Article

Adult Psychiatric Outcomes of Girls With Attention Deficit Hyperactivity Disorder: 11-Year Follow-Up in a Longitudinal Case-Control Study

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Objective: Few follow-up studies have been conducted of girls with ADHD, and none have followed girls into adulthood. The authors sought to estimate the prevalence of psychopathology in girls with and without ADHD followed into young adulthood.

Method: The authors conducted a longitudinal case-control study of 6- to 18-year-old girls with (N=140) and without (N=122) ADHD ascertained from psychiatric and pediatric sources. At the 11-year follow-up, 96 (69%) of the girls with ADHD and 91 (75%) of the comparison girls were reassessed (mean age=22 years). Participants were blindly assessed by structured diagnostic interviews.

Results: Lifetime and 1-year risks for all composite categories of psychopathology were significantly greater in girls with ADHD grown up relative to comparison girls; lifetime hazard ratios were 7.2 (95% CI=4.0–12.7) for antisocial disorders, 6.8 (95% CI=3.7–12.6) for mood disorders, 2.1 (95% CI=1.6–2.9) for anxiety disorders, 3.2 (95% CI=2.0–5.3) for developmental disorders, 2.7 (95% CI=1.6–4.3) for addictive disorders, and 3.5 (95% CI=1.6–7.3) for eating disorders. For lifetime psychopathology, all six composite categories remained statistically significant after controlling for other baseline psychopathology. Except for addictive disorders, significant 1-year findings remained significant after controlling for baseline psychopathology. The 1-year prevalences of composite disorders were not associated with lifetime or 1-year use of ADHD medication.

Conclusions: By young adulthood, girls with ADHD were at high risk for antisocial, addictive, mood, anxiety, and eating disorders. These prospective findings, previously documented in boys with ADHD, provide further evidence for the high morbidity associated with ADHD across the life cycle.

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Although attention deficit hyperactivity disorder (ADHD) is more prevalent in boys than in girls, there is little doubt that it is also an important cause of psychiatric disability in girls (1, 2). Yet, the scientific literature on girls with ADHD is scarce and mostly cross-sectional.

Mikami and Hinshaw (3) showed that girls with ADHD have more disruptive behaviors compared with girls who do not have ADHD. In a previous study, we compared 140 girls with ADHD and 122 comparison girls without ADHD and found that those with ADHD were more likely to have conduct, mood, and anxiety disorders (4). Similar findings were reported in a study of 140 girls with ADHD and 88 comparison girls by Hinshaw (5), who found associations between ADHD and mood and anxiety problems, disruptive behaviors, and language problems in girls with ADHD.

Because almost all the available literature on follow-up studies of ADHD is limited to studies of boys, there is a scarcity of follow-up studies of girls with ADHD. The first follow-up study of girls compared 12 girls and 24 boys with a DSM-II diagnosis of hyperactivity and 24 male comparison subjects (6). In a community survey (7), girls identified at baseline as hyperactive were more likely to report academic and interpersonal relationship problems at the adolescent follow-up. We reported results of a 5-year follow-up study into the mid-adolescent years from a sample of girls with DSM-III-R-defined ADHD and comparison subjects (8). Girls with ADHD were at significantly higher risk for disruptive behavior and mood, anxiety, and addictive disorders in adolescence. Hinshaw et al. (9) and Owens et al. (10) reported similar findings in girls followed into adolescence; the majority of girls with ADHD continued to struggle with functional impairments across multiple domains. Although these follow-up studies documented the high morbidity and disability associated with ADHD in girls, no information is available on whether these findings extend to adulthood.

Understanding of outcomes of girls with ADHD in adulthood has clinical and public health implications. Clinically, such information would help in prognosis and would alert clinicians to the importance of recognizing ADHD

This article is featured in this month's AJP Audio and is the subject of a CME course (p. 483).

TABLE 1. Baseline Characteristics of Girls With ADHD and Comparison Girls, Stratified by Attrition Status

Characteristic	Lost to Follow-Up		Assessed at Follow-Up	
	Girls with ADHD (N=44)		**Girls with ADHD (N=96)**	
	Mean	SD	Mean	SD
Hollingshead socioeconomic scale score	1.8	0.8	1.9	1.0
Age (years)	11.7	3.7	11.0	3.2
Lifetime Global Assessment of Functioning Scale score	55.5	6.9	54.1	6.6
	N	%	N	%
Caucasian	39	89	93	97
Intact family	31	70	70	73
Ascertained in major academic medical center[a]	19	43	44	46
Conduct disorder	2	5	9	9
Major depressive disorder	6	14	18	19
Any anxiety disorder	29	66	56	58
	Comparison girls (N=31)		**Comparison girls (N=91)**	
	Mean	SD	Mean	SD
Hollingshead socioeconomic scale score	1.8	0.7	1.7	0.8
Age (years)	12.9	3.4	12.0	2.8
Lifetime Global Assessment of Functioning Scale score	67.8	6.2	67.4	5.8
	N	%	N	%
Caucasian	29	94	79	87
Intact family	23	74	77	85
Ascertained in major academic medical center[a]	15	48	40	44
Conduct disorder	0	0	0	0
Major depressive disorder	0	0	1	1
Any anxiety disorder	6	19	22	24

[a] Study participants were ascertained either in a major academic medical center (pediatric psychopharmacology clinic for patients with ADHD and pediatric outpatient medical clinic for comparison subjects) or in the pediatric clinics of a major health maintenance organization.

and associated comorbid disorders in girls for treatment planning and early intervention strategies. From a public health perspective, the ability to predict the outcome of ADHD in girls would help focus limited resources on those individuals who are at higher risk for persistent illness with complicated outcomes.

Here we report results from an 11-year longitudinal study of psychiatrically and pediatrically referred girls with and without ADHD followed into young adulthood. Our main aim was to estimate the burden of psychopathology associated with ADHD in young adulthood. We hypothesized that girls with ADHD would show greater rates of disruptive behavior and mood and anxiety disorders than girls without ADHD. To our knowledge, this is the first prospective study of girls with ADHD followed into young adulthood.

Method

Participants

Details of the study methods have been reported elsewhere (4, 8). Participants were from a longitudinal case-control family study of girls with and without ADHD. At baseline, we ascertained girls 6–17 years of age with (N=140) and without (N=122) DSM-III-R-defined ADHD from pediatric and psychiatric clinics. We excluded patients who had been adopted, those whose nuclear family was not available for study, and those who had major sensorimotor disabilities (paralysis, deafness, blindness), psychosis, autism, inadequate command of the English language, or a full-scale IQ below 80. All girls in the ADHD group met DSM-III-R criteria for ADHD at the time of the clinical referral, and all had active symptoms of the disorder at the time of recruitment. Participants were recruited irrespective of comorbid disorders.

In this study, we analyzed data on 96 girls with ADHD and 91 comparison girls from the original sample who completed a full follow-up assessment a mean of 11 years (range=8 to 14 years) after enrollment. Participants ranged from 15 to 30 years of age (mean=22.1 years, SD=3.3) at follow-up. Eighty-three (86%) of the girls in the ADHD group and 90 (99%) of those in the comparison group had reached age 18 by the 11-year follow-up. Participants provided written informed consent, and parents also provided consent for offspring under the age of 18 and for their report on their offspring. Adolescents provided written assent to participate. The human research committee at Massachusetts General Hospital approved this study.

Follow-Up Assessment Procedures

We used the Structured Clinical Interview for DSM-IV (SCID) (11) supplemented with modules from the DSM-IV modified Schedule for Affective Disorders and Schizophrenia for School-Age Children–Epidemiologic Version (K-SADS-E) (12) to assess childhood diagnoses. The K-SADS-E was used for participants under age 18. We interviewed all participants and interviewed their mothers about their offspring. Of the 187 girls for whom a full diagnostic interview was conducted, the proportion for whom we had direct only, mother only, and both types of reports were 89%, 3%, and 8%, respectively (47%, 3%, and 50%, respectively, for the ADHD module). We combined data from direct and indirect interviews by considering a diagnostic criterion positive if it was endorsed in either interview.

Interviewers were blind to baseline ascertainment group, ascertainment site, and prior assessments. They had undergraduate degrees in psychology and were extensively trained. The principal investigator (J.B.) supervised them throughout the study. Kappa coefficients between interviewers and board-certified child and

TABLE 2. Demographic Characteristics of Girls With ADHD and Comparison Girls at 11-Year Follow-Up

Characteristic	Comparison Girls (N=91)		Girls With ADHD (N=96)	
	Mean	SD	Mean	SD
Age (years)[a]	22.7	2.9	21.6	3.6
Follow-up time (years)	10.7	1.3	10.6	1.2
Hollingshead socioeconomic scale score	1.9	0.8	2.1	0.9
	N	%	N	%
Ethnicity/race				
African American	4	4	1	1
Caucasian	80	88	93	97
Asian American	2	2	0	0
More than one	5	5	2	2
Ascertained in major academic medical center[b]	34	37	39	41

[a] Significant difference between groups, $p<0.05$.

