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Childhood ADHD, Sex and Obesity: a Longitudinal Population-based Study

Roxana L Aguirre Castaneda, MD¹, Seema Kumar, MD², Robert G Voigt, MD³, Cynthia L Leibson, PhD⁴, William J Barbaresi, MD⁵, Amy L Weaver, MS⁶, Jill M Killian, BS⁶, and Slavica K Katusic, MD⁴

¹Division of Pediatric Endocrinology and Metabolism, University of Illinois College of Medicine at Peoria, Peoria, Illinois

²Division of Pediatric Endocrinology and Metabolism, Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota

³Department of Pediatrics, Texas Children's Hospital, Baylor College of Medicine, Houston, Texas

⁴Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota

⁵Division of Developmental Medicine, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts

⁶Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota

Abstract

Objective—To assess obesity rates during childhood and young adulthood among attention-deficit hyperactivity disorder (ADHD) cases and age and sex-matched controls, from a population-based birth cohort, as cross-sectional studies suggest an association between ADHD and obesity.

Patients and Methods—Subjects included childhood ADHD cases (N=336) and age- and sex-matched non-ADHD controls (N=665) from a 1976-1982 birth cohort (N=5718). Height, weight and stimulant treatment were abstracted retrospectively from medical records documenting care provided from January 1, 1976 through August 31, 2010. The association between ADHD and obesity in ADHD cases relative to controls was estimated from Cox models.

Results—ADHD cases were 1.23 (95% CI, 1.00–1.50; $P<.05$) times more likely to be obese during the follow up period compared to non-ADHD controls. This association was not statistically significant in either sex (females HR, 1.49; 95% CI, 0.98–2.27; $P=.06$; males HR, 1.17, 95% CI, 0.92–1.48; $P=.20$). ADHD cases that were not obese as of date ADHD research diagnostic criteria were met were 1.56 (95% CI, 1.14–2.13; $P<.01$) times more likely to be obese during the

Corresponding Author: Seema Kumar, MD, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, Phone: (507) 284-3300, Fax: (507) 284-0727, kumar.seema@mayo.edu.

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subsequent follow-up compared to controls. This association was statistically significant only among females (HR, 2.02; 95% CI, 1.13-3.60; $P=.02$) but not among males (HR, 1.41; 95% CI, 0.97-2.05; $P=.07$). A higher proportion of ADHD subjects were obese after age 20 years compared to non-ADHD controls (34.4% vs. 25.1%, $P=.02$); this difference was observed only in females (41.6% vs 19.2%). There were no differences in obesity rates between stimulant treated and non-treated ADHD cases.

Conclusion—Childhood ADHD is associated with obesity during childhood and young adulthood in females. Treatment with stimulant medication is not associated with development of obesity up to young adulthood.

Introduction

The prevalence of childhood and adult obesity has increased markedly in the last three decades.¹ Obesity and its adverse health consequences have a significant economic impact.²⁻⁴ An understanding of risk factors for developing obesity is crucial in determining interventions for treatment or prevention. Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders of childhood with an estimated prevalence in school aged children between 8-16%.⁵⁻⁸ Clinical studies suggest that children with clinically diagnosed ADHD are heavier than the average child.⁹⁻¹¹ Conversely, overweight children are twice as likely to exhibit elevated rates of ADHD symptoms than their average-weight counterparts.^{11,12}

Cross sectional studies suggest an association between ADHD and obesity during childhood.¹¹⁻¹⁵ However, there are limited data on the association between obesity during adulthood in subjects with childhood ADHD.¹⁶⁻¹⁸ Mechanisms that could account for the association between ADHD and obesity include the presence of shared neurobiological dysfunction, involving the dopaminergic system and the behavioral impact of impulsivity and inattention in ADHD contributing to weight gain via dysregulated eating patterns.¹⁴ Stimulant medications, the most common treatment for ADHD, are known to cause appetite suppression; however,, the long-term impact of childhood treatment with stimulants on weight status during adulthood remains unknown.

The objective of this study was to examine the association between ADHD and obesity during childhood and young adulthood among research-identified ADHD subjects and age and sex matched non-ADHD controls from a population-based birth cohort. We also examined the association between treatment with stimulant medications and obesity.

