

Clinical and Functional Outcome of Childhood Attention-Deficit/Hyperactivity Disorder 33 Years Later

Rachel G. Klein, PhD; Salvatore Mannuzza, PhD; María A. Ramos Olazagasti, PhD; Erica Roizen, MS; Jesse A. Hutchison, BA; Erin C. Lashua, MA; F. Xavier Castellanos, MD

Context: Prospective studies of childhood attention-deficit/hyperactivity disorder (ADHD) have not extended beyond early adulthood.

Objective: To examine whether children diagnosed as having ADHD at a mean age of 8 years (probands) have worse educational, occupational, economic, social, and marital outcomes and higher rates of ongoing ADHD, antisocial personality disorder (ASPD), substance use disorders (SUDs), adult-onset psychiatric disorders, psychiatric hospitalizations, and incarcerations than non-ADHD comparison participants at a mean age of 41 years.

Design: Prospective, 33-year follow-up study, with masked clinical assessments.

Setting: Research clinic.

Participants: A total of 135 white men with ADHD in childhood, free of conduct disorder, and 136 men without childhood ADHD (65.2% and 76.4% of original cohort, respectively).

Main Outcome Measures: Occupational, economic, and educational attainment; marital history; occupational and social functioning; ongoing and lifetime psychiatric disorders; psychiatric hospitalizations; and incarcerations.

Results: Probands had significantly worse educational, occupational, economic, and social outcomes; more divorces; and higher rates of ongoing ADHD (22.2% vs 5.1%, $P < .001$), ASPD (16.3% vs 0%, $P < .001$), and SUDs (14.1% vs 5.1%, $P = .01$) but not more mood or anxiety disorders ($P = .36$ and $.33$) than did comparison participants. Ongoing ADHD was weakly related to ongoing SUDs ($\phi = 0.19$, $P = .04$), as well as ASPD with SUDs ($\phi = 0.20$, $P = .04$). During their lifetime, probands had significantly more ASPD and SUDs but not mood or anxiety disorders and more psychiatric hospitalizations and incarcerations than comparison participants. Relative to comparisons, psychiatric disorders with onsets at 21 years or older were not significantly elevated in probands. Probands without ongoing psychiatric disorders had worse social, but not occupational, functioning.

Conclusions: The multiple disadvantages predicted by childhood ADHD well into adulthood began in adolescence, without increased onsets of new disorders after 20 years of age. Findings highlight the importance of extended monitoring and treatment of children with ADHD.

Arch Gen Psychiatry. 2012;69(12):1295-1303.

Published online October 15, 2012.

doi:10.1001/archgenpsychiatry.2012.271

VIRTUALLY ALL AREAS OF adjustment have been found to be deficient in children with attention-deficit/hyperactivity disorder (ADHD), which has an estimated worldwide prevalence of 5%.¹ Consequently, the long-term outcome of childhood ADHD is a major concern. Previously, conventional wisdom held that ADHD symptoms dissipated by adolescence. However, controlled longitudinal studies have documented elevated rates of ADHD and conduct disorder, as well as multiple other dysfunctions, in adolescence.²⁻⁶

Five prospective investigations followed up preadolescents with ADHD into early adulthood (ages 21-27 years).⁶⁻¹² All

found higher rates of ADHD symptoms and antisocial personality disorders (ASPDs) in those with childhood ADHD compared with those without ADHD. In early adulthood (mean age, 25 years), we found a relative increase of non-alcohol-related substance disorders (SUDs) in probands but only in those who had developed conduct disorder during adolescence.^{9,12}

The few prospective, controlled studies have not gone beyond the third decade of life. Knowledge beyond this developmental period has been inferred from clinically referred adults diagnosed as having ADHD, whose reports of early ADHD symptoms relied on recall, which problematically has limited accuracy.^{13,14} Nevertheless, cross-sectional studies of indi-

Author Affiliations are listed at the end of this article.

viduals whose conditions were first diagnosed in adulthood indicate that ADHD occurs in adults and suggest associated disabilities and comorbidities. However, such studies do not document the frequency and range of outcomes into adulthood because dysfunctions may attenuate over time or new disorders may emerge. Functional impairment caused by childhood ADHD may vary through life because adults, unlike adolescents, are not as confined by standardized demands, such as those in school. Adults may modify their environment through occupational choices and selection of significant others. Therefore, the negative consequences of ADHD may be minimized in later life. Alternatively, new or more complex adult demands may aggravate the effect of persistent ADHD.

This report presents the adult outcome (follow-up at the mean age of 41 years [referred to as FU41]) of boys (mean age, 8 years) who were diagnosed as having ADHD (probands). Two previous follow-ups have been reported on this cohort. The first, a 10-year follow-up, compared the probands with men without ADHD (comparison participants) at the mean age of 18 years (referred to as FU18),^{4,5} and the second follow-up was at the mean age of 25 years (referred to as FU25).^{9,12}

We hypothesized that adults diagnosed as having ADHD in childhood have significantly worse outcome than those without ADHD with regard to the following: (1) educational attainment; (2) occupational level and functioning; (3) social functioning; (4) marital status (more divorced); (5) ongoing *DSM-IV* ADHD, ASPD, and SUDs (no directional hypotheses were proposed for other mental disorders, which we report); (6) psychiatric hospitalizations; (7) incarcerations; and (8) new onsets of psychiatric disorders from 21 years of age onward. We also posited positive significant associations among ongoing *DSM-IV* ADHD, ASPD, and SUDs in probands. Because childhood ADHD is believed to carry long-term disadvantages, even among individuals who no longer meet criteria for the disorder,¹⁵ we hypothesized that even probands without any ongoing mental disorder at follow-up would have relatively worse occupational and social functioning than those without childhood ADHD.

METHODS

The study was approved by the institutional review board of the New York University Langone Medical Center. Participants were informed fully of study procedures and provided signed consent. Two groups were studied. Probands were referred by teachers because of behavior problems. Another group, identified at FU18, was judged free of ADHD in childhood (comparison participants). Sample characteristics, described elsewhere,^{4,5,9} are summarized.

