ORIGINAL ARTICLE

Very Early Predictors of Adolescent Depression and Suicide Attempts in Children With Attention-Deficit/Hyperactivity Disorder

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Context: Major depression and dysthymia in adolescence are associated with substantial disability, need for mental health services, and risk for recurrence. Concrete suicidal ideation and attempts during adolescence are particularly associated with significant distress, morbidity, and risk for completed suicide.

Objectives: To test the hypothesis that young children with attention-deficit/hyperactivity disorder (ADHD) are at increased risk for depression and suicidal ideation and attempts during adolescence and to identify early predictors of which young children with ADHD are at greatest risk.

Design: Prospective follow-up study.

Setting: Chicago, Illinois, and Pittsburgh, Pennsylvania.

Patients: A cohort of 125 children who met *DSM-IV* criteria for ADHD at 4 to 6 years of age and 123 demographically matched comparison children without ADHD were prospectively followed up in 7 structured diagnostic assessments of depression and suicidal behavior in assessment years 6 through 14, spanning 9 through 18 years of age.

Main Outcome Measures: *DSM-IV* criteria for depressive disorders and suicidal behavior.

Results: Children with ADHD at 4 to 6 years of age were at greatly increased risk for meeting *DSM-IV* criteria for major depression or dysthymia (hazard ratio, 4.32) and for attempting suicide (hazard ratio, 3.60) through the age of 18 years relative to comparison children. There were marked variations in risk for these outcomes among children with ADHD, however. Within the ADHD group, children with each subtype of ADHD were at risk but for different adverse outcomes. Girls were at greater risk for depression and suicide attempts. Maternal depression and concurrent child emotional and behavior problems at 4 to 6 years of age predicted depression and suicidal behavior.

Conclusions: All subtypes of ADHD in young children robustly predict adolescent depression and/or suicide attempts 5 to 13 years later. Furthermore, female sex, maternal depression, and concurrent symptoms at 4 to 6 years of age predict which children with ADHD are at greatest risk for these adverse outcomes. Identifying high-risk young children with ADHD sets the stage for early prevention trials to reduce risk for later depression and suicidal behavior.

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Approximately 16% to 37% of clinically referred adults with attention-deficit/hyperactivity disorder (ADHD) have comorbid major depressive disorder (MDD) and/or dysthymia.[1-5] Furthermore, when MDD occurs concurrently with ADHD, MDD has an earlier age of onset, has a longer duration, and results in greater impairment.[6] These findings suggest a clear need to study and to better understand depression that emerges in persons with a childhood history of ADHD, but prospective studies examining risk for depression among children with ADHD have yielded inconsistent findings.

A number of previous longitudinal studies[7-13] of either all male or predominantly male samples found no increased rates of diagnoses of MDD during adolescence and adulthood among children with ADHD relative to control individuals. In contrast, 2 longitudinal studies[10,14] reported higher levels of depressive symptoms among girls with ADHD, and several other studies found higher rates of the diagnosis of depression. A 13-year follow-up of 4- to 12-year-old children (90% males) found that children with ADHD were more likely to meet criteria for MDD during adolescence and early adulthood (27%) than controls (4%).[15] Likewise, 46% of males with ADHD ascertained at 6 to 18 years of age vs 7% of controls met lifetime MDD criteria 10 years later (mean age, 22 years).[16] In parallel studies[6,17] of females, logistic regression using the same covariates showed that the adjusted odds of MDD 5 years later were 5.1

times greater in 6- to 18-year-old girls with ADHD than controls. Furthermore, females with ADHD at 6 to 18 years of age were more likely to experience later suicidal ideation than controls,[6] and more children with ADHD (90% males) reported suicidal ideation and attempts during high school than controls.[18]

Thus, current evidence is mixed as to whether children with ADHD are at risk for later depression and suicidal behavior. The present study contributes to the resolution of this issue in 3 ways. First, rather than assessing later depression at a single point in time like previous studies, these outcomes were assessed in multiple follow-up waves in the present study. Because depression is episodic, this method of assessment provides a more comprehensive assessment of future depression and suicidality. Second, we examined factors that may increase risk for these negative outcomes among children with ADHD (eg, the child's sex or maternal history of depression). This is important because variations in these factors may have been responsible for the inconsistent findings of previous studies. Furthermore, identifying early child and family characteristics that predict which children with ADHD are most at risk for depression will inform *early* prevention efforts. Third, although suicidal ideation and attempts are symptoms of depression, we separately tested potential predictors of these outcomes because they are strongly associated with morbidity, mortality, and high-end treatment.

