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Childhood ADHD is Strongly Associated with a Broad Range of Psychiatric Disorders during Adolescence: a Population-Based Birth Cohort Study

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Abstract

Background—To evaluate associations between ADHD and comorbid psychiatric disorders using research-identified incident cases of ADHD and population-based controls.

Methods—Subjects included a birth cohort of all children born 1976–1982 remaining in Rochester, MN after age five ($n = 5718$). Among them we identified 379 ADHD incident cases and 758 age-sex matched non-ADHD controls, passively followed to age 19 years. All psychiatric diagnoses were identified and abstracted, but only those confirmed by qualified medical professionals were included in the analysis. For each psychiatric disorder, cumulative incidence rates for subjects with and without ADHD were estimated using the Kaplan-Meier method. Corresponding hazard ratios (HR) were estimated using Cox models adjusted for gender and mother's age and education at the subject's birth. The association between ADHD and the likelihood of having an internalizing or externalizing disorder was summarized by estimating odds ratios (OR).

Results—ADHD was associated with a significantly increased risk of adjustment disorders (HR=3.88), conduct/oppositional defiant disorder (HR=9.54), mood disorders (HR=3.67), anxiety disorders (HR=2.94), tic disorders (HR=6.53), eating disorders (HR=5.68), personality disorders (HR=5.80), and substance-related disorders (HR=4.03). When psychiatric comorbidities were classified on the internalization-externalization dimension, ADHD was strongly associated with coexisting internalizing/externalizing (OR=10.6), or externalizing-only (OR=10.0) disorders.

Conclusion—This population-based study confirms that children with ADHD are at significantly increased risk for a wide range of psychiatric disorders. Besides treating the ADHD, clinicians should identify and provide appropriate treatment for psychiatric comorbidities.

Keywords

ADD/ADHD; psychiatric practice; epidemiology

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Attention-deficit/hyperactivity disorder (ADHD) has been reported in clinical and community samples, often accompanied by psychiatric disorders (e.g., mood, anxiety, conduct (CD), oppositional-defiant disorders (ODD) (Angold, Costello & Erkanli, 1999, Barkley, 2006, Brown, 2009, Wilens, et al., 2002, Young, 2008). Comorbidity rates between ADHD and psychiatric disorders are inconsistent, since many studies included clinic-referred subjects, had relatively small sample sizes and included only limited types of comorbid psychiatric disorders (Barkley, 2006, Spencer, 2006). Thus, a broader range of comorbid psychiatric disorders in ADHD requires further exploration. Children with ADHD and comorbid psychiatric disorders have poorer outcomes: significantly greater social, emotional, and psychological difficulties than those with ADHD alone (Spencer, 2006). Furthermore, those with ADHD and comorbid depression had significantly increased risk for psychiatric hospitalization, substance abuse, and suicidality compared to children with ADHD or depression alone (Biederman, et al., 2008a, Blackman, Ostrander & Herman, 2005, Daviss, 2008, Quinn, 2008). In addition, comorbidities greatly influence presentation of ADHD symptoms, the diagnosis/prognosis, and complicates treatment (Kunwar, Dewan & Faraone, 2007). Clinical studies show that combinations of ADHD with ODD/CD, and/or anxiety, should be strictly distinguished since the most effective treatment differs among these conditions (Jensen, et al., 2001).

The impact of gender on psychiatric comorbidities and ADHD has not been adequately addressed (Bauermeister, et al., 2007, Levy, Hay, Bennett & McStephen, 2005, Romano, Tremblay, Vitaro, Zoccolillo & Pagani, 2005). Externalizing disorders (e.g., ODD and CD) are believed to be more frequent among boys, and girls are more prone to internalizing disorders (e.g., anxiety, depression) (Quinn, 2008, Romano, et al., 2005), but definitive gender differences in these externalize or internalize dimensions of psychiatric disorders with regard to ADHD status are unclear.

Population-based birth cohort epidemiologic studies on rates of psychiatric comorbidities by gender and internalizing/externalizing disorder among children with ADHD are rare in spite of increased importance in managing psychiatric comorbidities of ADHD (Bussing, Mason, Bell, Porter & Garvan, 2010, Ford, Goodman & Meltzer, 2003, Kadesjo & Gillberg, 2001, Romano, et al., 2005, Smalley, et al., 2007, Volk, Neuman & Todd, 2005). Such community-based studies may not be as representative of the entire community as are population-based birth cohorts.