Materials and Methods

Study Setting/Design/Data Sources

This population-based longitudinal birth-cohort study was conducted in Rochester, MN. In 1990, when birth-cohort subjects were in school, the Rochester Census showed 70,745 residents, (96% white, 72% 45 years old, primarily middle class). Through the Rochester Epidemiology Project (REP), all diagnoses and surgical procedures recorded at essentially all Rochester medical facilities are indexed for automated retrieval.^{19,20} The indices are linked to patient-based medical records that include detailed information on all medical

encounters from birth until death or emigration from community. Through a contractual research agreement, all 41 public, parochial and private schools in Minnesota Independent School District (ISD) No. 535, the school system for the city of Rochester, MN, provided permission to access their cumulative education records for every child from the birth cohort. The study was approved by the Institutional Review Boards of Mayo Clinic and Olmsted Medical Center.

Birth Cohort

Birth cohort consisted of all children born between 1/1/1976 and 12/31/1982 to mothers residing in townships comprising Minnesota ISD No. 535 ($n = 8458$). The target population consisted of 5,718 children (2,956 boys, 2,762 girls) who remained in Rochester at or after age five years.²¹

Identification of Childhood ADHD Cases and Controls

ADHD incidence cases were identified by research criteria applied to the 1,961 children (34% of the birth cohort) from our birth cohort who had any recorded behavioral or learning concerns. Subjects were defined as research-identified ADHD incidence cases ($N=379$) if their school and/or medical records included various combinations of the following three different categories of information: 1) meets criteria for ADHD from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision 2) positive ADHD questionnaire results, 3) documented clinical diagnosis of ADHD (with or without specific subtype).²² For each case, we randomly selected two age- and sex-matched controls without ADHD from the birth cohort after excluding those with severe intellectual disability. The school and medical records for subjects who had not denied access to medical records for research purposes were reviewed in accordance with Minnesota statute 144.

Obesity Identification

Height and weight measurements were abstracted from the medical records for each subject from birth (January 1, 1976 onwards) through August 31, 2010 with the exception of measurements during pregnancy for female subjects (the antenatal period and 6 weeks postpartum). In addition, for 34% of subjects, a weight and height measurement was also obtained prospectively if they participated in the prospective phase of an ADHD research study conducted during January 2004 – December 2009 involving subjects from the same birth cohort. For the retrospectively abstracted data, weight and height measurements were obtained by clinical staff and recorded in kilograms and inches/centimeters rounded to the nearest 0.1 and 0.5 respectively. During the prospective study, trained research staff obtained weight and height measurements during study visits to the nearest 0.1 kilogram and millimeter using a Seca Medical Scale (Seca Corporation, Issaquah, Washington). For ages 2-19 years, obesity was defined as a body mass index (BMI) $\geq 95^{\text{th}}$ percentile for age and sex using 2000 Centers for Disease Control and Prevention (CDC) growth charts.²³ In adults 20 years of age and older, obesity was defined as BMI $\geq 30 \text{ kg/m}^2$, whereas overweight, normal and underweight were defined as BMI between 25 and 29.9 kg/m^2 , between 18.5 and 24.9, and $< 18.5 \text{ kg/m}^2$, respectively. Final BMI for each subject was determined using the last available weight after age 20 years and the subject's adult height. Adult height was

defined as the average of all height measurements recorded at age 18 years for females and 20 years for males, consistent with criteria used in other studies.²⁴⁻²⁶

Stimulant Medication Treatment

For each stimulant treatment episode documented in the medical record, the dose and associated start and stop dates, based on the dates of visits at which medications were prescribed and when prescription refills were written, were abstracted as part of a prior study.²⁷ The cumulative duration of stimulant treatment was derived by summing the durations of the individual treatment episodes.²⁷ Subjects were considered “stimulant treated” if they were treated for a cumulative duration of 3 months or more between ages 2 and <21 years of age; otherwise they were considered “non treated”.

Data Analysis—Statistical analyses were performed using the SAS version 9.2 software package (SAS Institute, Inc.; Cary, NC) and R version 2.14. Data were summarized using frequencies and percentages for categorical variables and means and standard deviations (SD) or medians and interquartile ranges (IQR) for continuous variables. Comparisons between groups (ADHD cases versus controls) and stimulant treated versus stimulant “non treated” ADHD cases were evaluated using the chi-square test for sex, the two-sample t-test for birth length, birth weight and age, and Wilcoxon rank sum test for maternal education categories and number of height measurements. All calculated *P*-values were two-sided and *P*-values less than .05 were considered statistically significant.

Cumulative incidence and risk of obesity: In order to avoid misclassification of individuals as obese due to an error in measurement or recording of weight and height, a subject was considered to have met criteria for obesity if the BMI was at or above the cut off for obesity on at least two occasions; the second of the two dates was used as the date for meeting criteria for obesity. The risk of obesity in ADHD cases relative to non-ADHD controls was estimated from the hazard ratio (HR) obtained from fitting a Cox proportional hazards regression model. Additional models were fit to assess the association after adjusting for birth weight and maternal age at birth. The analysis was conducted by defining the ‘start date’ in two ways by starting the period of observation at: 1) the earliest recorded BMI from 2 to <4 years of age, and 2) the index date (i.e., the date the subject met research criteria for ADHD; this same date was used for the corresponding case's matched control.) Duration of follow-up was calculated from each defined start date to the date the subject either met criteria for obesity or date of their last medical visit with a documented BMI. In the second analysis, i.e., starting at the index date, subjects who met criteria for obesity before the index date were excluded from analysis, and Cox models were fit on an age-scale to allow for complete age adjustment.

The association between stimulant medication treatment and meeting criteria for obesity was evaluated by handling stimulant usage (yes vs. no) as a time-varying covariate in a Cox model. The counting process functionality of the Cox model was utilized to model cumulative duration of stimulant treatment as a time-varying covariate, allowing the cumulative duration to change daily throughout follow-up.²⁸ In addition, to estimate the risk effect of the cumulative duration of stimulant treatment on meeting the BMI criteria for

obesity, a penalized smoothing spline was used to model the nonlinear relationship of duration of treatment in a separate Cox model.

Young Adult BMI: The proportion of patients in various weight classifications was compared between groups (cases versus controls, stimulant treated versus stimulant non treated cases) using the chi-square test. The correlation between the final BMI and duration of stimulant treatment, average daily dose, and age at onset of treatment, respectively, was estimated using the Spearman rank correlation coefficient (r_s).

Results

Characteristics of ADHD Cases and Controls

Of the 379 research-identified ADHD cases, 340 individuals had not denied authorization for use of medical records for research. Among these 340 and the corresponding 680 age and sex matched non-ADHD controls, 336 ADHD cases and 665 non-ADHD controls had at least two sets of height and weight measurements recorded on or after 2 years of age and were included in the analysis. Mean age at last recorded BMI was 26.4 and 23.4 years, respectively, for cases and controls (Table 1).

Among the 336 childhood ADHD cases, 219 (65.2%) were treated with stimulants for 3 months ("treated"). The most commonly prescribed stimulants were methylphenidate (189 cases) and dextroamphetamine (92 cases). Many ADHD cases (35.6%) were prescribed more than one type of stimulant medication at various times, precluding an analysis of the association between type of stimulant and obesity. We classified subjects as "non treated" if they were treated with stimulants for a cumulative total < 3 months ($n=32$; 9.5%) or if they had no stimulant treatment ($n=76$; 22.6%). The median age at onset of treatment was 9.8 years (IQR, 7.6-13.0 months); median duration of treatment was 40.5 months (IQR, 18.5-71.7 months); and median average daily dosage in methylphenidate equivalent units was 24.4 MEUs (IQR, 19.4-31.3 MEUs). (Table 1).

Cumulative Incidence and Risk of Obesity

During the follow-up period, 387 subjects (155 cases and 232 controls) met the BMI criteria for obesity. ADHD cases were 1.23 (95% CI, 1.00–1.50; $P=.05$) times more likely to meet obesity criteria during follow-up compared to non-ADHD controls. This association was not statistically significant in either sex; females (HR, 1.49; 95% CI, 0.98-2.27; $P=.06$) and males (HR, 1.17; 95% CI, 0.92-1.48; $P=.20$). Estimated hazard ratios were unchanged after adjusting for birth weight and maternal age at birth (all sexes, HR, 1.23; 95% CI, 1.00-1.51; females HR, 1.51; 95% CI, 0.99-2.29; males HR, 1.16; 95% CI, 0.92-1.47).

The criterion for obesity was met before the "index date" by 75 (22.3%) cases and 141 (21.2%) controls ($P=.68$, chi-square test). These rates were similar among cases and controls when stratified by sex (females, 16.7% vs. 16.5%; males, 24.2% vs. 22.8%). In order to study the association between ADHD and subsequent development of obesity, we examined data for cases and controls that were not obese at or before the index date. Among the 252 cases and 473 controls that did not meet criteria for obesity before the index date and had at least two BMI measurements after the index date, ADHD cases were 1.56 (95% CI, 1.14 –

2.13; $P=.006$) times more likely to meet obesity criteria following the index date compared to controls (Table 2). This association was statistically significant among females (HR, 2.02; 95% CI, 1.13-3.60; $P=.02$) but not among males (HR, 1.41; 95% CI, 0.97-2.05; $P=.07$, Figures 1a and 1b). The gender x ADHD case status interaction was not statistically significant ($P=.29$). Estimated hazard ratios were unchanged after adjusting for birth weight and maternal age at birth (Table 2).