[b] Study participants were ascertained either in a major academic medical center (pediatric psychopharmacology clinic for patients with ADHD and pediatric outpatient medical clinic for comparison subjects) or in the pediatric clinics of a major health maintenance organization.

adult psychiatrists and licensed clinical psychologists have been reported elsewhere (8); the median kappa coefficient for individual disorders was 0.98.

We considered a disorder present if DSM-IV diagnostic criteria were unequivocally met. Diagnostic uncertainties were resolved by a committee of board-certified child and adult psychiatrists and child psychologists blind to the participant's ADHD status, referral source, and all other data. Diagnoses presented for review were considered positive only if diagnostic criteria were met to a clinically meaningful degree. We estimated the reliability of the diagnostic review process by computing kappa coefficients of agreement for clinician reviewers. Kappa coefficients between individual clinicians and the review committee have been reported elsewhere (8); the median kappa coefficient for individual disorders was 0.87. Participants were asked to describe the degree of impairment in daily functioning associated with each positive disorder on a three-level ordinal scale: minimal (little to no impairment), moderate (difficulties in daily life tasks), or severe (unable to perform essential daily tasks). To avoid false positive diagnoses, we diagnosed major depression only if it was associated with severe impairment. This is consistent with prior research (13) and comparable to what we did at prior assessments. Because there is not a similar precedent for bipolar disorder, we adopted a less stringent approach and made the diagnosis only when symptoms were associated with at least moderate impairment.

Persistent ADHD was defined as meeting full or subthreshold criteria for DSM-IV ADHD during the interval between the 5-year and 11-year assessments. Participants were defined as having subthreshold ADHD if they endorsed more than half of, but less than full, diagnostic criteria (i.e., four or five ADHD symptoms) but met all other diagnostic requirements (e.g., age at onset). Socioeconomic status was measured with the 5-point Hollingshead scale (14). To measure overall lifetime functioning, we used the DSM-IV Global Assessment of Functioning Scale (GAF) (12).

Statistical Analysis

Analyses of demographic factors relied on Pearson chi-square tests and t tests for binary and dimensional variables, respectively. We examined psychopathology throughout the lifespan and within the past year (1-year prevalence), using a three-pronged strategy to avoid the inflated type I error rate that could result from multiple statistical testing. First, to decrease the initial number of tests, we aggregated diagnostic outcomes into composite categories: mood disorders comprised major depression and bipolar disorder; anxiety disorders comprised separation anxiety, panic disorder, agoraphobia, specific phobia, social phobia, generalized anxiety disorder, and obsessive-compulsive disorder (separation anxiety was not included in the analysis of 1-year outcomes); antisocial disorders comprised conduct disorder, oppositional defiant disorder, and antisocial personality disorder; developmental disorders comprised enuresis, encopresis, language disorder, and Tourette's/tic disorders (developmental disorders were not included in the analysis of 1-year prevalences); substance dependence comprised alcohol dependence, drug dependence, and nicotine dependence; and eating disorders comprised full or subthreshold anorexia nervosa and bulimia nervosa. These summary disorders were coded positive if any of the constituent diagnoses were endorsed, and negative otherwise.

Second, we conducted a set of six tests (the six composite diagnostic categories) that each compared the ADHD and comparison groups using Holm's sequential Bonferroni method (15) to correct for multiple testing and maintain a family-wise error rate of 0.05. Third, for any composite category that was significant, we tested each of the constituent diagnoses using Holm's method.

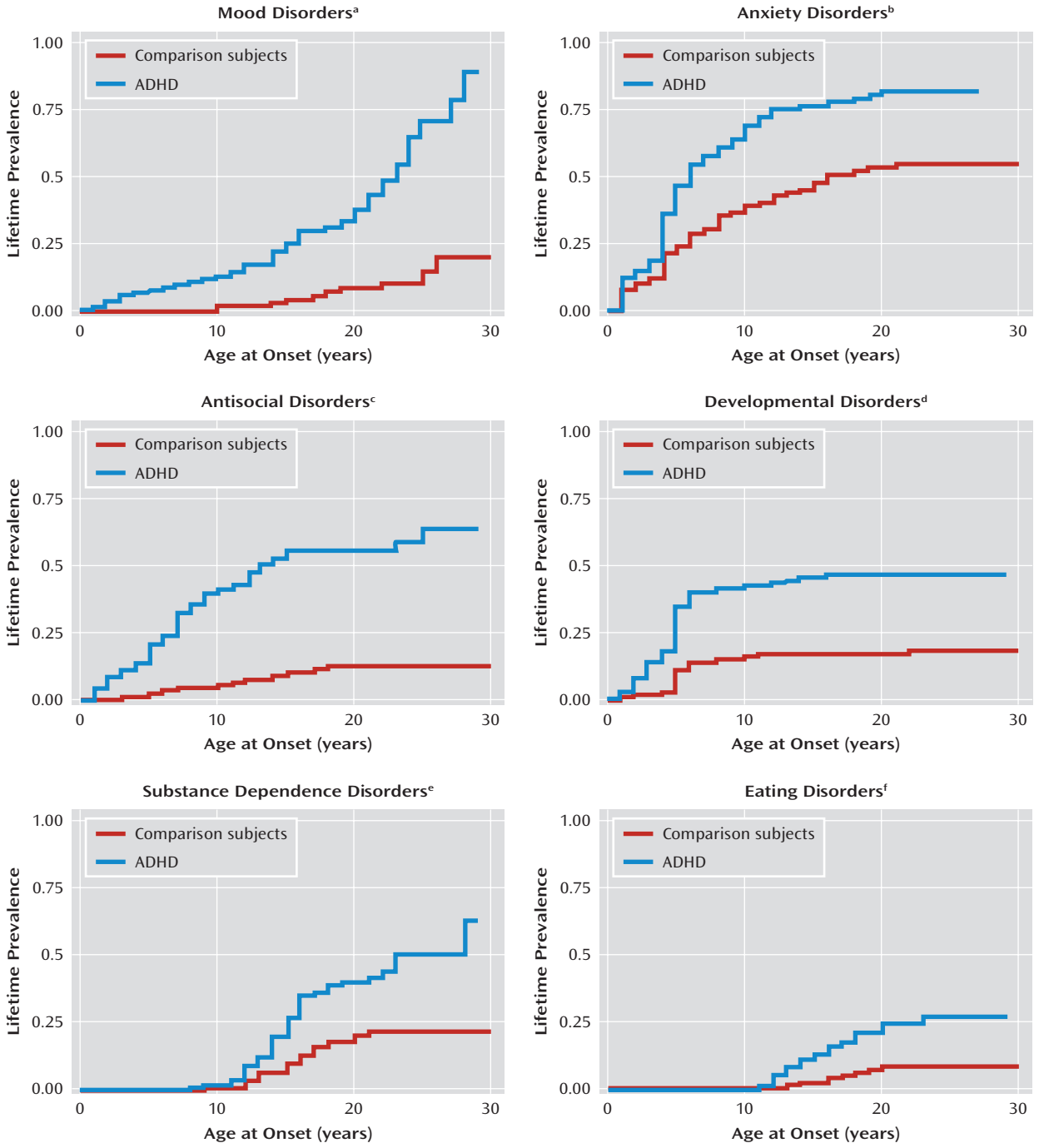
To estimate the lifetime prevalence of psychopathology, we used Cox proportional hazards survival models. For each disorder, lifetime history of any disorder was defined as positive if a positive response was given at any assessment (baseline, 5-year follow-up, or 11-year follow-up). These models used all available data for each participant, including those not assessed at the 11-year follow-up; thus, all 262 girls are included. We used the earliest age at onset in computing the survival time for case subjects and the age at the most recent interview as the time of censoring for noncase subjects. To estimate cumulative prevalence, we calculated Kaplan-Meier morbidity risks in the ADHD and comparison groups up to age 22 (the mean age of the sample). For the 1-year prevalence analysis, we used logistic regression to compare the ADHD and comparison groups. One-year prevalence was defined as positive if the participant met criteria for a given disorder in the year prior to the 11-year follow-up.

Results

Participant Characteristics

Of the 140 girls with ADHD and 122 comparison girls recruited at baseline, 96 (69%) and 91 (75%), respectively, were reassessed at the 11-year follow-up. The follow-up rate did not differ between the groups. There were no significant differences between girls successfully followed up and those lost to follow-up on socioeconomic status, age, race, GAF score, familial intactness, ascertainment source, or psychiatric outcomes (Table 1). At the 11-year follow-up, girls in the ADHD group were on average 1 year young-

FIGURE 1. Cumulative Risks for Disorders in Girls With ADHD Relative to Comparison Girls for Six Composite Diagnostic Categories



[a] Hazard ratio=6.8, 95% CI=3.7–12.6, p<0.001.
[b] Hazard ratio=2.1, 95% CI=1.6–2.9, p<0.001.
[c] Hazard ratio=7.2, 95% CI=4.0–12.7, p<0.001.
[d] Hazard ratio=3.2, 95% CI=2.0–5.3, p<0.001.
[e] Hazard ratio=2.7, 95% CI=1.6–4.3, p<0.001.
[f] Hazard ratio=3.5, 95% CI=1.6–7.3, p=0.001.