PROBANDS

Probands were 6- to 12-year-old boys (8.3 [1.6] years), all referred by teachers between 1970 and 1978. They had to be rated as hyperactive by teachers and by a parent or psychiatrist, have a history of behavior problems, have an IQ of 85 or higher, and have no history of psychosis or neurologic disorder. At the time, the diagnosis and treatment of hyperactive children were poorly un-

derstood. To study a relatively homogeneous syndrome, we excluded children when teachers' referrals involved aggressive or other antisocial behaviors or when the psychiatric assessment with the parent and child indicated a pattern of antisocial activities. This approach was guided by the belief that hyperactive/impulsive disorder differed from conduct disorder. A total of 207 white boys were enrolled. Children's clinical status was consistent with *DSM-IV* ADHD, combined type, because symptoms were impairing and cross-situational; teachers' inattentive and hyperactivity/impulsivity ratings were high (rated on a scale of 0 to 3)¹⁶ (inattentive/distractible, 2.52 [0.7]; restless/overactive, 2.71 [0.6]; and excitable/impulsive, 2.34 [0.9]). In contrast, ratings of conduct problems were low (0.70 [0.4]),¹⁷ documenting exclusion of conduct disorder.

COMPARISON PARTICIPANTS

At FU18, we identified white men matched for age with probands. They had sought medical attention in the same medical center, between the ages of 6 and 12 years, for routine physical examination or acute conditions. Medical records regularly noted the child's school adjustment. Children whose medical records indicated unremarkable school behavior and whose parents' occupation appeared to match the probands' were selected. Parents were called, informed of the study, and asked whether any elementary schoolteacher had ever complained about their child's behavior. If not, the child was recruited. Refusal rate was low (approximately 5%).

ASSESSMENT AT FU41

At FU41, 135 of 207 probands (65.2%) and 136 of 178 comparison participants (76.4%) were interviewed. Trained and closely supervised doctoral-level clinical psychology candidates, masked to all antecedent data, obtained detailed information about educational attainment, employment history, occupational adjustment, marital history, family composition, living circumstances, social functioning, medical history, and psychiatric status. Informant interviews were conducted for 9 of 135 probands and 7 of 136 comparison participants who could not, or refused to, be interviewed but consented to an informant interview.

Because FU41 included a brain scan,¹⁸ transportation was provided for individuals to come to New York University. Those who did not travel to New York were interviewed by telephone (24 of 135 probands [17.8%] and 25 of 136 comparison participants [18.4%]). Rates of mental disorders did not differ significantly between telephone and direct interviews.

Educational and Occupational Attainment and Function

Years of education and highest degree define educational attainment. Occupational attainment was classified according to Hollingshead and Redlich¹⁹ (on a scale of 1 to 8). "Currently employed" reflects employment at follow-up. Queries included work history (ie, jobs held, job satisfaction, work relationships, lateness, job changes, and firings). Incorporating all information, interviewers rated occupational function during the previous 6 months, regardless of type of employment, on an anchored scale (1, superior; 2, very good; 3, good; 4, average; 5, fair; and 6, poor).

Social Functioning

We inquired about friendships and social and leisure activities. Social functioning was rated on a 6-point scale (1 indicating superior to 6 indicating poor).

Incarcerations

Incarceration was broadly defined as having been in a reform school or jail for 1 day or more (not restricted to jail sentences for convicted offenses).

Psychiatric Diagnoses

DSM-IV disorders, as well as multiple aspects of function, were assessed for the interval between FU25 and FU41 (mean, 16 years) with the nonpatient edition of the Structured Clinical Interview for DSM-IV Axis I Disorders.²⁰ We designed an interview to evaluate adult ADHD symptoms and directly related impairment.²¹ Because childhood ADHD had been established in probands and ruled out in comparison participants, ongoing ADHD was diagnosed when all clinical criteria were met, without recalled onset age (ie, the person “often” experienced the stipulated criteria, had significant related impairment or distress, and had cross-situationality).

Interviewers inquired whether each symptom cluster (inattention, hyperactivity, and impulsivity) had interfered with work, home, or social life. If so, probes followed for examples of interference. Impairment was rated on a scale of 1 to 5. Scores of 3 to 5 were considered to indicate significant impairment (3, definitely a problem at times, somewhat of a problem on numerous occasions, with some interference in functioning, or clinically significant distress; 5, symptom compromises functioning and is a major problem).

Interviewers formulated definite and probable DSM-IV diagnoses. They wrote narratives summarizing overall function, clinical picture, and justified diagnoses. Definite diagnoses indicate that DSM-IV criteria were fulfilled. Probable diagnoses indicate that the person reported fewer symptoms than required but reported impairment or distress specifically related to the symptoms (subthreshold disorders). Ongoing ADHD, ASPD, and SUDs were defined as occurring in the previous 6 months. A window of 2 months defined other disorders as ongoing. For ongoing disorders, we rely on definite diagnoses so that our results may be compared with others who do not report “probable” diagnoses. For rates of lifetime disorders, we combined probable and definite diagnoses because retrospective self-reports may underestimate past symptoms; however, there is support for their clinical significance when symptoms caused impairment. Lifetime disorders are based on findings from all follow-ups (FU18, FU25, and FU41) and necessarily span different DSMs. However, this applied to both probands and comparison participants. Disorders with an onset during adulthood are exclusively those that were reported to have emerged de novo from 21 years of age onward. Adult-onset disorders were generated by combining diagnoses made at the previous and current follow-ups, which regularly inquired about first onset.

MISSING STUDY PARTICIPANTS

Probands

Of 207 probands, 72 (34.8%) were lost to follow-up: 21 were not located, 13 refused, information was not obtained for 11 of the 15 deceased, interviews were denied in 4 of the 6 incarcerated probands, and grant support ended before 23 were evaluated. Childhood characteristics of assessed and lost probands did not differ significantly. Of the 135 probands evaluated at FU41, 97.0% had been assessed at FU18 and 95.6% at FU25 (Figure). At FU25, probands assessed and lost to FU41 did not differ significantly on rates of ADHD, ASPD, and SUDs.