To address limitations of available studies and inform clinical practice, we studied the associations between ADHD and a wide range of comorbid psychiatric disorders in a large population-based birth cohort, and analyzed gender differences. This included assessment of the magnitude of associations between ADHD and comorbid psychiatric disorders and the frequency of externalizing and/or internalizing psychiatric disorders, between boys and girls, with and without ADHD.

Method

Study setting and data sources

Rochester, Minnesota, is 90 miles southeast of Minneapolis-St Paul, the closest urban center. In 1990, when our subjects were school-aged, there were 70,745 Rochester residents: 96% white, 72% 45 years of age, primarily middle class, resembling US white population (Melton, 1996).

Our capability for population-based epidemiologic research on psychiatric comorbidity of ADHD results from a unique set of circumstances. First, Rochester is relatively isolated and virtually all medical care is provided by Mayo Clinic, Olmsted Medical Center and three

affiliated hospitals. The Rochester Epidemiology Project (REP) has a unique medical record-linkage system of Rochester and Olmsted County residents. All diagnoses and surgical procedures from affiliated medical facilities are indexed for computerized retrieval (Kurland & Molgaard, 1981, Melton, 1996). Records include detailed histories of all medical encounters in the community (psychiatry/psychology reports, psychological test results, correspondence regarding treatment by private psychiatry facilities, ambulatory medical and social services; hospital, emergency department, home visits), from birth until death or emigration from the community. Second, through a contractual research agreement, all 41 public and private schools in Minnesota Independent School District (ISD) No. 535, our local school system, gave permission to access their richly documented cumulative educational records for every child in the birth cohort. These school records are permanently maintained for all children who have attended public, private, or home school in the district. Third, under a separate research agreement we obtained permission to access records from the only private community psychiatric practice. This study was approved by the Institutional Review Boards of Mayo Clinic and Olmsted Medical Center.

Birth cohort

Our birth cohort consisted of all children born between January 1, 1976 and December 31, 1982, to mothers residing Rochester ($n = 8548$). The target population consisted of 5718 children (2956 boys; 2762 girls) living in Rochester at or after the age of five, followed retrospectively from birth. The methods used for identification and follow-up of this birth cohort, and analysis of potential influence of migration bias, have been previously reported (Katusic, Colligan, Barbaresi, Schaid & Jacobsen, 1998).

ADHD incident case identification

Our strategy in identifying ADHD incidence cases consisted of several steps, used multiple sources of information, and relied on recorded history of symptoms, individual test results, and treatment documented in medical, school, and private psychiatric practice records. Details of this process were previously reported (Barbaresi, et al., 2002, Katusic, et al., 2005). Briefly, several steps were used to narrow the pool of potential ADHD incident cases, starting with cumulative school records of each child in the birth cohort ($n = 5718$). School records were searched for indications of concern about learning and/or behavior; 1961 children were identified with such concerns documented by teachers, parents, school psychologists, physicians, social workers, or/and school nurses. Next, we abstracted all descriptions of ADHD symptoms consistent with DSM-IV, results from teacher/parent questionnaires and clinical diagnoses of ADHD from school, medical records and those from the private community psychiatric practice.

Identification of ADHD incident cases consisted of applying research criteria to these 1961 children. Subjects were defined as research-identified ADHD incident cases if their school/medical records included various combinations of three different categories of information: 1) met DSM-IV criteria for ADHD, 2) positive ADHD questionnaire results, 3) clinical diagnosis of ADHD. A total of 379 ADHD incident cases were identified. All cases and their controls were followed from birth until emigration, death, high school graduation, drop out or age 19.

Non-ADHD controls

For each ADHD incident case, two controls were selected from the birth cohort. Controls were matched on gender and birth date (± 6 months) using an optimal matching algorithm applied to the values of these matching factors (Bergstralh, Kosanke & Jacobsen, 1996). No control (nor case) had a diagnosis of pervasive developmental disorder, severe intellectual disability, schizophrenia, nor any psychotic disorder.

Psychiatric disorder identification

The identification of comorbid psychiatric disorders among ADHD cases and controls consisted of a systematic, multistage process, utilizing detailed, routinely collected data as part of the Rochester Epidemiology Project (Kurland & Molgaard, 1981, Melton, 1996). First, a list of all possible psychiatric diagnoses given to ADHD cases and controls prior to age 19 years was produced using our computerized medical index retrieval system (Kurland & Molgaard, 1981, Melton, 1996). Second, members of the research team (two psychologists, two developmental-behavioral pediatricians, one physician-epidemiologist) individually reviewed this list. Consensus determined that 299 diagnoses could be classified as psychiatric disorders in any version of the Diagnostic and Statistical Manual of Mental Disorders. Many different terms, over the time span of our study, were used to describe similar psychiatric conditions (e.g., neurotic anxiety, over-anxious disorder specific to childhood and adolescence, unspecified state anxiety, generalized anxiety disorder, etc.). During step three, medical records were abstracted for all ADHD cases and controls who had at least one of the 299 diagnoses before age 19. To be classified with a psychiatric disorder, we required documentation of (a) the initial diagnosis and (b) separate confirmation of the initial diagnosis. Trained abstractors, blinded for ADHD case/control status, collected the following information: psychiatric diagnosis, earliest date of diagnosis, professional making the initial psychiatric diagnosis, date of confirmation and by whom (medical professional). Documented diagnoses were considered to have been confirmed when the confirmatory diagnosis was made by a qualified professional with appropriate credentials and expertise (Table 2). In step four we collapsed these diagnoses into 10 categories based on DSM-IV-TR (Table 2) (American Psychiatric Association, 2000).

Subjects subsequently were classified into four Internalization-Externalization categories: internalizing-only (mood disorders, anxiety disorders, somatoform disorders), externalizing-only (ODD/CD, impulse-control disorders, substance-use-related disorders), combined internalization-externalization, and indeterminate (insufficient information to classify). Subjects with disorders of adjustment, personality, eating, and tics were classified into one of these four categories based on clinical descriptions in the medical record.

Data analysis

Demographic and perinatal factors were compared between ADHD incident cases and non-ADHD controls using the chi-square test or Fisher's exact test for categorical variables and the Wilcoxon rank sum test for parental age.

Separate analyses were performed for each of the 10 psychiatric-disorder-categories. Cumulative incidence, the probability that a subject from the cohort would be diagnosed with a particular comorbid psychiatric disorder, was calculated according to the Kaplan and Meier method, accounting for the varying duration of follow-up (Kaplan & Meier, 1958). Duration of follow-up was calculated from birth until the date when a subject was diagnosed/ confirmed with a particular psychiatric disorder prior to 19 years of age. For subjects not diagnosed with that particular psychiatric disorder, their durations of follow-up were censored prior to age 19 at either their date of death or date of last medical follow-up (or age 19). Cumulative incidence rates for each of the 10 psychiatric comorbidities were calculated separately for ADHD cases and non-ADHD controls.

For each psychiatric disorder, the association between ADHD and time to the diagnosis of that disorder was evaluated by fitting a Cox proportional hazards model. These associations were summarized by estimating the hazard ratio (HR) and corresponding 95% confidence interval (CI). Both unadjusted and adjusted (i.e. multivariable) models were fitted. In the multivariable model, the child's sex, mother's education, and age at birth of child, were

included. To assess whether the association between ADHD and each psychiatric disorder was different between boys and girls, an interaction term (gender $\times$ ADHD status) was included in the multivariable Cox regression model.

The number of comorbid psychiatric disorder categories identified in each subject (0, 1, 2, 3+) was compared between ADHD cases and non-ADHD controls using the Wilcoxon rank sum test. A multinomial logistic regression analysis was used to calculate odds ratios (OR) and 95% CIs for evaluating the associations between ADHD and the four Internalization-Externalization categories (i.e. the unordered categorical dependent variable). To assess whether these associations were different between boys and girls, an interaction term was included in the logistic model. Two-sided p -values $< .05$ were considered statistically significant. All analyses were performed using SAS (version 9.2 software package: SAS Institute, Inc., Cary, NC).

Results

Among the 5,718 children in the birth cohort, 19 subjects with severe intellectual disability were excluded. A total of 379 incident cases with ADHD and 758 non-ADHD controls fulfilled study criteria. In addition, 36 ADHD cases and 46 controls without research authorization at the time of our study were excluded, yielding 343 ADHD cases and 712 non-ADHD controls.

Biological and socioeconomic factors from birth certificates are shown in Table 1. Subjects with ADHD were significantly more likely to be Caucasian ($p = .02$), have mothers with lower education ($p = .01$), and younger mothers at birth ($p < .01$), compared to controls. There were no significant differences regarding perinatal factors between cases and controls.

The medical professional who confirmed the psychiatric diagnoses, and the child's age at confirmation, are summarized in Table 2. The majority were confirmed by a psychologist or psychiatrist.

Among the 343 ADHD cases, 213 (62%) had one or more comorbid psychiatric disorders by 19 years of age compared with 19% of the 712 controls (Table 3). The number of comorbid psychiatric disorders (0, 1, 2, 3+) was significantly higher for ADHD cases than non-ADHD controls for both boys ($p < .001$) and girls ($p < .001$). However, the number of comorbid psychiatric disorders was not significantly different between boys and girls with ADHD ($p = .47$), nor between non-ADHD boys and non-ADHD girls ($p = .53$).

ADHD was significantly associated with an increased risk for 8 of the 10 categories, excluding somatoform and impulse-control disorders (Table 4). The strongest association was between ADHD and ODD/CD. For each psychiatric disorder, the gender $\times$ ADHD interaction was not statistically significant (Table 4), indicating that the estimated association between ADHD and each of the psychiatric disorders was similar for boys and girls. For example, the unadjusted HR for the association between ADHD status and mood disorders was 3.7 (boys) and 3.3 (girls).

ADHD was significantly associated with the comorbid condition of combined externalizing-internalizing disorders (OR = 10.6 versus none; 95% CI = 6.6–17.0), externalizing-only (OR = 10.0 versus none; 95% CI = 6.0–16.4) and internalizing-only (OR = 4.1 versus none; 95% CI = 2.6–6.4) (Figure 1). Odds ratios of similar magnitude were obtained when the analysis was performed separately for girls and boys ($p = .59$ for gender $\times$ ADHD interaction). Among children with ADHD, girls were significantly more likely to have internalizing-*only* comorbidities than boys with ADHD (20.9% vs. 11.3%, $p = .02$). Conversely, boys with ADHD were significantly more likely to have externalizing-*only* comorbidities than girls

with ADHD (20.2% vs. 7.0%, $p < .01$). The same patterns emerged when comparing non-ADHD girls with non-ADHD boys.

Discussion

The strength of our epidemiologic study is the population-based birth cohort, with carefully defined, research-identified incident ADHD cases and non-ADHD controls, and their, documented comorbid psychiatric conditions. Our longitudinal methodology add significantly to understanding the natural history of the comorbidity between ADHD and psychiatric disorders from childhood through adolescence.

Our results indicate strong associations between ADHD and a broad range of psychiatric disorders. The strongest association was between ADHD and ODD/CD, generally consistent with previous school/community-based studies (Ford, Goodman & Meltzer, 2003, Kadesjo & Gillberg, 2001, Romano, et al., 2005, Smalley, et al., 2007). However, comorbid ODD/CD in our population-based sample was only half that reported in previous non-population-based study (Biederman, et al., 2008b). We found ADHD was associated with more than a four-fold increased risk of any psychiatric disorder. Approximately 60% of both boys and girls with ADHD had at least one comorbid psychiatric condition beside ADHD, and 35% had two or more, consistent with the suggestion that 'pure' ADHD is rare in clinical samples (Wilens, et al., 2002) and the general population (Kadesjo & Gillberg, 2001). Previous community and/or school samples show similar findings using questionnaires or structured/semi-structured interviews with parents and/or adolescents to establish the presence of a comorbid psychiatric disorder (Bussing, et al., 2010, Ford, Goodman & Meltzer, 2003, Kadesjo & Gillberg, 2001, Kessler, et al., 2005, Romano, et al., 2005, Smalley, et al., 2007, Volk, Neuman & Todd, 2005). While such interviews permit researchers to elicit details of the symptoms, they may be affected by rater or self-report gender bias (Romano, et al., 2005, Rucklidge & Tannock, 2001). Our methodology was based on clinical diagnoses of psychiatric comorbidities documented in the medical records, and confirmed by medical professionals, diminishing potential effects of rater and self-report biases. It also enabled us to consider adjustment disorders not usually evaluated by structured interview.