er than comparison girls (Table 2). Survival models for lifetime disorders accounted for this difference in age, and age was used as a covariate in logistic regression models of 1-year prevalence. At the 11-year follow-up, 93% of the girls in the ADHD group had received some form of treatment for ADHD during their lives; 1% received counseling alone (N=1), 21% received medication alone (N=20), and 71% (N=68) received both counseling and medication. During the 1-year period before the 11-year follow-up assessment, 42% were receiving some form of treatment

TABLE 3. Cumulative Morbidity Risks and Hazard Ratios for Psychiatric Disorders in Girls With ADHD and Comparison Girls

	Comparison Girls (N=122)		Girls With ADHD (N=140)		Analysis			
Disorder	Morbidity Risk[a]	95% CI	Morbidity Risk[a]	95% CI	Hazard Ratio	95% CI	Test Statistic	p
Mood disorders								
Major depressive disorder (with severe impairment)	0.08	0.04–0.16	0.34	0.26–0.45	5.8	3.0–11.0	z=5.32	<0.001
Bipolar disorder (with moderate or severe impairment)	0.03	0.01–0.08	0.25	0.18–0.34	10.7	3.3–35.1	z=3.92	<0.001
Anxiety disorders								
Separation anxiety disorder	0.16	0.11–0.24	0.39	0.31–0.48	2.7	1.6–4.5	z=3.80	<0.001
Agoraphobia	0.10	0.06–0.17	0.40	0.31–0.49	4.7	2.5–8.9	z=4.85	<0.001
Social phobia	0.20	0.14–0.29	0.46	0.37–0.56	2.8	1.7–4.5	z=4.10	<0.001
Obsessive-compulsive disorder	0.05	0.02–0.12	0.11	0.07–0.18	2.3	0.9–5.9	z=1.67	0.09
Specific phobia	0.28	0.21–0.37	0.56	0.47–0.65	2.3	1.6–3.5	z=4.05	<0.001
Panic disorder	0.15	0.09–0.23	0.30	0.22–0.40	2.4	1.3–4.3	z=2.97	0.003
Generalized anxiety disorder	0.13	0.08–0.21	0.35	0.27–0.45	3.4	1.8–6.1	z=3.93	<0.001
Antisocial disorders								
Oppositional-defiant disorder	0.10	0.06–0.18	0.55	0.47–0.63	8.0	4.4–14.8	z=6.68	<0.001
Conduct disorder	0.03	0.01–0.08	0.26	0.19–0.35	12.1	3.7–39.3	z=4.13	<0.001
Antisocial personality disorder[b]	0.01	0.001–0.07	0.11	0.06–0.20	14.4	1.9–109.9	z=2.57	0.01
Developmental disorders								
Tourette's/tic disorders	0.07	0.03–0.14	0.21	0.14–0.29	3.8	1.6–8.7	z=3.12	0.002
Language disorder	0.03	0.01–0.08	0.17	0.12–0.25	5.7	2.0–16.4	z=3.24	0.001
Enuresis	0.09	0.05–0.16	0.28	0.21–0.36	3.3	1.7–6.4	z=3.46	0.001
Encopresis	0.00	—	0.05	0.02–0.10	NA[c]	NA[c]	χ^2=6.27	0.01
Substance dependence disorders								
Nicotine dependence	0.18	0.12–0.27	0.37	0.29–0.47	2.6	1.5–4.5	z=3.53	<0.001
Alcohol dependence	0.08	0.04–0.16	0.18	0.11–0.28	2.4	1.1–5.6	z=2.10	0.04
Drug dependence	0.07	0.03–0.13	0.24	0.17–0.35	3.7	1.6–8.6	z=3.05	0.002
Eating disorders								
Anorexia nervosa	0.06	0.03–0.12	0.11	0.07–0.18	2.2	0.8–5.7	z=1.58	0.11
Bulimia nervosa	0.05	0.02–0.12	0.20	0.13–0.30	5.2	2.0–13.7	z=3.36	0.001

[a] Cumulative morbidity risk of disorder by age 22 as estimated by Kaplan-Meier failure function.
[b] Estimates based only on participants who were interviewed with the Structured Clinical Interview for DSM-IV at least once.
[c] Not available because there were no comparison subjects with encopresis; Pearson's chi-squared test was used instead.

for the disorder; 17% (N=16) were receiving medication alone and 25% (N=24) were receiving both counseling and medication. Among the 96 girls in the ADHD group reascertained at the 11-year follow-up, the rate of full or subthreshold ADHD during the interval between the year 5 and year 11 assessments was 69% (N=66), and the rate of current (i.e., in the past month) full or subthreshold DSM-IV ADHD was 62% (N=60).

Risk for Lifetime Psychiatric Disorders

The risks for all six composite lifetime diagnostic categories were higher in the ADHD group than in the comparison group; hazard ratios were 6.8 (95% CI=3.7–12.6) for mood disorders, 2.1 (95% CI=1.6–2.9) for anxiety disorders, 7.2 (95% CI=4.0–12.7) for antisocial disorders, 3.2 (95% CI=2.0–5.3) for developmental disorders, 2.7 (95% CI=1.6–4.3) for substance dependence disorders, and 3.5 (95% CI=1.6–7.3) for eating disorders (Figure 1). All six composite categories remained statistically significant after controlling for baseline psychopathology for each of the other four categories.

ADHD girls had significantly higher lifetime prevalences of major depression, bipolar disorder, separation anxiety disorder, agoraphobia, social phobia, specific phobia, panic disorder, generalized anxiety disorder, oppositional defiant disorder, conduct disorder, antisocial personality disorder, Tourette's/tic disorders, language disorder, enuresis, encopresis, nicotine dependence, alcohol dependence, drug dependence, and bulimia nervosa (Table 3). However, when we corrected for other baseline psychopathology, the lifetime risks for encopresis, nicotine dependence, alcohol dependence, and drug dependence lost statistical significance.

Risks for 1-Year Psychiatric Disorders

The ADHD group had significantly higher 1-year prevalences of composite mood, anxiety, antisocial, and substance dependence disorders relative to the comparison group (Table 4). The 1-year prevalence of eating disorders was not significantly different between the ADHD and comparison groups (7% versus 3%, z=1.07, p=0.29). Except for substance dependence disorders (p=0.07),

TABLE 4. Adjusted 1-Year Prevalence Estimates for Psychiatric Disorders in ADHD and Comparison Subjects at the 11-Year Follow-Up

					Analysis			
	Comparison Group (N=91)		ADHD Group (N=96)		Controlling for Age		Controlling for Age and Baseline Psychopathology[a]	
Disorder	Prevalence	95% CI	Prevalence	95% CI	Test Statistic[b]	p	Test Statistic[b]	p
Mood disorders	0.07	0.03–0.14	0.23	0.15–0.32	z=2.91	0.004	z=2.23	0.03
Major depressive disorder (with severe impairment)	0.07	0.03–0.14	0.20	0.13–0.29	z=2.47	0.014	z=1.77	0.08
Bipolar disorder (with moderate or severe impairment)	0.01	0.002–0.07	0.07	0.03–0.15	z=1.78	0.08	z=1.50	0.13
Anxiety disorders	0.21	0.14–0.31	0.47	0.37–0.57	z=3.49	<0.001	z=2.83	0.006
Agoraphobia	0.02	0.01–0.08	0.25	0.18–0.35	z=3.60	<0.001	z=3.46	0.001
Social phobia	0.07	0.03–0.14	0.20	0.13–0.29	z=2.57	0.010	z=2.34	0.02
Obsessive-compulsive disorder	0.04	0.02–0.11	0.07	0.03–0.14	z=0.69	0.49	z=0.16	0.87
Specific phobia	0.07	0.03–0.14	0.14	0.08–0.22	z=1.64	0.10	z=1.84	0.06
Panic disorder	0.08	0.04–0.15	0.15	0.09–0.24	z=1.35	0.18	z=1.46	0.14
Generalized anxiety disorder	0.03	0.01–0.10	0.13	0.07–0.21	z=2.15	0.03	z=2.48	0.013
Antisocial disorders	0.04	0.02–0.11	0.21	0.14–0.31	z=3.03	0.002	z=2.37	0.02
Oppositional-defiant disorder	0.04	0.02–0.11	0.17	0.10–0.26	z=2.47	0.01	z=1.67	0.10
Conduct disorder	0.00	—	0.03	0.01–0.16	Exact	0.48	Exact	1.00
Antisocial personality disorder[d]	0.00	—	0.06	0.02–0.14	Exact	0.04	Exact	0.10
Substance dependence disorders	0.07	0.04–0.15	0.31	0.22–0.41	z=3.73	<0.001	z=1.80	0.07
Nicotine dependence	0.04	0.02–0.11	0.17	0.11–0.26	z=2.55	0.011	z=1.58	0.11
Alcohol dependence	0.05	0.02–0.12	0.11	0.06–0.20	z=1.57	0.12	z=–0.06	0.95
Drug dependence	0.02	0.01–0.08	0.07	0.04–0.15	z=1.56	0.12	z=0.08	0.93
Eating disorders	0.03	0.01–0.10	0.07	0.03–0.14	z=1.07	0.29	z=0.91	0.36
Anorexia nervosa	0.01	0.001–0.08	0.00	—	Exact	1.00	Exact	1.00
Bulimia nervosa	0.02	0.01–0.09	0.07	0.03–0.14	z=1.42	0.16	z=1.42	0.16

[a] Baseline status of the disorder predicted at follow-up and baseline values of the other composite categories (except substance dependence and eating disorders).

[b] Exact=exact logistic regression, used in lieu of logistic regression.

[c] Estimates based only on participants who were interviewed with the Structured Clinical Interview for DSM-IV at least once.

significant findings remained significant after controlling for all baseline psychopathology (i.e., baseline mood, anxiety, and antisocial disorders), including the baseline status of the disorder predicted at follow-up. Corrections for baseline psychopathology in this latter analysis did not include eating disorders or substance dependence at baseline because they were rare at baseline (N=5 and N=9, respectively).

Similar findings were observed for 1-year rates of individual disorders. The rates of major depression, agoraphobia, social phobia, oppositional defiant disorder, and nicotine dependence were higher in the ADHD group relative to the comparison group (Table 4). However, when findings were adjusted for baseline psychopathology (including the baseline status of the disorder predicted at follow-up), only agoraphobia remained statistically significant ($p<0.001$). The 1-year prevalences of composite psychiatric disorders were not associated with lifetime or 1-year medication use for ADHD.

Discussion

This is the first follow-up study of girls with ADHD into young adulthood and the longest follow-up study of girls with ADHD (11 years). By a mean age of 22 years, 62% of girls with ADHD continued to have impairing ADHD symptoms, which is consistent with a meta-analysis of ADHD follow-up studies (16). They also had significantly greater lifetime and 1-year risks for antisocial, mood, and anxiety disorders relative to comparison subjects, even after correcting for baseline psychopathology. These results extend to girls findings that were previously documented in boys (17), stressing the significant psychiatric morbidity associated with ADHD in both sexes across the lifespan. They also stress the critical importance of early recognition of this disorder for prevention and early intervention strategies.

Strengths of this study include the large sample of well-characterized girls with and without ADHD and the long follow-up into young adulthood. This is especially important since few studies have followed youths with ADHD into adulthood, and none has examined girls with ADHD. The lifetime prevalences of psychiatric disorders in the comparison girls are consistent with the prevalences of psychiatric disorders reported in epidemiological studies (18), supporting the validity of the assessment methodology.

Comparisons of 1-year prevalence estimates between this study and our study of boys with ADHD (17) reveal a similar pattern of risk for comorbid disorders, which could

not be accounted for by either lifetime or 1-year medication use for ADHD. Notable differences include a higher rate of antisocial personality disorder in boys with ADHD grown up compared with girls with ADHD grown up (13% and 6%, respectively) and higher rates of major depressive disorder and anxiety disorders in girls with ADHD grown up compared with boys with ADHD grown up (major depressive disorder, 20% and 8%, respectively; agoraphobia, 25% and 3%, respectively; social phobia, 20% and 4%, respectively). Although boys and girls with ADHD share significant risks for a variety of comorbid disorders, these rates identify different profiles of comorbidity between the sexes in young adulthood.

Our finding that girls with ADHD had significantly greater risks for antisocial disorders, major depression, and anxiety disorders in young adulthood is consistent with the results we obtained at the adolescent follow-up assessment (8). They are also consistent with Hinshaw and colleagues' report (9) of elevated rates of externalizing and internalizing disorders in girls with ADHD followed into adolescence. Our results at the adolescent follow-up showed lifetime prevalence rates up to age 25 (8), while the present analysis shows rates up to age 30. Although lifetime rates of antisocial and anxiety disorders were shown to flatten by age 25, rates of mood disorders continued to climb between ages 25 and 30 (Figure 1). Therefore, some comorbidities associated with ADHD in girls do not develop until after age 25, which highlights the importance of following this population into adulthood.

The increasing risk for major depression into young adulthood confirms epidemiological surveys (19), family study data (20–23), studies of adults with ADHD (24), and meta-analytic studies (25) showing that ADHD is a significant risk factor for major depression. Our findings also confirm studies of referred female adults with ADHD (24, 26), as well as a report from the National Comorbidity Survey Replication study's representative sample of the U.S. population, which documented elevated rates of major depression and antisocial, addictive, and anxiety disorders in adults with ADHD relative to comparison subjects (27).