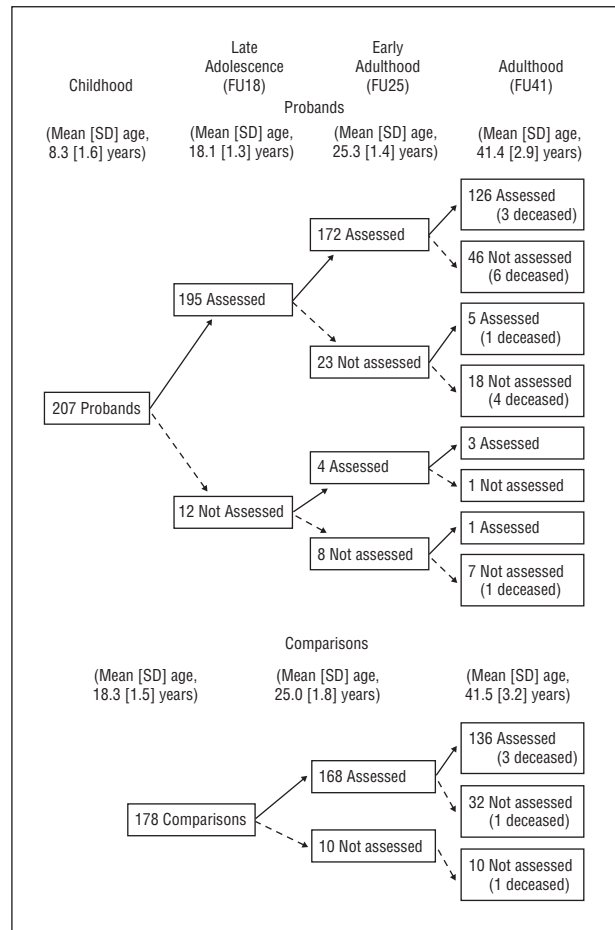


Figure. Flow of assessed and not-assessed probands and comparison participants. FU18 indicates follow-up at 18 years of age; FU25, follow-up at 25 years of age; and FU41, follow-up at 41 years of age.

Comparison Participants

Of 178 comparison participants, 42 (23.5%) were lost to follow-up: 20 were not located, 15 refused, and informant interviews were not obtained for 2 of the 5 deceased comparison participants: 1 was incarcerated and grant funds ended before 4 were scheduled. The evaluated comparisons tended to have higher socioeconomic status ($P = .07$), had significantly higher IQs than lost comparison participants at FU18 ($P = .001$), and tended to have lower rates of any substance disorder ($P = .10$) at FU25. All comparison participants (100%) who were interviewed at FU41 had been evaluated at FU25.

STATISTICAL ANALYSIS

Group contrasts for continuous measures relied on unpaired t tests, uncorrected χ^2 for dichotomous variables, and Fisher exact tests when expected cell frequencies were less than 5. The ϕ coefficients provide effect sizes of χ^2 values. Because IQ has not previously been found to be significantly related to mental disorders, analyses were not adjusted for IQ (no relationship was noted at FU41). The α value was set at $P \leq .05$, 2-tailed. Seventy-five audiotapes that represented multiple disorders were rated independently (S.M.). The κ values²² (ADHD=0.95, any SUD=0.97, any mood=0.90, and any anxiety=0.92) indicated high chance-corrected interrater reliability.

Table 1. Demographic Characteristics and Social and Occupational Functioning at the 33-Year Follow-up^a

Variable	Probands (n = 135)	Comparison Participants (n = 136)	t (df) or χ^2 Test	P Value
Age, mean (SD) [range], y	41.4 (2.9) [30-47]	41.5 (3.2) [33-48]	0.29 (269)	.78
Educational attainment, mean (SD) [range], y	13.3 (2.1) [8-20]	15.8 (2.3) [11-20]	9.52 (269)	<.001
Highest grade completed				
Less than high school	17 (12.6)	1 (0.7)	FET	<.001
GED	25 (18.5)	5 (3.7)	15.16	<.001
High school	32 (23.7)	14 (10.3)	8.64	.004
Some college	35 (25.9)	29 (21.3)	0.79	.39
Bachelor's degree	21 (15.6)	47 (34.6)	13.02	<.001
Higher degree	5 (3.7)	40 (29.4)	32.33	<.001
Hollingshead occupational level, mean (SD) [range] ^b	4.7 (2.0) [1-8]	3.0 (1.8) [1-8]	7.12 (269)	<.001
SES, mean (SD) [range] ^c	3.4 (1.0) [1-5]	2.4 (1.1) [1-5]	8.39 (269)	<.001
Employed	113 (83.7)	129 (94.9)	8.81	.003
Annual salary, \$ ^d				
Mean (SD) [range]	93 317 (158 414) [4000-1 500 000]	175 058 (224 957) [15 000-1 500 000]	3.20 (217) ^e	.002
Median	60 000	100 000		<.001
Occupational functioning ^{d,f}				
Mean (SD) [range]	3.2 (1.1) [1-6]	2.5 (0.9) [1-5]	5.82 (240)	<.001
Median	3	2		
Social functioning ^f				
Mean (SD) [range] ^f	3.8 (1.3) [2-6]	2.9 (1.0) [1-6]	6.61 (269)	<.001
Median	4	3		
Marital status				
Single (never married)	13 (9.6)	13 (9.6)	0.01	.95
Married/cohabiting	94 (69.6)	107 (78.7)	2.89	.10
Separated	15 (11.1)	12 (8.8)	0.4	.90
Divorced	13 (9.6)	4 (2.9)	5.15	.02
Ever divorced	42 (31.1)	16 (11.8)	15.07	<.001
Currently incarcerated ^g	6/161 (3.7)	1/149 (0.7)	FET	.12

Abbreviations: FET, Fisher exact test; GED, Graduate Educational Development; SES, socioeconomic status.

^aData are given as number (percentage) of study participants unless otherwise indicated.

^b1 indicates higher executives; 8, unemployed.

^c1 indicates highest social class; 5, lowest.

^dAmong employed study participants.

^e† Test for unequal variances.

^f1 indicates superior; 2, very good; 3, good; 4, average; 5, fair; and 6, poor.

^gOf those located at the 41-years-of-age follow-up (161 of 207 probands and 149 of 178 comparison participants).

RESULTS

EDUCATIONAL AND OCCUPATIONAL ATTAINMENT

On average, probands had 2½ fewer years of schooling than comparison participants. Their relative disadvantage is indicated in **Table 1**: 31.1% did not complete high school (vs 4.4% of comparison participants) and hardly any (3.7%) had higher degrees (whereas 29.4% of comparison participants did). Similarly, probands had significantly lower occupational attainment levels. On average, the comparison group had mid-level to high-level occupational attainment (3.0 [1.8]), whereas the index cases were at the low end (4.7 [2.0]). Given the probands' worse educational and occupational attainment, their relatively poorer socioeconomic status at FU41 is to be expected ($P < .001$). Although significantly fewer probands than comparison participants were employed ($P = .003$), most were holding jobs (83.7%). However, the disparity of \$40 000 between the median annual salary of employed probands and comparisons is striking.

OCCUPATIONAL AND SOCIAL FUNCTIONING

Employed probands, as a whole, had average to good work performance (3.2 [1.1]). However, comparison participants were significantly superior ($P < .001$), with good to very good functioning (2.5 [0.9]) (Table 1). Similarly, probands' mean overall social functioning was relatively worse but not clinically impaired. Probands had average to good social functioning (3.8 [1.3]), whereas comparisons had good to very good social adjustment (2.9 [1.0]) ($P < .001$). Although most individuals in both groups were cohabiting with a spouse (69.6% and 78.7%) (Table 1), significantly more probands were currently divorced (9.6% vs 2.9%, $P = .02$) and had ever been divorced (31.1% vs 11.8%, $P < .001$).

ONGOING PSYCHIATRIC DISORDERS AT FU41

Attention-Deficit/Hyperactivity Disorder

As hypothesized, at FU41, ADHD was significantly more prevalent in probands than in comparison participants

Table 2. Rates of Ongoing DSM-IV Disorders at the 33-Year Follow-up

DSM-IV Diagnosis	No. (%) of Study Participants		χ^2 Test	P Value
	Probands (n = 135)	Comparison Participants (n = 136)		
ADHD	30 (22.2)	7 (5.1)	16.76	<.001
Combined	9 (6.7)	1 (0.7)	FET	.01
Predominantly inattentive	10 (7.4)	2 (1.5)	5.64	.02
Predominantly hyperactive-impulsive	11 (8.1)	4 (2.9)	3.51	.06
Antisocial personality disorder	22 (16.3)	0	FET	<.001
Alcohol-related disorder	13 (9.6)	21 (15.4)	2.09	.20
Substance use disorder ^a	19 (14.1)	7 (5.1)	6.23	.01
Nicotine dependence	41 (30.4)	12 (8.8)	19.99	<.001
Any mood disorder	12 (8.9)	8 (5.9)	0.90	.36
Any anxiety disorder	17 (12.6)	12 (8.8)	1.01	.33

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; FET, Fisher exact test.

^aOther than alcohol-related disorder and nicotine dependence.

Table 3. Relationship Between Ongoing ADHD, Antisocial Personality Disorder, and Substance Disorders Among Probands at the 33-Year Follow-up

DSM-IV Diagnosis	ADHD Patients, No. (%)		χ^2 Test	ϕ	P Value
	Yes (n = 30)	No (n = 105)			
Antisocial personality disorder	7 (23.3)	15 (14.3)	1.40	.10	.24
Alcohol-related disorder	4 (13.3)	9 (8.6)	FET	.07	.49
Substance use disorder ^a	8 (26.7)	11 (10.5)	FET	.19	.04
Nicotine dependence	13 (43.3)	28 (26.7)	3.07	.15	.08
Antisocial personality disorder and substance use disorder ^a	4 (13.3)	3 (2.8)	FET	.20	.04

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; FET, Fisher exact test.

^aOther than alcohol-related disorder and nicotine dependence.

(22.2% vs 5.1%, $P < .001$) (**Table 2**). The 3 types of ADHD—combined, inattentive, and hyperactive/impulsive—were equally frequent in probands (6.7%, 7.4%, and 8.1%, respectively).

Antisocial Personality Disorder

As hypothesized, ongoing ASPD was elevated in probands; 22 of 135 probands (16.3%), but no comparison participant, had ASPD at FU41 ($P < .001$) (Table 2).

Alcohol Disorders and SUDs

Prevalence of alcohol-related disorders did not differentiate the groups ($P = .20$). In contrast, probands had a 3-fold greater rate of ongoing SUDs and nicotine dependence than comparison participants ($P = .01$ and $< .001$, respectively) (Table 2).

Mood and Anxiety Disorders

Groups did not differ in frequency of ongoing mood (8.9% and 5.9%) or anxiety disorders (12.6% and 8.8%) for probands and comparison participants, respectively ($P = .36$ and $.33$) (Table 2).

Comorbidity in Probands With Persistent ADHD, ASPD, and SUDs

Contrary to our hypothesis, ongoing ADHD was not related to ASPD ($P = .24$), but it was to ongoing SUDs ($P = .04$) at FU41 (**Table 3**). Probands with ongoing ADHD were 3 times more likely to have a drug use disorder than probands without ADHD. The association between ADHD and concurrent diagnoses of both ASPD and SUDs was also significant, with a 4-fold increase in ASPD and SUDs in probands with ongoing ADHD ($P = .04$). No significant elevation of alcohol-related disorders or nicotine dependence was found as a function of ongoing ADHD (Table 3).

LIFETIME FUNCTIONING

Incarcerations and Deaths

Relative to comparison participants, a significantly larger proportion of probands had been incarcerated (36.3% vs 11.8%; $P < .001$) and were deceased (7.2% vs 2.8%; $P = .05$) (**Table 4**).

Table 4. Lifetime Rates of Incarcerations,^a Deaths, and Mental Disorders^b

Outcome	No. (%) of Study Participants		χ^2 Test	P Value
	Probands (n = 135)	Comparisons Participants (n = 136)		
Incarcerated	49 (36.3)	16 (11.8)	22.36	<.001
Deceased	15/207 (7.2)	5/178 (2.8)	3.83	.05
Conduct disorder ^{b, c}	84 (62.2)	36 (26.5)	35.10	<.001
Antisocial personality disorder ^d	44 (32.6)	5 (3.7)	38.24	<.001
Alcohol-related disorder	61 (45.2)	56 (41.2)	0.44	.51
Substance use disorder ^e	76 (56.3)	52 (38.2)	8.87	.003
Nicotine dependence	81 (60.0)	42 (30.9)	23.17	<.001
Any mood disorder ^f	66 (48.9)	58 (42.6)	1.06	.30
Any anxiety disorder	25 (18.5)	28 (20.6)	0.18	.67

^aFor 1 day or more (not restricted to jail sentences).

^bProbable and definite diagnoses.

^cBefore 18 years of age.

^dBy definition, all participants with antisocial personality disorder had a previous history of conduct disorder.

^eOther than alcohol-related disorder and nicotine dependence.

^fMostly major depressive disorder: 51 of 66 probands (77.3%) and 54 of 58 comparison participants (93.1%).

Rates of Lifetime Mental Disorders

During their lifetime, probands had significantly elevated rates of ASPD, SUDs, and nicotine dependence ($P = .003$ to $<.001$) (Table 4). Lifetime rates of SUDs and nicotine dependence were not low among comparison participants (38.2% and 30.9%, respectively), yet probands significantly exceeded these frequencies (56.3% and 60.0%). Probands did not differ in lifetime alcohol-related disorders ($P = .51$) or lifetime mood and anxiety disorders ($P = .30$ and $.67$). We note lifetime prevalence of bipolar disorder because of interest in its relationship to childhood ADHD.²³ Two probands (1.5%) had bipolar disorder; another was frankly psychotic.

Psychiatric Hospitalizations

Thirty-three of 135 probands (24.4%) had been hospitalized in a psychiatric facility compared with 9 of 136 comparison participants (6.6%; $P < .001$). Moreover, hospitalized probands had significantly more hospitalizations (3.36 [4.26]; range, 1-24) than hospitalized comparison participants (1.56 [0.88]; range, 1-3; $P = .03$). In both groups, most hospitalizations were related to substance abuse (78.8% and 77.7%).

ONSET OF MENTAL DISORDERS IN ADULTHOOD

We posited that childhood ADHD would increase the risk of psychiatric disorders throughout life (other than ADHD and ASPD, which require childhood onsets). This common expectation was not supported. Probands were not significantly more likely to incur new mental disorders in adulthood (21 years and older), but a trend was found for elevated mood disorders in probands (31.1% vs 22.1%, $\chi^2 = 2.85$, $P = .09$).

SOCIAL AND OCCUPATIONAL FUNCTIONING IN PROBANDS WITHOUT AN ONGOING MENTAL DISORDER

At FU41, 44 of 135 probands (32.6%) did not meet criteria for any mental disorder. As predicted, these probands had significantly worse social functioning than comparison participants (3.55 [1.25] and 2.89 [0.97]; $t = 3.19$, $P = .002$). However, only a trend for worse occupational functioning was found (2.98 [1.2] and 2.62 [1.1]; $t = 1.84$, $P = .07$).

COMMENT

This prospective follow-up of children diagnosed as having ADHD at a mean age of 8 years, selected to be free of conduct disorder, reaches into the fourth and fifth decades. Previous longitudinal studies have been limited to the second and third decades of life.

Compared with peers without ADHD, probands displayed dysfunction in multiple domains as adults. Educational and occupational attainment was significantly compromised, leading to a relative economic disadvantage. Although most probands were employed (83.7%) and their median income was above that for white males in New York State (in 2007: \$52 370),²⁴ they fared much more poorly economically than their non-ADHD peers. It is only relative to children without evidence of childhood ADHD that decrements in adult economic attainment become evident. The same pattern occurred with regard to occupational and social functioning. On average, probands had adequate adjustment, but it was inferior to that of comparison participants. Similarly, rates of currently and ever divorced of the index group were not especially high (9.6% and 31.1%, respectively), but they were 3-fold higher than that of comparison participants (2.9% and 11.8%).

As anticipated, ongoing ADHD was relatively more prevalent in the group with childhood ADHD, but the rate in comparison participants was not nil (5.1%), similar to the 4% prevalence reported in a population whose childhood ADHD was retrospectively established.²⁵

We suspected that comparison participants' ADHD symptoms might have emerged during adulthood. However, all 7 comparison participants with ongoing ADHD reported impairing ADHD symptoms before the age of 12 years, and all but 1 indicated an onset before the age of 7 years. Yet, only 1 of 7 comparison participants with ADHD at FU41 had ADHD at FU18, based on parent- and self-report. Similarly, probands' self-reports of ADHD at FU25 were much lower than at FU41 (5.7% vs 22.2%).^{9,12} Increases in self-reported ADHD, over time, have also been reported by Barkley et al.⁸ Inconsistencies in adults' retrospective reports of childhood ADHD raise questions about our ability to generate meaningful estimates of the disorder from adult recall.

Why is there an increase in self-reported ADHD in adults with childhood ADHD over time? We relied on *DSM-III-R* criteria at FU25 and *DSM-IV* at FU41, whose standards for diagnosing ADHD differed. Higher rates of ADHD have been reported using *DSM-IV* than *DSM-III-R*²⁶; however, this feature does not seem explanatory because ADHD at the 25-year follow-up was only 7.4% in probands if criteria include any significant inattention, hyperactivity, or impulsivity symptom.^{9,12} A possible factor may be greater awareness of ADHD due to wide media coverage, which has even promoted ADHD as reflecting special, positive attributes.²⁷ Alas, advantages associated with ADHD have yet to be documented. It may be that the popularity of ADHD in the media has fostered erroneous self-identification, leading to secular changes in self-identified ADHD rather than true changes in prevalence. It is also possible that impairing inattention, hyperactivity, and impulsivity develop in later life, when mental alacrity and resources decline or accruing demands may exceed capacity (ie, the Peter Principle). In such instances, adults may reinterpret their early history as a function of current difficulties. On the other hand, media promotion of ADHD may attune people to it and foster accurate recognition and recall of dysfunction in childhood.