Our findings, in a population-based birth cohort, did not detect any significant gender $\times$ ADHD interactions on the rate of psychiatric comorbidities. This suggests the strength of the association between ADHD and psychiatric comorbidities does not differ between boys and girls. These findings are generally consistent with those of Biederman et al. who showed no gender $\times$ ADHD interaction on psychiatric disorders among child (except for substance-related disorders) and adult clinical samples (Biederman, et al., 2002, Biederman & Faraone, 2004, Biederman, Faraone, Monuteaux, Bober & Cadogen, 2004). Another community-based study reported no significant gender $\times$ ADHD interactions for disruptive, mood, and anxiety disorders, (Bauermeister, et al., 2007).

It has been reported that boys have more externalizing disorders (e.g., ODD/CD), whereas girls tend toward internalizing disorders (e.g., anxiety, depression) (Bussing, et al., 2010, Quinn, 2008, Romano, et al., 2005). Our population-based study showed that even with a diagnosis of ADHD, girls tended to have more internalizing disorders than boys; boys with ADHD were at higher risk for externalizing psychiatric comorbidities than girls. Levy et al. (Levy et al., 2005), however, reported no significant gender differences in comorbidity with ADHD and ODD/CD (externalizing) while anxiety disorders (internalizing) were more apparent in girls with ADHD. This might be partially due to a small number of CD cases that make results imprecise (Levy et al., 2005). Other studies on this issue have not always been consistent, probably due to differences in study design. Biederman et al. found that among children with ADHD referred to a psychiatric clinic, girls with ADHD were at lower

risk for comorbid major depression, CD, and ODD than boys with ADHD (Biederman, et al., 2002). In two other studies, the proportion of major DSM-IV or ICD-9 disorders did not differ between boys and girls with ADHD (Rucklidge & Tannock, 2001, Tai & Chiu, 2009). However, detailed analyses in the later (Tai & Chiu, 2009) showed that among children with ADHD, internalizing disorders (e.g., major or neurotic depression) were slightly more frequent in girls, while CD as an externalizing disorder was more frequent in boys, consistent with our findings.

We also found ADHD to be associated with *combined* externalizing-internalizing disorders (Figure 1). The coexistence of externalizing and internalizing disorders has been reported by others (Boylan, Vaillancourt, Boyle & Szatmari, 2007, Boylan, Georgiades & Szatmari, 2010, Romano, et al., 2005.). Cosgrove et al. reported in a twin study that co-occurrence of internalizing and externalizing psychopathology in adolescents resulted from both common genetic and non-shared environmental influences (Cosgrove, et al., 2011).

Several limitations should be considered when interpreting our findings. First, as this investigation is a retrospective cohort study in which the relevant information depended on retrospective review of medical and school records, the precise age of onset of ADHD among children in our sample was not possible to determine. Rather, we report the age at which sufficient information had been documented in the medical and school records to fulfill research criteria for ADHD. Therefore, it is difficult to ascertain whether ADHD developed in these children before they had recognizable symptoms of the comorbid psychiatric disorders. Second, it is possible that some comorbid psychiatric disorders were not identified. However, multiple independent complementary sources of data were used for the identification of these disorders. Third, the retrospective nature of this study and changes in the terminology for ADHD subtypes over time prevented us from obtaining precise information about ADHD subtypes. Thus, we were unable to address the issue of ADHD subtype on comorbidity and gender differences. Fourth, we did not have sufficient data to evaluate the severity of the psychiatric comorbidities. Finally, at the time of the study, Rochester, Minnesota was primarily a white, middle class community, so inferences to other populations or settings may be limited. However, the residents of Rochester have excellent access to medical care and comprise a homogeneous population (95% white) thereby minimizing the confounding effects of SES, ethnicity, and race on the study questions.

Conclusion

We found that ADHD is significantly associated with an increased risk for a broad range of psychiatric comorbidities. The strength of these associations did not differ between boys and girls. Furthermore, ADHD was primarily associated with co-existing externalizing-internalizing disorders. However, girls were significantly more likely to have internalizing disorders than boys regardless of ADHD status.

Clinicians should be aware that children and adolescents with ADHD are at significant risk for a wide range of psychiatric disorders. Screening for evaluating and managing such comorbid conditions will reduce the likelihood of the adverse social and emotional outcomes reported in the research literature. Furthermore, the burden on the families and on society as a whole will be lessened. Finally, our results emphasize the importance of remaining alert to the potential occurrence of internalizing and externalizing psychiatric disorders for both girls and boys as an essential element of comprehensive clinical care for children and adolescents with ADHD.