METHODS

STUDY PARTICIPANTS

Two cohorts of 3.8- to 7.0-year-old children were ascertained in consecutive years in Chicago, Illinois, and Pittsburgh, Pennsylvania. Participants lived with their biological mothers; half the participants met *DSM-IV* diagnostic criteria for ADHD. In Chicago, children with ADHD were recruited from a child psychiatry clinic. In Pittsburgh, 42.0% of children with ADHD were recruited from a child psychiatry clinic and 58.0% were recruited through advertisements. Five potential participants were excluded because of pervasive developmental disorder, intellectual disability, or seizure disorder.[19] Comparison children were recruited from similar schools and neighborhoods and matched the probands regarding sex, race/ethnicity, and age. Comparison children had never been referred for mental health problems, but they were not excluded if they met criteria for a disorder other than ADHD. Of 310 eligible participants, 259 participated.[19,20]

LONGITUDINAL ASSESSMENTS

Participants underwent approximately annual assessments during years 1 through 4, 6 through 9, and 12 through 14. The comparison group was reduced during years 12 through 14 because of funding limitations. All comparison girls were retained, but 50% of other comparison children were randomly dropped within each year of age and race/ethnicity group. If a retained comparison child declined assessment in year 12, a dropped comparison child or adolescent (randomly selected within age and race/ethnicity) was substituted and assessed in years 12 and beyond; no subsequent substitutions were made. Retention was high, with 79.8% to 91.5% of eligible cases assessed in each of waves 6 through 14. When parents were interviewed, the child or adolescent was interviewed 94.6% to 97.8% of the time. Families that did not participate in one year typically participated in the next year. The present analyses were based on the 95.8% of the original sample (N = 248; 125 with ADHD in year 1 and 123 comparison children without ADHD) who were reassessed 1 time or more in years 6 through 9 and/or years 12 through 14.

OUTCOME MEASURES

In each assessment, the Diagnostic Interview Schedule for Children[21] was administered to mothers or the primary caretaker. Information was obtained with regard to *DSM-IV* criteria during the past 12 months for ADHD, oppositional defiant disorder, conduct disorder (CD), mood disorders (MDD and dysthymia), and anxiety disorders.[22] Teachers completed the *DSM-IV* version of the Disruptive Behavior Disorders Rating Scale[23] each year, assessing symptoms of ADHD, oppositional defiant disorder, and CD. On the basis of standard procedures, symptoms rated "pretty much" or "very much" were scored as present.[23] Beginning in year 6, when the children were 9 to 11 years old, independent interviews of the mother and the child were conducted. The Diagnostic Interview Schedule for Children was administered to the youth in assessment years 6 through 14, querying *DSM-IV* criteria for CD, mood, and anxiety disorders.

DIAGNOSTIC ASSESSMENTS OF THE MOTHER AND CHILD

We assessed the well-established risk factor of maternal depression. To do so, we administered the Structured Clinical Interview for *DSM-III-R*, Non-Patient Edition[24] module assessing lifetime MDD to biological mothers in year 1.[25]

Diagnosis of ADHD in Year 1

On the basis of research regarding the independent contribution of each informant to the external validity of each diagnosis[26-28] and the *DSM-IV* field trials,[29] symptoms of ADHD were considered to be present in the child if reported by either the parent or teacher. Impairment was assessed in 2 ways for the diagnosis of ADHD in year 1. First, parents were asked in the Diagnostic Interview Schedule for Children whether the child's ADHD symptoms had caused problems (1) at home or with friends or (2) at school. Second, parents and teachers completed the Impairment Rating Scale,[30] in which the child's need for treatment was rated across multiple domains of functioning on 7-point scales. Children were considered impaired if they received a rating of 3 or higher on at least 1 scale.[30]

Children were given the diagnosis of ADHD in year 1 if they met *DSM-IV* symptom criteria and exhibited impairment in at least 1 setting (home/peer environments or school). Because of their young age in year 1, all met the age of onset criterion, but cross-situational impairment was not required because not all children with ADHD had (yet) exhibited impairment in school. During the next 7 assessments, 96.0% of children with ADHD exhibited impairment in both home/peer environments and school.[20] