the effects of medication status (use of psychostimulants), pubertal status, changes in depressive symptoms and quality of family functioning during adolescence and early adulthood were examined as time varying confounders. Given that these variables are associated with both ADHD and BMI, changes in these variables may confound the estimates of potential longitudinal effects of ADHD and BMI if not adjusted for. Socioeconomic status was a time-invariant covariate. Furthermore, as little is known about potential sex differences in the longitudinal associations between ADHD and BMI, the role of sex was additionally explored. The literature is consistent in showing a lower prevalence of normal weight in adults compared to children aged 12 or younger with ADHD,3,17,18 although adolescence has hardly been studied so far.18 Based on this difference we expected a potential build-up of weight through bidirectional relationships between ADHD symptoms and BMI such that ADHD symptoms predict BMI and vice versa from late childhood up to early adulthood.

**Methods**

**Participants**

Participants were drawn from the Tracking Adolescents’ Individual Lives Survey (TRAILS), a prospective cohort study of Dutch adolescents consisting of a population cohort (n=2230) and a clinical cohort (n=543) of adolescents (52.5% males) with follow-up assessments done biannually or triennially for the past 19 years.19 The clinical cohort was set up to complement the population sample to increase the variance in problem behaviors by oversampling children at high risk of psychopathology, based on them being in contact with outpatient services before age 11. We used five measurement waves from TRAILS. The average age of participants in the sample was 11.1 (SD =0.54) years at baseline and 22.2 (SD =0.68) years at time (wave) 5 (see Table 1). Each study wave was approved by the Dutch Central Committee on Research Involving Human Subjects (CCMO) and conducted according to the principles of the Declaration of Helsinki. Informed consent was obtained from parents and adolescents.

**Measures**

ADHD symptoms and depressive symptoms were assessed using the Achenbach System of Empirically Based Assessment tools.20 We used the average of parent and self-report.21 BMI was computed based on objectively measured height and weight. Family functioning was measured by the general functioning scale of the Family Assessment Device, completed by parents.22 Extensive description of these measurement instruments, as well as of the measurement of socioeconomic status (SES), pubertal status, medication use, and imputation procedure for missing data is available in Supplementary material 1.

**Statistical analyses**

Intra-class correlations were computed for item mean scores of ADHD symptom domains, depressive symptoms, family functioning scores and BMI, as measures of the within-person variability over time and the between-person variation.

The longitudinal relationships between the ADHD symptom domains and BMI were examined by using the Random Intercept Cross-Lagged Panel Model (RI-CLPM) in a multigroup analyses of male and female participants. The RI-CLPM is an extension of the traditional cross-lagged panel model in which a random intercept is included in the model. The inclusion of a random intercept allows for parsing the variance of a repeatedly measured variable into a part that is stable across the measurement waves and a changing part.23 Traditional cross-lagged models and other panel data analysis techniques fail to adequately account for trait-like stability of constructs as captured by the autoregressive relationships. As a result, the cross-lagged parameters do not represent the actual within-person relationships over time and this may lead to a biased conclusion on longitudinal relationships.23 Thus, the dissection of stable from variable variance over time in RI-CLPM is an important improvement relative to the traditional cross-lagged model. The core of the RI-CLPM model was comprised of the relations among the study variables of interest, i.e., hyperactivity/impulsivity, attention problems, and BMI, at waves one, two, three, four and five. The estimated model parameters were the cross-lagged effects showing how ADHD symptoms predicts BMI, and vice versa, over time, as well as the autoregressive effects and correlated changes between the two ADHD symptom domains and BMI at the within-person level. In addition, the stable associations between these variables of interest were estimated. In the same way, time varying depressive symptoms and family functioning for the five measurement waves were incorporated in the model. In addition, baseline SES and concurrent time varying pubertal stage and concurrent psychostimulant use were co-modelled as possible confounders. Equality constraints between males and females on groups of parameters in the model (i.e., stepwise, in blocks: effects of confounders, stable correlations among variables, residual correlations, cross-lagged paths and autoregressive paths) were used to evaluate the equivalence of the estimates across the sexes.