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Key points

- In spite of increased interest in adolescent psychiatric comorbidities of ADHD, evidence from non-referred samples is limited and the impact of gender has not been adequately addressed.
- To overcome these limitations, we used a population-based, longitudinally-followed birth cohort, to evaluate the associations between childhood ADHD and adolescent comorbid psychiatric disorders, and assess gender differences.
- We found ADHD to be associated with a significantly increased risk for a broad range of psychiatric comorbidities in both boys and girls; strength of these associations did not differ between them.

¹ None – no comorbid psychiatric disorder present

² Indeterminate – insufficient information

FIGURE 1.

Proportion of internalizing, externalizing, and combined disorders by ADHD status

¹ None – no comorbid psychiatric disorder present

² Indeterminate – insufficient information

Table 1Demographic and perinatal risk factors^a between children with and without ADHD

Factor	<i>N</i> missing	ADHD ^b (<i>N</i> = 343)	Non-ADHD ^b (<i>N</i> = 712)	<i>p</i> -value
Children				
Boys, <i>n</i> (%)	0	257 (74.9)	534 (75.0)	.98
White, <i>n</i> (%)	0	341 (99.4)	692 (97.2)	.02
Birth weight <2500 g, <i>n</i> (%)	0	16 (4.7)	19 (2.7)	.09
Parents				
Father's age, mean (SD)	49	28.6 (5.4)	29.2 (5.6)	.16
Mother's age, mean (SD)	0	26.0 (4.8)	26.8 (4.7)	< .01
Father White, <i>n</i> (%)	33	330 (99.4)	674 (97.7)	.05
Mother White, <i>n</i> (%)	0	342 (99.7)	696 (97.8)	.02
Married, <i>n</i> (%)	0	315 (91.8)	663 (93.1)	.45
Mother's education level, <i>n</i> (%)	107			
Less than high school graduate		24 (7.7)	43 (6.8)	.01
High school graduate		125 (39.9)	194 (30.6)	
Some college		105 (33.6)	222 (35.0)	
College graduate		59 (18.9)	176 (27.7)	
Pregnancy/Labor/Delivery				
Pregnancy complications, <i>n</i> (%)	0	33 (9.6)	57 (8.0)	.38
Labor/delivery complications, <i>n</i> (%)	0	124 (36.2)	252 (35.4)	.81
Congenital anomalies, <i>n</i> (%)	0	4 (1.1)	7 (1.0)	.76

^aComputerized birth certificate information for all birth cohort children were obtained from the Minnesota Department of Health.

^bResearch authorization among 379 ADHD cases and 758 non-ADHD controls was denied for 36 ADHD cases and 46 non-ADHD controls, yielding 343 ADHD cases and 712 non-ADHD controls.

Table 2

Distribution of medical professionals who confirmed the comorbid psychiatric diagnoses by 19 years of age and age confirmed

Psychiatric Disorder Category	No. of subjects with each disorder	Medical professional who confirmed the diagnosis		Age confirmed Mean (SD)
		Psychologist/psychiatrist N (%)	Other medical professionals ^a N (%)	
Adjustment disorders	183	166 (90.7)	17 (9.3)	12.5 (4.2)
ODD/CD	93	86 (92.5)	7 (7.5)	11.5 (4.4)
Mood disorders	121	106 (87.6)	15 (12.4)	15.9 (1.9)
Anxiety disorders	54	46 (85.2)	8 (14.8)	14.6 (3.7)
Tic disorders	10	5 (50.0)	5 (50.0)	11.2 (3.5)
Eating disorders	8	6 (75.0)	2 (25.0)	16.3 (1.3)
Impulse/control disorders	8	7 (87.5)	1 (12.5)	12.8 (5.4)
Personality disorders	7	6 (85.7)	1 (14.3)	15.5 (2.6)
Somatoform disorders	4	3 (75.0)	1 (25.0)	12.9 (4.6)
Substance-related disorders	109	106 (97.3)	3 (2.8)	16.7 (1.3)

^aOther medical professionals included: pediatricians, family physician, nurse practitioners, neurologists, emergency/critical care physicians.