Our findings about bipolar disorder are particularly interesting given controversies about diagnosing the disorder in children, especially those with ADHD, and about discriminating manic symptoms from severe chronic irritability, hyperarousal, and hyperreactivity (28, 29). Reports of comorbidity between ADHD and bipolar disorder have been questioned because some diagnostic criteria are shared by both disorders. Thus, it is possible that the comorbidity of bipolar disorder and ADHD is due to overlapping diagnostic criteria. However, when Milberger et al. (30) accounted for overlapping diagnostic criteria, they continued to find significant comorbidity between the two disorders.

Despite ongoing controversy about the diagnosis of pediatric bipolar disorder, these concerns should be interpreted in the context of a large emerging literature supporting the validity of diagnosing bipolar disorder in youths and the fact that two medications, risperidone and aripiprazole, have already gained approval from the U.S. Food and Drug Administration for the treatment of pediatric bipolar disorder as monotherapy. Notably, a practice parameter from the American Academy of Child and Adolescent Psychiatry (31) and two independent reviews of phenomenological, longitudinal, treatment-response, neuroimaging, neuropsychological, and genetic studies (32, 33) concluded that bipolar disorder can be validly diagnosed in youths. This literature also shows that pediatric bipolar disorder is frequently persistent, is highly morbid, is commonly associated with significant functional impairment in multiple domains, and is associated with elevated risks for psychiatric hospitalization, antisocial behaviors, addictions, and suicidal ideation. The review by Geller and Tillman (33) is of particular interest because it showed that pediatric bipolar disorder meets the Robins and Guze criteria for a valid psychiatric disorder.

Our work adds to this literature by reporting that girls with ADHD grown up continue to have an increased risk for bipolar disorder. This finding confirms results from our adolescent follow-up (8, 34) and is consistent with our studies of female adults with ADHD (24, 26). It is also consistent with results from the National Comorbidity Survey Replication study (27) documenting a significant and bidirectional association between ADHD and bipolar disorder in adults of both sexes. Moreover, this overrepresentation of bipolar disorder in girls with ADHD grown up is consistent with studies of pediatric (35) and adult ADHD samples (24) as well as studies of bipolar children (36) and adults (37) documenting a bidirectional association between ADHD and bipolar disorder in both sexes across the lifespan.

The finding that girls with ADHD had an elevated risk for eating disorders in adulthood confirms our report from the 5-year follow-up (8) and Hinshaw and colleagues' (9) finding of elevated eating disorder symptoms in their adolescent follow-up study of girls with ADHD. Studies of adult females have also found an elevated prevalence of bulimia in females with ADHD (24). These results should alert clinicians to a need to monitor young female patients with ADHD for eating disorder pathology.

Our results must be interpreted in the context of methodological limitations. Our lifetime psychopathology outcomes are potentially subject to recall bias, especially in the context of comorbidity. However, in our own work, lifetime diagnoses have shown excellent interrater reliability, as noted in the Method section, and good to excellent test-retest reliability over 1 year (38). Because our diagnoses of ADHD in some participants relied on self-report, our estimates of prevalence may be lower than they would have been if reports from parents or spouses had been incorporated. Because our sample was referred and mostly Caucasian, our results may not be generalizable to the general population or to other racial or ethnic groups. However, our results

should generalize to ADHD girls seen in pediatric and psychiatric settings. Because we did not manipulate treatment as an independent variable, we cannot use our study to determine treatment effectiveness (39) or to describe the untreated course of ADHD. While our main aim was to assess the outcome of ADHD girls in young adulthood, a small portion of our sample had not yet reached adulthood. Our sample was originally ascertained according to DSM-III-R criteria, and it is possible that our results may not generalize to samples ascertained by DSM-IV criteria. However, considering the very high overlap between the two definitions (93% of DSM-III-R cases received a DSM-IV diagnosis [40]), any effect should be minimal.

Despite these limitations, in a large sample of girls with and without ADHD followed into young adulthood originally ascertained from pediatric and psychiatric sources, our 11-year follow-up confirms and extends results from the baseline and mid-adolescent assessments. We observed a strong association between ADHD and lifetime risks for antisocial, mood, anxiety, developmental, and substance dependence disorders at the 11-year follow-up. These data provide further evidence for the morbidity and disability associated with ADHD from childhood into young adulthood in individuals of both sexes with ADHD.

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