Mplus version eight was used with Full Information Maximum Likelihood (FIML) estimation. Model fit was determined based on the Comparative Fit Index (CFI), the Tucker–Lewis Fit Index (TLI), the Root Mean Square Error of Approximation (RMSEA) and the Standardized Root Mean Squared Residual (SRMR) with good fit indicated by values CFI>0.95, TLI>0.05, RMSEA<0.08 and SRMR<0.05.24 Chi-square difference tests using the Satorra-Bentler scaling correction were used to evaluate potential model fit deterioration of increasingly stringent nested models due to increasing equality constraints on the estimated parameters for males and females (see Supplemental information 2 for additional information).

**Results**

**Descriptive findings**

Descriptive statistics of the variables included in our model across all waves are shown in Table 1. Both hyperactivity/impulsivity and attention problems showed a decline across development. The percentage overweight increased from 15.2% at measurement wave one, age 11, to 30.2% at measurement wave five, age 22. Figure 1 confirms that stimulant use may be an important confounder and needs to be adjusted for when studying the reciprocal effects of BMI and ADHD symptoms over time: on average, stimulant users have consistently lower BMI than non-users and discontinuation of such treatment is associated with increased BMI. Based on the intra-class correlation, 62% of the variance in the five measures of hyperactivity/impulsivity score was explained by stable differences between persons across the five measurement times and the remainder 38% by within-person variation at different measurement times. Likewise, 59% of the variance in attention problems and 47% of the variance in BMI across the measurement waves were explained by differences between persons, while the remainder of each by within-person variation. This shows that there is substantial within person change in this developmental period which is studied by fitting RI-CLPMs to the data.

**Main findings**

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The RI-CLPM with freely estimated parameters achieved a good fit [χ2 (540) = 950.37, CFI = 0.98, TLI = 0.97, RSMEA = 0.023 and SRMR = 0.02] (see Supplementary material 2). Next, potential similarities between males and females in the RI-CLPM were examined in nested multi-group analyses by testing the invariance of groups of parameter estimates across sex. The model was built up by adding equality constraints between estimates for males and females in a stepwise manner and evaluating model fit deterioration using the Chi-square difference test (detailed procedures and model fits of this multistep procedure can be found in Supplementary material 2). The fit statistics for the final constrained model were χ2 (665) = 1082.31, CFI = 0.99, TLI = 0.98, RSMEA = 0.021, and SRMR = 0.03. This final model indicated that males and females did not differ in the cross-lagged paths of either main variables (hyperactivity/impulsivity, attention problems and BMI), other variables (depression, family functioning) and effects of potential confounders (pubertal stage, psychostimulant use and SES), but they differed in the stable correlations, residual correlations and autoregressive paths (see Figure 2 for part of the final estimated model focused on hyperactivity/impulsivity, attention problems and BMI; see Supplementary material 3 for the full estimated model including family functioning and depressive symptoms; see Supplementary material 4 for associations between psychostimulant use and BMI and ADHD symptoms).

As indicated by the estimated correlations between hyperactivity/impulsivity and BMI of our final model, Figure 2 shows that, for both sexes, hyperactive/impulsive symptoms and BMI have a stable modest association between age 11 and age 22 (females: r=0.102; males: r=0.086). Such stable association was not found between attention problems and BMI (females: r=0.065; males: r= 0.015). Importantly, Figure 2 also shows that there are virtually no cross-lagged paths from either hyperactive/impulsive and attention problems to BMI or from BMI to hyperactive/impulsive and attention problems, indicating the absence of potentially causal effects (β-coefficients range between -0.03 and 0.08). One exception was a longitudinal effect in both males and females between hyperactive/impulsive symptoms at age 16 and BMI at age 19 (β=0.06 in both males and females, p = 0.026 (males) and 0.029 (females)). This cross-lagged effect was studied further in post-hoc analyses, making the distinction between no use of stimulants, discontinued use of stimulants and continued use of stimulants (see Figure 1). In doing so we checked if found cross-lagged effect of hyperactivity/impulsivity could have been confounded by a rebound effect from individuals who discontinued stimulant use. Following this, the cross-lagged increase in BMI at age 19 by hyperactivity at age 16 became non-significant. This also happened when we removed all individuals who discontinued medication from the sample. We checked, finally, if the absence of longitudinal effects was explained by family functioning or depression by removing both variables at all timepoints from the RI-CLPM and refitting it. This was not the case, leaving the finding that there are no direct links between ADHD and BMI in this developmental period unaltered.

**Discussion**

The current study examined the longitudinal effects between ADHD symptoms and BMI from pre-adolescence to young adulthood, as separate from the stable associations between these variables in this period. Except for a weak positive cross-lagged effect from hyperactive/impulsive symptoms at age 16 to BMI at age 19 found in both males and females, there was no evidence of reciprocal effects between ADHD symptoms and BMI over time. Our data further indicated a modest and stable positive association between the hyperactive/impulsive domain of ADHD and BMI. We conclude that over the course of adolescence the link between ADHD and BMI is highly stable and is predominantly with hyperactive/impulsive symptoms rather than attention problems. Neither depressive symptoms nor poor family functioning explained the absence of effects between ADHD and BMI over time. The findings thus point to a shared genetic or familial background and/or causal effects established already earlier in childhood.

The association between ADHD and BMI, overweight or obesity has rarely been studied in adolescence18 and longitudinal studies are even rarer. The current study was the first longitudinal study that modelled stable relationship as separate from direct effects over time from late childhood through adolescence to young adulthood. Another study that bears resemblance to our cross-lagged approach and which, so far, is the only study that separated stable from direct effects over time focused on childhood. It found that ADHD symptoms at age 3 and 6 predicted fat mass and BMI at age 9.10 This may potentially indicate that the longitudinal effect of ADHD on BMI may be established early in childhood which later presents as a stable correlation during the adolescent period as shown by the current findings. Of note, neither that nor our study showed evidence of a reverse effect, i.e., high BMI leading to more hyperactivity/impulsivity or attention problems.

The absence of a reverse effect contrasts with recent findings from MR analysis, a technique using genetics as an instrumental variable for causal inference. Building on the most recent GWAS of ADHD, the first published MR study suggested stronger evidence for an effect of high BMI on ADHD liability than for an effect in the opposite direction.9 More recently published MR and polygenic score analyses reported bidirectional causal effect between ADHD and BMI9 and between ADHD and childhood obesity, but not BMI (GWAS on adult sample).7,8 Thus, based on the combined evidence from genetic and longitudinal studies, the direction of causality between ADHD symptoms and BMI is still unclear although findings do point to an important role of genetics in the co-occurrence of ADHD and high BMI,6–9,25 with current evidence pointing to childhood rather than adolescence as a key developmental period in which the association between ADHD and high BMI is established.7,10 Note, however, that MR studies are still subject to environmental confounding.13,26

Reviews and meta-analyses of cross-sectional data have firmly established that the co-occurrence rates of ADHD and obesity are higher in adulthood than in early life.3,17,18 Our study was set up to identify direct effects between ADHD symptoms and BMI in between childhood and adulthood, but they were absent so we could not bridge this gap. ADHD symptoms during adulthood are associated with poor occupational outcomes, being arrested, sedentary behavior, poor diet, financial struggle and divorce,27–30 all of which are associated with an unhealthy life style and consequently overweight/obesity. Thus, it might be speculated that the stronger association between ADHD and BMI in adulthood may become established later when lifestyle habits outside the family of origin become engrained. Importantly, such changes may still be genetically driven, consistent with age-dependent genetic influences.8,25 The mechanisms leading to higher comorbidity between ADHD and BMI in adults relative to primary-school aged children3,18,30 needs to be studied in future research in order to develop effective interventions.

The current study has several key strengths. Studies on the (cross-sectional) association between ADHD and BMI tend to focus on either childhood or adulthood with a notable lack of studies on adolescence.18 Moreover, the longitudinal nature of our study with five repeated measurement waves providing for the first time the bridge from childhood to adulthood, the inclusion of critical time covarying confounders, and the large sample size are important assets of the study. To avoid mono-informant bias, the study used both parent- and self-reported ADHD symptoms. Another strength was the inclusion of important and time varying confounders. Lastly, the RI-CLPM model used in the current study disentangles, unlike the previous cross-lagged panel models, trait-like associations between the variables from changing relation predicted by each other over time. To the extent that direct cross-lagged associations over time can be identified, and provided that appropriate time varying covariates are co-modelled, the use of the RI-CLPM is an important first step in establishing potential causality. Their absence, as currently found for most of the estimated paths in our study, is likewise highly informative.

The absence of parent report at wave four and the selective attrition were limitations of the study. The missing parent report at wave four was imputed using all available parent and self-report information in the other waves, estimating individual trajectories using state-of-the-art methods (see Supplementary material 1b.). Regarding selective attrition, although the missing values were treated using FIML, the findings of this study may underestimate the relationship between ADHD symptoms and BMI given that more severely affected participants dropped out of the study somewhat more often. However, the inclusion of the TRAILS clinical cohort that oversamples individuals with ADHD symptoms and overweight makes underestimation of the associations when the aim is to generalize to the general population less likely. Given that in the present study we combined a general population sample and a clinical sample, a further limitation of this study was that the effects of stimulant use could only be studied in a relatively small proportion of the total sample. Despite this, we illustrated differences in BMI between no, continued and discontinued medication use over time. We confirmed previous findings that stimulant use goes together with reduced BMI, including the rebound effect that discontinuation of stimulants leads to higher BMI,14,15 such that over time persons with ADHD who discontinued over time approached the BMI of persons with ADHD who did not use stimulants. A final limitation is that the RI-CLPM has not been developed, so far, for categorical outcome variables. Therefore, we could not analyze dichotomous outcomes (by dichotomizing ADHD scores at, e.g., the 80th percentile). Given that associations may strengthen at the highest levels of symptom severity, current findings may have underestimated effects over time. Together, these two limitations indicate the usefulness of method development and future study of longitudinal effects in a large clinically diagnosed sample.

In conclusion, this study showed no evidence of longitudinal bi-directional association where ADHD symptoms lead to greater BMI and/or high BMI leads to enhanced persistence or deterioration of ADHD symptoms during adolescence and young adulthood. Thus, our hypothesis that weight build-up may occur between childhood and adulthood through direct effects over time by ADHD symptoms and BMI reciprocally influencing one another was not born out. Rather, our main finding was that the association between hyperactive/impulsive symptoms and BMI in this developmental period is highly stable. An exception to this was a small direct effect of hyperactivity/impulsivity on BMI in both men and women between age 16 and 19, which requires further replication. Therefore, the outcome of this study mainly points to a shared genetic or familial background and/or potential direct causal effects already established earlier in childhood, although, direct effects may be present again in adulthood. From a clinical point of view, clinicians should be aware that adolescents presenting with overweight/obesity might have concurrent ADHD and that intervention/preventive strategies should be implemented early on in the development before the association becomes stable when evidence based interventions for ADHD may have a significant impact in terms of preventing or reducing overweight/obesity.31

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**Data Availability Statement**

The data underlying this article were provided by TRAILS consortium by permission. Data will be shared on request to the corresponding author with permission of TRAILS consortium. The availability of TRAILS data is communicated through DANS EASY (https/easy.dans.knaw.nl) and more information can be obtained via the website (trails@umcg.nl).

**Statement of Ethics**

Institutional review board (IRB) approval statement is not applicable to this specific study. However, the TRAILS cohort was approved by the IRB and strictly complies with the Helsinki Declaration.

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**Table Heading**

Table 1. Descriptive statistics

**Figure Legend**

Figure 1. Mean body mass index for five measurement waves as a function of ADHD and stimulant use

Figure 2. Summary of multigroup RI-CLPM showing the standardized estimates of stable between-person correlations and within-person autoregressive paths, and cross-lagged paths in females and males separately

**Supplementary materials**

Supplementary material 1: Measurements and Imputation procedure

Supplementary material 2: Description of model comparisons in testing male-female differences

Supplementary material 3: The Full Random-Intercepts Cross-Lagged Panel Model (RI-CLPM) with standardized estimates for male and female participants separately

Supplementary material 4: Time covarying associations between psychostimulant use and BMI, hyperactivity/impulsivity, and attention problem derived from model 5 in Table S1.