Table 3
Burden of Comorbid Psychiatric Disorders^a among ADHD Cases and Controls, Overall and by Gender

Number of psychiatric disorders	ADHD			Non-ADHD		
	Overall (N=343)	Boys (N=257)	Girls (N=86)	Overall (N=712)	Boys (N=534)	Girls (N=178)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
0	130 (37.9)	94 (36.6)	36 (41.9)	580 (81.5)	438 (82.0)	142 (79.8)
1	95 (27.7)	73 (28.4)	22 (25.6)	77 (10.8)	55 (10.3)	22 (12.4)
2	76 (22.2)	58 (22.6)	18 (20.9)	36 (5.1)	27 (5.1)	9 (5.1)
3+	42 (12.2)	32 (12.5)	10 (11.6)	19 (2.7)	14 (2.6)	5 (2.8)
1 or more of the 10 disorders	213 (62.1)	163 (63.4)	50 (58.1)	132 (18.5)	96 (18.0)	36 (20.2)
2 or more of the 10 disorders	118 (34.4)	90 (35.0)	28 (32.6)	55 (7.7)	41 (7.7)	14 (7.9)

^a All comorbid psychiatric disorders were confirmed by age 19.

Table 4

Risk of Comorbid Psychiatric Disorders among ADHD Cases and Non-ADHD Controls

Psychiatric Disorder Category	ADHD (N=343)			Non-ADHD (N=712)			Gender × ADHD Interaction ^b , <i>p</i> -value
	Number diagnosed by age 19	Cumulative incidence by age 19 % (95% CI)	Number diagnosed by age 19	Cumulative incidence by age 19 % (95% CI)	ADHD/Non-ADHD Unadjusted HR (95% CI), <i>p</i> -value	ADHD/Non-ADHD Adjusted HR ^a (95% CI), <i>p</i> -value	
Adjustment disorders	115	34.5 (29.1–39.4)	68	10.2 (7.8–12.4)	4.01 (2.97–5.42), < .01	3.88 (2.82–5.33), < .01	.52
ODD/CD	75	22.5 (17.9–26.9)	18	2.7 (1.4–3.9)	9.50 (5.68–15.90), < .01	9.54 (5.33–17.05), < .01	.96
Mood disorders ^c	74	22.9 (18.2–27.4)	47	7.2 (5.2–9.1)	3.51 (2.44–5.06), < .01	3.67 (2.44–5.54), < .01	.88
Anxiety disorders ^d	31	9.6 (6.3–12.7)	23	3.5 (2.1–4.9)	2.84 (1.66–4.87), < .01	2.94 (1.64–5.24), < .01	.29
Tic disorders	6	1.8 (4–3.2)	4	0.6 (0–1.2)	3.07 (.87–10.88), .08	6.53 (1.29–33.03), .02	.71
Eating disorders	6	1.9 (4–3.3)	2	0.3 (0–0.7)	6.15 (1.24–30.47), .03	5.68 (1.14–28.21), .03	.67
Impulse control disorders	5	1.5 (2–2.9)	3	0.4 (0–0.9)	3.41 (.82–14.27), .09	1.49 (0.24–9.16), .67	.94
Personality disorders	5	1.5 (2–2.9)	2	0.3 (0–0.7)	5.12 (.99–26.38), .05	5.80 (1.12–30.04), .04	.15
Somatiform disorders	2	0.6 (0–1.5)	2	0.3 (0–0.7)	2.03 (.29–14.43), .48	1.96 (.27–14.14), .51	.51
Substance-related disorders	68	21.2 (16.6–25.5)	41	6.3 (4.4–8.1)	3.70 (2.51–5.46), < .01	4.03 (2.62–6.20), < .01	.85
Any psychiatric disorder	213	63.9 (58.3–68.7)	132	19.8 (16.7–22.8)	4.71 (3.79–5.86), < .01	4.89 (3.85–6.20), < .01	.34

^a Adjusted for sex, mother's age at birth, and mother's education level at birth. 107 subjects were not included in the model due to missing values for mother's education.^b *p*-value for gender × ADHD interaction from model which included gender, ADHD, mother's age at birth, mother's education level at birth, and gender × ADHD interaction.^c Major depressive disorder, depressive disorder, dysthymia, and bipolar disorders.^d General anxiety disorder, phobia, post-traumatic stress disorder, and obsessive-compulsive disorder.