Among the 252 cases (65 females, 187 males) who had not met criteria for obesity before the index date, 173 had a known duration of stimulant treatment for ≥ 3 months, 50 were never treated, 21 were treated for <3 months, and 8 had unknown treatment duration. There was no association between treatment with stimulants and obesity, either overall (HR, 0.85; 95% CI, 0.52-1.39; $P=.52$) or among females (HR 0.91; 95% CI, 0.39-2.16; $P=.84$) or males (HR, 0.84; 95% CI, 0.46-1.54; $P=.58$). In addition, obesity risk was not associated with the preceding cumulative duration of stimulant treatment.

Young Adult BMI

Among the 336 ADHD cases and 665 non-ADHD controls, 285 cases and 450 controls had a BMI measurement after 20 years of age (maximum age, 34.3 years) and were utilized in the analysis of final BMI. The mean age at the final BMI measurement for these 735 subjects was 28.4 years for ADHD cases and 27.6 years for non-ADHD controls. The distribution of BMIs using the standard classification of underweight, normal, overweight and obese, was significantly different between ADHD cases and non-ADHD controls ($P=.02$, Figure 2a). Specifically, a higher proportion of ADHD cases were obese compared to non-ADHD controls (34.4% vs. 25.1%). This difference was observed in females ($P<.01$) but not among males ($P=.1$) (Figures 2b and 2c). Among ADHD cases, the BMI classification was not significantly different between those treated with stimulants for ≥ 3 months versus those not ($P=.84$, Figure 2d). Furthermore, among those treated for ≥ 3 months, there was little correlation between the final BMI and treatment duration ($r_s = 0.05$) or average daily dosage ($r_s = 0.02$). However, there was an inverse correlation with age at treatment onset; ADHD cases who began stimulant treatment earlier tended to have a higher final BMI ($r_s = -0.14$, $P=.05$).

Discussion

In this population-based longitudinal study of childhood ADHD cases and non-ADHD controls, in females childhood ADHD was associated with obesity during childhood and young adulthood. The incidence of obesity was not associated with stimulant treatment, among childhood ADHD cases. To our knowledge, this is the first population-based longitudinal study to examine the association between ADHD and development of obesity using ADHD cases and controls of both sexes derived from the same birth cohort.

Our findings of an association between ADHD and childhood and young adulthood obesity in females are consistent with those from a birth cohort based prospective study from the Netherlands in which the association between ADHD and obesity in girls was noted to be age-dependent, with the strongest association between the ages of 10-12 years.²⁹ An association between ADHD and obesity in children has also been noted in several cross

sectional studies.^{10,11,13,30} Our findings however are in contrast to the longitudinal case control study by Biederman and colleagues that revealed no difference between females with ADHD and non-ADHD controls at 10-11 year follow up.³¹ The Biederman study, however, was limited by a smaller sample size overall, decreased number of ADHD cases and controls that had weight status information at age 20 years or older and shorter duration of follow up (mean age at follow up of 21.1 years versus 26.4 years in our study).³¹

We did not find an association of ADHD with obesity in males. Several other studies, however, suggest an association between ADHD and obesity in males.^{11,16,18,29} These differences may be related to differences in methodology, such as criteria used for childhood ADHD (research-identified versus those diagnosed in clinic on the basis of parent interviews with three questions without evidence that DSM-IV criteria were met)¹¹, self-reported weight and height information¹⁸ and reference values used for definition of obesity.²⁹ Differences in the ethnic makeup of the study population as well as differences in duration of follow up may also account for these differences.¹⁸

The association between ADHD and obesity may reflect shared underlying abnormalities in the neural dopaminergic pathways that mediate not only impulse control and reward sensitivity but also appetite and satiety.^{32,33} Additionally, poor executive functioning in individuals with ADHD³⁴ may lead to less regular eating patterns, overeating, impulsivity as well as decreased physical activity, thereby leading to excessive weight gain.^{35,36} Sleep difficulties, often present in children with ADHD³⁷ may also lead to excess weight gain as a result of behavioral and hormonal factors.³⁸ Our findings of an association between ADHD and obesity in females highlight the need for monitoring of weight status of children with ADHD for overweight/obesity and need for obesity prevention efforts via healthy lifestyle (dietary and physical activity related) within the home as well as in schools and health care providers' offices for children with ADHD.