In childhood, all probands had combined ADHD. At follow-up, each type of ADHD was equally prevalent. However, assuming absence of inattention in probands with predominantly hyperactive/impulsive ADHD conveys an erroneous clinical message because all reported impairing inattention (median, 3 symptoms) but failed to meet the diagnostic threshold of 6 of 9 inattention symptoms. This finding is in accord with Barkley et al,⁸ who posit that ADHD types are not clinically meaningful in adults.

It has been argued that standards for diagnosing ADHD should be lower in adults than children, requiring 4 of 9 instead of 6 of 9 clinical criteria.⁸ In this study, applying the 4 of 9 standard increases ADHD in probands by nearly half, from 22.2% to 31.9%, and more than doubles the rate in comparison participants (from 5.1% to 11.8%), possibly leading to false-positive diagnoses.

Although findings do not suggest a grim outcome for most children with ADHD, quite a few had very nega-

tive outcomes. Death and incarceration, arguably the worst possible lifetime events, were significantly elevated in those with childhood ADHD. Almost one-fifth had ASPD, a disorder that carries multiple serious consequences. Of probands who had probable or definite conduct disorder, at some point during adolescence (84 of 135), one-quarter (22 of 84) had ASPD at FU41. In contrast, of comparison participants with an adolescent history of conduct disorder (36 of 136), none had ASPD at FU41 (Tables 2 and 4).

Only a proportion of children with conduct disorder have been found to develop ASPD in adulthood.²⁸ In this study also, most children with ADHD who developed conduct disorder during adolescence did not have ASPD at FU41. Thus, some dysfunctions of children with ADHD do attenuate during adulthood.

Childhood ADHD, without conduct disorder, elevated the risk for development and, importantly, maintenance of antisocial disorders. As previously reported,²⁴ these, in turn, were associated with drug abuse and dependence, which had a profoundly negative effect through their associated criminality.²⁹ Elevated rates of SUDs cannot be attributed to differential rates of exposure to drugs of abuse during adolescence by probands and comparison participants; in both groups, most individuals (90.0% and 83.0% of probands and comparison participants, respectively) had tried drugs, defined as using at least 5 times.³⁰

Consistent with other prospective studies,^{14,31} findings do not support that ADHD per se places children at increased risk for mood and anxiety disorders, as suggested elsewhere.³² Lifetime rates of these disorders were not low in probands but no higher than in comparison participants. A study by Barkley et al³ is unique in reporting significantly more major depression in probands than comparison participants at 21 years of age, but this difference disappeared at the next follow-up 6 years later.⁸

No follow-up of children has found differential rates of bipolar and anxiety disorders in adulthood. In this study, 2 probands had definite bipolar disorder and 1 had late-onset psychosis. Frequencies do not exceed population prevalences and are too low for meaningful contrasts but might suggest distinct psychopathologic processes in a small subset of children with ADHD.

Our findings in a relatively severe clinical sample of children with ADHD, free of conduct disorders, are consistent with several population studies³³⁻³⁷ that have reported that ADHD or ADHD symptoms do not predict SUDs when controlling for conduct disorder or problems. Rather, conduct problems mediate the predictive relationship between childhood ADHD and subsequent SUDs. At FU18, we found high comorbidity among patients with persistent ADHD, ASPD, and SUDs.⁴ At FU25, ASPD and SUDs were no longer significantly associated with ongoing ADHD.^{9,12}

Thus, ASPD and SUDs developed while ADHD persisted, but they continued even after ADHD remitted.^{9,12} In contrast, at FU41, ongoing ADHD and SUDs were significantly, but not strongly, related ($\varphi = 0.19$) (Table 3). Interpretation of this association is not straightforward because some drugs of abuse may have behavioral effects that mimic ADHD symptoms.

The study excluded children who have both ADHD and conduct disorder between the ages of 6 and 12 years. Therefore, results may not apply to such children. However, this diagnostic restriction was planned, and results apply to a well-defined clinical group of ADHD children, independent of the confounding effect of co-occurring conduct disorder in childhood. Estimates of prevalence of conduct disorder in children with ADHD vary.³⁸ In the Multimodal Treatment Study of Children with ADHD, which included children of both sexes and all racial groups, the rate of conduct disorder was 14.3%.³⁹ Therefore, study findings appear relevant to most children with ADHD. Nevertheless, the exclusion of conduct disorder may suggest that children in the current study had relatively mild forms of ADHD. Although this possibility cannot be ruled out, it does not seem probable because the teacher-rated hyperactivity factor score of this cohort was 2.11 (0.46) (on a scale of 0 to 3), which is somewhat higher than the Multimodal Treatment Study of Children with ADHD sample, which had a score of 1.82 (0.49) (no other longitudinal study reports teacher ratings).

We note several limitations. The design precludes generalizing to women and all ethnic and social groups because probands were white men of average intelligence who were referred to a clinic because of combined-type ADHD. They do not generalize to predominantly inattentive ADHD, especially if there is no history of impairing hyperactivity/impulsivity.

Comparison participants lost to follow-up had lower IQs than those assessed; they also tended to have lower socioeconomic statuses and more previous drug-related disorders, and information could not be obtained for the 2 with ASPD at FU25 (1 was deceased). Therefore, contrasts between probands and comparison participants may exaggerate somewhat the relative dysfunctions of adults who had ADHD in childhood. In addition, study diagnoses reflect self-reports, and different results might emerge with input from significant others. Another limitation concerns missing study participants. Of 192 living probands, 61 (31.8%) were lost to follow-up. In addition, some contrasts had limited power, which may have precluded the detection of significant associations.

Comparison participants had far superior median incomes than probands. However, comparison participants do not appear to represent an exceptionally normal group. A sizable proportion had conduct disorder in adolescence (26.5%), and their incarceration rate (≥ 1 day in jail) is not very low (11.8%). Furthermore, a large proportion of comparison participants qualified for a lifetime psychiatric diagnosis (combining subthreshold and full diagnoses) (Table 4), sometimes exceeding population rates.⁴⁰ It seems more compelling that differences at the mean age of 41 years between probands and comparison participants reflect differential development, especially because findings are highly consistent with other, briefer follow-up studies.

In conclusion, the course of childhood ADHD reveals a consistent clinical pattern from late adolescence well into adulthood. The longitudinal findings support the diagnostic validity of ADHD, as defined in this sample, because ADHD did not predict a medley of disorders in adulthood. At the same time, longitudinal findings point

to clinical heterogeneity in childhood ADHD because the course was negative in only a subset.

Although the pattern of psychopathologic processes from early to later adulthood in probands did not show striking changes, rates of dysfunction diminished. The trajectory of antisocial disorders in probands was consistent with reports of the disorders' gradual remission over time.⁴¹ However, through life, those who had developed conduct disorder fared relatively badly, with a substantial number having very negative life circumstances. The period of increased relative risk for new psychopathologic processes was limited to adolescence. This finding should not be construed to mean that probands were not worse off in adulthood than comparison participants. They were, but relative disadvantages in adulthood reflect persistent malfunction with earlier origin. As such, findings stress the importance of continued monitoring and treatment of children with ADHD, even when conduct disorder is not evident.

Submitted for Publication: November 3, 2011; final revision received January 31, 2012; accepted March 9, 2012.

Published Online: October 15, 2012. doi:10.1001/archgenpsychiatry.2012.271

Author Affiliations: Anita Saltz Institute for Anxiety and Mood Disorders (Dr Klein), Phyllis Green and Randolph Cowen Institute for Pediatric Neuroscience (Drs Olazagasti and Castellanos), and Institute for Prevention Science (Ms Lashua), New York University Child Study Center, and Department of Counseling and Clinical Psychology, Teachers College, Columbia University (Ms Roizen), New York, New York; Department of Psychology, American University, Washington, DC (Mr Hutchison); and Nathan S. Kline Institute for Psychiatric Research, Orangeburg, New York (Dr Castellanos). Dr Mannuzza is retired.

Correspondence: Rachel G. Klein, PhD, New York University Child Study Center, One Park Ave, Seventh Floor, New York, NY (rachel.klein@nyumc.org).

Conflict of Interest Disclosures: None reported.

Funding/Support: This research was supported by grant MH-18579 (Dr Klein) and grant T32 MH-067763 (Dr Castellanos) from the National Institute of Mental Health (Dr Klein) and grant DA-16979 from the National Institute on Drug Abuse (Dr Castellanos).

Additional Contributions: Donald F. Klein, MD, provided valuable comments.

REFERENCES

1. Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA. The worldwide prevalence of ADHD: a systematic review and meta-regression analysis. *Am J Psychiatry*. 2007;164(6):942-948.
2. Barkley RA, Fischer M, Edelbrock CS, Smallish L. The adolescent outcome of hyperactive children diagnosed by research criteria. I: an 8-year prospective follow-up study. *J Am Acad Child Adolesc Psychiatry*. 1990;29(4):546-557.
3. Bussing R, Mason DM, Bell L, Porter P, Garvan C. Adolescent outcomes of childhood attention-deficit/hyperactivity disorder in a diverse community sample. *J Am Acad Child Adolesc Psychiatry*. 2010;49(6):595-605.
4. Gittelman R, Mannuzza S, Shenker R, Bonagura N. Hyperactive boys almost grown up. I: psychiatric status. *Arch Gen Psychiatry*. 1985;42(10):937-947.
5. Mannuzza S, Klein RG, Bonagura N, Malloy P, Giampino TL, Addalli KA. Hyperactive boys almost grown up. V: replication of psychiatric status. *Arch Gen Psychiatry*. 1991;48(1):77-83.

6. Weiss G, Hechtman L, Milroy T, Perlman T. Psychiatric status of hyperactives as adults: a controlled prospective 15-year follow-up study of 63 children. *J Am Acad Child Psychiatry*. 1985;24(2):211-220.
7. Barkley RA, Fischer M, Smallish L, Fletcher K. Young adult follow-up of hyperactive children: antisocial activities and drug use. *J Child Psychol Psychiatry*. 2004; 45(2):195-211.
8. Barkley RA, Murphy KR, Fischer M. *ADHD in Adults: What the Science Says*. New York, NY: Guilford Press; 2010.
9. Mannuzza S, Klein RG, Bessler A, Malloy P, LaPadula M. Adult outcome of hyperactive boys: educational achievement, occupational rank, and psychiatric status. *Arch Gen Psychiatry*. 1993;50(7):565-576.
10. Mannuzza S, Gittelman R. Informant variance in the diagnostic assessment of hyperactive children as young adults. In: Barrett JE, Rose RM, eds. *Mental Disorders in the Community: Progress and Challenge*. New York, NY: Guilford Press; 1986:243-254.
11. Rasmussen P, Gillberg C. Natural outcome of ADHD with developmental coordination disorder at age 22 years: a controlled, longitudinal, community-based study. *J Am Acad Child Adolesc Psychiatry*. 2000;39(11):1424-1431.
12. Mannuzza S, Klein RG, Bessler A, Malloy P, LaPadula M. Adult psychiatric status of hyperactive boys grown up. *Am J Psychiatry*. 1998;155(4):493-498.
13. Mannuzza S, Klein RG, Klein DF, Bessler A, Shrout P. Accuracy of adult recall of childhood attention deficit hyperactivity disorder. *Am J Psychiatry*. 2002;159(11):1882-1888.
14. Barkley RA, Fischer M, Smallish L, Fletcher K. The persistence of attention-deficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder. *J Abnorm Psychol*. 2002;111(2):279-289.
15. Faraone SV, Biederman J, Spencer T, Mick E, Murray K, Petty C, Adamson JJ, Monuteaux MC. Diagnosing adult attention deficit hyperactivity disorder: are late onset and subthreshold diagnoses valid? *Am J Psychiatry*. 2006;163(10):1720-1729.
16. Conners CK. A teacher rating scale for use in drug studies with children. *Am J Psychiatry*. 1969;126(6):884-888.
17. Mannuzza S, Klein RG, Abikoff H, Moulton JL III. Significance of childhood conduct problems to later development of conduct disorder among children with ADHD: a prospective follow-up study. *J Abnorm Child Psychol*. 2004;32(5):565-573.
18. Proal E, Reiss PT, Klein RG, Mannuzza S, Gotimer K, Ramos-Olazagasti MA, Lerch JP, He Y, Zijdenbos A, Kelly C, Milham MP, Castellanos FX. Brain gray matter deficits at 33-year follow-up in adults with attention-deficit/hyperactivity disorder established in childhood. *Arch Gen Psychiatry*. 2011;68(11):1122-1134.
19. Hollingshead AB, Redlich FC. *Social Class and Mental Illness*. New York, NY: Wiley; 1958.
20. First MB, Spitzer RL, Gibbon M, Williams JBW. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders Research Version, Non-Patient Edition (SCID-I/NP)*. New York: Biometrics Research, New York State Psychiatric Institute; 2002.
21. Mannuzza S, Castellanos FX, Roizen ER, Hutchison JA, Lashua EC, Klein RG. Impact of the impairment criterion in the diagnosis of adult ADHD: 33-year follow-up study of boys with ADHD. *J Atten Disord*. 2011;15(2):122-129.
22. Shrout PE, Spitzer RL, Fleiss JL. Quantification of agreement in psychiatric diagnosis revisited. *Arch Gen Psychiatry*. 1987;44(2):172-177.
23. Kim EY, Miklowitz DJ. Childhood mania, attention deficit hyperactivity disorder and conduct disorder: a critical review of diagnostic dilemmas. *Bipolar Disord*. 2002;4(4):215-225.
24. US Census Bureau. S0201. Selected population profile in the United States. <http://factfinder2.census.gov/faces/nav/jsf/pages/index.html>. Accessed January 5, 2012.
25. Kessler RC, Adler L, Barkley R, Biederman J, Conners CK, Demler O, Faraone SV, Greenhill LL, Howes MJ, Secnik K, Spencer T, Ustun TB, Walters EE, Zaslavsky AM. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. *Am J Psychiatry*. 2006; 163(4):716-723.
26. Faraone SV, Sergeant J, Gillberg C, Biederman J. The worldwide prevalence of ADHD: is it an American condition? *World Psychiatry*. 2003;2(2):104-113.
27. Hallowell EM, Ratey JJ. *Driven to Distraction*. New York, NY: Pantheon; 1994.
28. Robins LN. Sturdy childhood predictors of adult antisocial behaviour: replications from longitudinal studies. *Psychol Med*. 1978;8(4):611-622.
29. Mannuzza S, Klein RG, Moulton JL III. Lifetime criminality among boys with attention deficit hyperactivity disorder: a prospective follow-up study into adulthood using official arrest records. *Psychiatry Res*. 2008;160(3):237-246.
30. Klein RG, Mannuzza S, Bailly A, Venisse JL, eds. Importance de l'hyperactivité de l'enfance dans le développement des troubles liés à l'utilisation de substances [Importance of childhood hyperactivity in the development of substance-related disorders]. In: *Addictions et Psychiatrie*. Paris, France: Masson; 1999:107-122.
31. Bagwell CL, Molina BSG, Kashdan TB, Pelham WE, Hoza B. Anxiety and mood disorders in adolescents with childhood attention-deficit/hyperactivity disorder. *J Emot Behav Disord*. 2006;14(3):178-187.
32. Biederman J, Monuteaux MC, Mick E, Spencer T, Wilens TE, Silva JM, Snyder LE, Faraone SV. Young adult outcome of attention deficit hyperactivity disorder: a controlled 10-year follow-up study. *Psychol Med*. 2006;36(2):167-179.
33. August GJ, Winters KC, Realmuto GM, Fahnhorst T, Botzet A, Lee S. Prospective study of adolescent drug use among community samples of ADHD and non-ADHD participants. *J Am Acad Child Adolesc Psychiatry*. 2006;45(7):824-832.
34. Cadoret RJ, Stewart MA. An adoption study of attention deficit/hyperactivity/aggression and their relationship to adult antisocial personality. *Compr Psychiatry*. 1991;32(1):73-82.
35. Flory K, Lynam DR. The relation between attention deficit hyperactivity disorder and substance abuse: what role does conduct disorder play? *Clin Child Fam Psychol Rev*. 2003;6(1):1-16.
36. Elkins IJ, McGue M, Iacono WG. Prospective effects of attention-deficit/hyperactivity disorder, conduct disorder, and sex on adolescent substance use and abuse. *Arch Gen Psychiatry*. 2007;64(10):1145-1152.
37. Fergusson DM, Horwood LJ, Ridder EM. Conduct and attentional problems in childhood and adolescence and later substance use, abuse and dependence: results of a 25-year longitudinal study. *Drug Alcohol Depend*. 2007;88(suppl 1):S14-S26.
38. Biederman J, Newcorn J, Sprich S. Comorbidity of attention deficit hyperactivity disorder with conduct, depressive, anxiety, and other disorders. *Am J Psychiatry*. 1991;148(5):564-577.
39. The MTA Cooperative Group (Multimodal Treatment Study of Children with ADHD). A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry*. 1999;56(12):1073-1086.
40. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication [published correction appears in *Arch Gen Psychiatry*. 2005;62(7):768]. *Arch Gen Psychiatry*. 2005;62(6):593-602.
41. Martens WHJ. Antisocial and psychopathic personality disorders: causes, course, and remission: a review article. *Int J Offender Ther Comp Criminol*. 2000;44(4):406-430.