Our finding of sex-specific differences in the association between ADHD and obesity may be partly related to unique differences in ADHD subtypes, such as the higher prevalence of the inattentive subtype of ADHD in females versus the hyperactive-impulsive subtype, which is more prevalent among males, as well as differences in associated co-morbidities between males and females.³⁹⁻⁴¹ It is also likely that lower self-efficacy and poorer coping strategies as well as higher rates of depression, anxiety and eating disorder in girls with ADHD, may contribute to habits that predispose to excess weight gain.⁴¹⁻⁴³ The increased resting energy expenditure seen in boys in hyperactive-impulsive type of ADHD may be protective against weight gain.⁴⁴

Our findings of no association between obesity during young adulthood and ADHD stimulant usage are consistent with those reported in two other case-control longitudinal studies.^{29,31} However, we did note a higher final BMI in ADHD cases that began stimulant treatment earlier. These findings suggest that longer follow up in children and adults that use stimulants is warranted. A recent study utilizing longitudinal electronic health record data in children ages 3-18 years reported an association between stimulant use in ADHD children with slower early BMI growth, but a rebound later in adolescence to levels above children without a history of ADHD or stimulant use.⁴⁵ The diagnosis of ADHD in that study, unlike

in our study was based on diagnosis codes. Additionally, the duration of follow-up in that study ranged between 2.4 and 4.6 years only and it did not provide any information on outcomes during adulthood.

Strengths of our study include the population-based longitudinal study design, sample size, inclusion of males and females and use of strict research-based criteria for ADHD and non-ADHD controls. Weight and height of subjects were recorded by clinical staff or by trained study personnel instead of being self-reported.

Our study has several limitations. Height and weight measurements taken from retrospective record review were those recorded during a clinic visit, and standardized methodologies were not necessarily employed. Additionally, as ADHD cases had more frequent height and weight measurements, there could be potential bias in the timing of obesity diagnosis with ADHD cases more likely to be diagnosed with obesity at an earlier age and the subsequent time to event analyses for ADHD cases. Another limitation was that the research criteria for ADHD being applied were based on retrospective review and were not obtained from prospective application of standardized measures. Further we did not adjust for various psychosocial or behavioral morbidities such as anxiety, depression, eating disorders and substance abuse that are common in patients with ADHD as well as in patients with obesity.^{9,42,43,46} We also did not examine neurodevelopmental disorders and conduct disorders common to both ADHD and obesity. Additionally, socioeconomic status that can impact weight status both during childhood and adulthood and persistence of ADHD during the adult life were not addressed in this study. Finally, Rochester is primarily a white, middle-class community, so inferences to more diverse populations may be limited. The study findings reflect an association and not causation.

Conclusion

ADHD in females is associated with obesity during childhood and young adulthood. Stimulant medication treatment during childhood does not appear to be associated with obesity up to young adulthood. There is a need for greater awareness regarding the association between ADHD and obesity in females among patients, care givers and healthcare providers. Preventive measures targeting healthy eating and active lifestyle should be incorporated as part of routine care of all patients with ADHD.

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References

1. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA. 2014; 311:806–814. [PubMed: 24570244]

2. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988-1994. *Arch Pediatr Adolesc Med.* 2003; 157:821–827. [PubMed: 12912790]
3. Hammond RA, Levine R. The economic impact of obesity in the United States. *Diabetes Metab Syndr Obes.* 2010; 3:285–295. [PubMed: 21437097]
4. Marcus MD, Baranowski T, DeBar LL, et al. Severe obesity and selected risk factors in a sixth grade multiracial cohort: the HEALTHY study. *J Adolesc Health.* 2010; 47:604–607. [PubMed: 21094439]
5. Akinbami, Ij. Attention Deficit Hyperactivity Disorder Among Children Aged 5-17 years in the United States, 1998-2009. NCHS data brief. 2011; 70
6. Barbaresi WJ, Katusic SK, Colligan RC, et al. How common is attention-deficit/hyperactivity disorder? Incidence in a population-based birth cohort in Rochester, Minn. *Arch Pediatr Adolesc Med.* 2002; 156:217–224. [PubMed: 11876664]
7. Scahill L, Schwab-Stone M. Epidemiology of ADHD in school-age children. *Child Adolesc Psychiatr Clin N Am.* 2000; 9:541–555. vii. [PubMed: 10944656]
8. Wolraich M, Brown L, Brown RT, et al. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics.* 2011; 128:1007–1022. [PubMed: 22003063]
9. Cortese S, Angriman M, Maffei C, et al. Attention-deficit/hyperactivity disorder (ADHD) and obesity: a systematic review of the literature. *Crit Rev Food Sci.* 2008; 48:524–537.
10. Erhart M, Herpertz-Dahlmann B, Wille N, Sawitzky-Rose B, Holling H, Ravens-Sieberger U. Examining the relationship between attention-deficit/hyperactivity disorder and overweight in children and adolescents. *Eur Child Adolesc Psy.* 2012; 21:39–49.
11. Kim J, Mutyal B, Agiovlasis S, Fernhall B. Health behaviors and obesity among US children with attention deficit hyperactivity disorder by gender and medication use. *Prev Med.* 2011; 52:218–222. [PubMed: 21241728]
12. Waring ME, Lapane KL. Overweight in children and adolescents in relation to attention-deficit/hyperactivity disorder: results from a national sample. *Pediatrics.* 2008; 122:e1–6. [PubMed: 18595954]
13. Byrd HC, Curtin C, Anderson SE. Attention-deficit/hyperactivity disorder and obesity in US males and females, age 8-15 years: National Health and Nutrition Examination Survey 2001-2004. *Pediatr Obes.* 2013; 8:445–453. [PubMed: 23325553]
14. Cortese S, Vincenzi B. Obesity and ADHD: Clinical and Neurobiological Implications. *Curr Top Behav Neurosci.* 2012; 9:199–218. [PubMed: 21845534]
15. Holtkamp K, Konrad K, Muller B, et al. Overweight and obesity in children with Attention-Deficit/Hyperactivity Disorder. *Int J Obes Relat Metab Disord.* 2004; 28:685–689. [PubMed: 15024399]
16. Cortese S, Ramos Olazagasti MA, Klein RG, Castellanos FX, Proal E, Mannuzza S. Obesity in men with childhood ADHD: a 33-year controlled, prospective, follow-up study. *Pediatrics.* 2013; 131:e1731–1738. [PubMed: 23690516]
17. de Zwaan M, Gruss B, Muller A, et al. Association between obesity and adult attention-deficit/hyperactivity disorder in a German community-based sample. *Obes Facts.* 2011; 4:204–211. [PubMed: 21701236]
18. Pagoto SL, Curtin C, Lemon SC, et al. Association between adult attention deficit/hyperactivity disorder and obesity in the US population. *Obesity.* 2009; 17:539–544. [PubMed: 19131944]
19. Melton LJ 3rd. History of the Rochester Epidemiology Project. *Mayo Clin Proc.* 1996; 71:266–274. [PubMed: 8594285]
20. Rocca WA, Yawn BP, St Sauver JL, Grossardt BR, Melton LJ 3rd. History of the Rochester Epidemiology Project: half a century of medical records linkage in a US population. *Mayo Clin Proc.* 2012; 87:1202–1213. [PubMed: 23199802]
21. Katusic SK, Colligan RC, Barbaresi WJ, Schaid DJ, Jacobsen SJ. Potential influence of migration bias in birth cohort studies. *Mayo Clin Proc.* 1998; 73:1053–1061. [PubMed: 9818038]
22. Katusic SK, Barbaresi WJ, Colligan RC, Weaver AL, Leibson CL, Jacobsen SJ. Case definition in epidemiologic studies of AD/HD. *Ann Epidemiol.* 2005; 15:430–437. [PubMed: 15967390]

23. Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC Growth Charts for the United States: methods and development. *Vital Health Stat.* 2002; 11:1–190.
24. Lee JJ, Escher JC, Shuman MJ, et al. Final adult height of children with inflammatory bowel disease is predicted by parental height and patient minimum height Z-score. *Inflamm Bowel Dis.* 2010; 16:1669–1677. [PubMed: 20127995]
25. Fine RN, Sullivan EK, Tejani A. The impact of recombinant human growth hormone treatment on final adult height. *Pediatr Nephrol.* 2000; 14:679–681. [PubMed: 10912542]
26. Kelly HW, Sternberg AL, Lescher R, et al. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med.* 2012; 367:904–912. [PubMed: 22938716]
27. Barbaresi WJ, Katusic SK, Colligan RC, Weaver AL, Leibson CL, Jacobsen SJ. Long-term stimulant medication treatment of attention-deficit/hyperactivity disorder: results from a population-based study. *J Dev Behav Pediatr.* 2006; 27:1–10. [PubMed: 16511362]
28. Therneau Terry M GPM. Modeling Survival data: Extending the Cox model. Vol. XIV. New York: Springer; 2000. p. 350
29. Fliers EA, Buitelaar JK, Maras A, et al. ADHD is a risk factor for overweight and obesity in children. *J Dev Behav Pediatr.* 2013; 34:566–574. [PubMed: 24131879]
30. van Egmond-Frohlich AW, Widhalm K, de Zwaan M. Association of symptoms of attention-deficit/hyperactivity disorder with childhood overweight adjusted for confounding parental variables. *Int J Obesity.* 2012; 36:963–968.
31. Biederman J, Spencer TJ, Monuteaux MC, Faraone SV. A naturalistic 10-year prospective study of height and weight in children with attention-deficit hyperactivity disorder grown up: sex and treatment effects. *J Pediatr.* 2010; 157:635–640. 640 e631. [PubMed: 20605163]
32. Swanson JM, Kinsbourne M, Nigg J, et al. Etiologic subtypes of attention-deficit/hyperactivity disorder: brain imaging, molecular genetic and environmental factors and the dopamine hypothesis. *Neuropsychol Rev.* 2007; 17:39–59. [PubMed: 17318414]
33. Volkow ND, Wang GJ, Baler RD. Reward, dopamine and the control of food intake: implications for obesity. *Trends Cogn Sci.* 2011; 15:37–46. [PubMed: 21109477]
34. Graziano PA, Bagnier DM, Waxmonsky JG, Reid A, McNamara JP, Geffken GR. Co-occurring weight problems among children with attention deficit/hyperactivity disorder: the role of executive functioning. *Int J Obesity.* 2012; 36:567–572.
35. Khalife N, Kantomaa M, Glover V, et al. Childhood attention-deficit/hyperactivity disorder symptoms are risk factors for obesity and physical inactivity in adolescence. *J Am Acad Child Adolesc Psychiatry.* 2014; 53:425–436. [PubMed: 24655652]
36. van den Berg L, Pieterse K, Malik JA, et al. Association between impulsivity, reward responsiveness and body mass index in children. *Int J Obesity.* 2011; 35:1301–1307.
37. Cortese S, Faraone SV, Konofal E, Lecendreux M. Sleep in children with attention-deficit/hyperactivity disorder: meta-analysis of subjective and objective studies. *J Am Acad Child Adolesc Psychiatry.* 2009; 48:894–908. [PubMed: 19625983]
38. Carter PJ, Taylor BJ, Williams SM, Taylor RW. Longitudinal analysis of sleep in relation to BMI and body fat in children: the FLAME study. *BMJ.* 2011; 342:d2712. [PubMed: 21622518]
39. Gaub M, Carlson CL. Gender differences in ADHD: a meta-analysis and critical review. *J Am Acad Child Adolesc Psychiatry.* 1997; 36:1036–1045. [PubMed: 9256583]
40. Graetz BW, Sawyer MG, Baghurst P. Gender differences among children with DSM-IV ADHD in Australia. *J Am Acad Child Adolesc Psychiatry.* 2005; 44:159–168. [PubMed: 15689729]
41. Rucklidge JJ. Gender differences in attention-deficit/hyperactivity disorder. *Psychiatr Clin North Am.* 2010; 33:357–373. [PubMed: 20385342]
42. Mikami AY, Hinshaw SP, Patterson KA, Lee JC. Eating pathology among adolescent girls with attention-deficit/hyperactivity disorder. *J Abnorm Psychol.* 2008; 117:225–235. [PubMed: 18266500]
43. Surman CB, Randall ET, Biederman J. Association between attention-deficit/hyperactivity disorder and bulimia nervosa: analysis of 4 case-control studies. *J Clin Psychiatry.* 2006; 67:351–354. [PubMed: 16649819]

44. Mueller TF, Brielmaier S, Domsch H, Luyckx VA, Ehlers T, Krowatschek D. Increased resting energy expenditure in children with attention-deficit-hyperactivity disorder. *Eat Weight Disord.* 2010; 15:e144–151. [PubMed: 20212347]
45. Schwartz BS, Bailey-Davis L, Bandeen-Roche K, et al. Attention deficit disorder, stimulant use, and childhood body mass index trajectory. *Pediatrics.* 2014; 133:668–676. [PubMed: 24639278]
46. Yoshimasu K, Barbaresi WJ, Colligan RC, Voigt RG, Killian JM, Weaver AL, Katusic SK. Childhood ADHD is strongly associated with a broad range of psychiatric disorders during adolescence: a population-based birth cohort study. *J Child Psychol Psychiatry.* 2012; 53(10): 1036–43. [PubMed: 22647074]

List of Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder
BMI	Body Mass Index

Figure 1.
Cumulative Incidence of Meeting the BMI Criteria for Obesity Following the Index Date, Separately for Females (1a) and Males (1b).

Figure 2.
Summary of last BMI Between 20 and 34 Years of Age.

Table 1
Baseline and Follow-up Characteristics of ADHD Cases and non-ADHD Controls; ADHD Cases Separately by Stimulant Treatment Status^a

Characteristic	ADHD Case Status	P		ADHD Cases Treated With Stimulants for 3 months ^b		P
		ADHD Cases (N=336)		Non-ADHD Controls (N=665)		
				Yes (N=219)	No (N=108)	
<u>Baseline</u>						
Male sex, n (%)	252 (75.0%)	495 (74.4%)		170 (77.6%)	75 (69.4%)	.11
Birth length (cm), mean (SD)	51.7 (3.0)	51.9 (2.7)		51.8 (3.0)	51.5 (3.1)	.42
Birth weight (g), mean (SD)	3464.4 (570.1)	3534.1 (541.9)		3471.9 (550.6)	3449.4 (615.4)	.74
Maternal education at subject's birth, n (%)						.07
Not available, n	30	73		22	8	
Less than high school	25 (8.2%)	37 (6.3%)		15 (7.6%)	9 (9.0%)	
High school graduate	122 (39.9%)	180 (30.4%)		87 (44.2%)	31 (31.0%)	
Some college	101 (33.0%)	216 (36.5%)		63 (32.0%)	36 (36.0%)	
College graduate	58 (19.0%)	159 (26.9%)		32 (16.2%)	24 (24.0%)	
Maternal age at subject's birth (y), Mean (SD)	25.9 (4.8)	26.8 (4.8)		26.2 (4.6)	25.7 (5.2)	.40
Age- and sex-specific BMI percentile, Mean (SD) ^c	64.7 (29.1)	62.0 (30.7)		64.7 (29.4)	64.8 (28.5)	.98
<u>Follow-up</u>						
Age met ADHD research criteria (y)						
Overall: Mean (SD)	10.4 (3.7)	n/a		10.0 (3.6)	11.2 (3.7)	<.01
Females: Mean (SD)	11.4 (4.1)	n/a		10.6 (3.9)	12.4 (4.4)	.05
Males: Mean (SD)	10.0 (3.4)	n/a		9.8 (3.5)	10.6 (3.9)	.07
Age at last recorded BMI measurement (y), Mean (SD)	26.4 (5.7)	23.4 (7.1)		26.5 (5.4)	26.2 (6.2)	.69
Number of BMI measurements after age 2y, Median (IQR) ^d	31 (19-45)	21 (12-34)		32 (23-50)	26 (14-37)	<.001

^aBMI= body mass index; SD= standard deviation; IQR= interquartile range^bIn total, 260 ADHD cases were treated with stimulants included 32 for <3 months and 9 for whom the duration was unknown^cAge- and sex-specific BMI percentile based on earliest recorded BMI between 2 and <4 years of age^dIf more than 2 height and weight measurements were recorded on the same date, then just one set of measurements was counted for that date.

Table 2
Association between ADHD Status and Meeting the Obesity BMI^a Criteria Following the Index Date, Among Subjects Not Obese at the Index Date^b

	No. at risk ^c	Unadjusted analysis		Adjusted analysis ^d	
		HR (95% CI)	P	HR (95% CI)	P
Overall			<.01		<.01
ADHD cases	252	1.56 (1.14-2.13)		1.55 (1.13-2.12)	
Non-ADHD controls	473	Referent		Referent	
Females			.02		.02
ADHD cases	65	2.02 (1.13-3.60)		1.95 (1.09-3.49)	
Non-ADHD controls	131	Referent		Referent	
Males			.07		.08
ADHD cases	187	1.41 (0.97-2.05)		1.40 (0.96-2.04)	
Non-ADHD controls	342	Referent		Referent	

^a BMI=body mass index

^b The "index date" for each ADHD case and their non-ADHD matched controls is defined as the date when then case met the research criteria for ADHD.

^c The number at risk is the number of subjects who had not met the obese BMI criteria prior to the index date.

^d Adjusted for subject's birth weight and maternal age at birth.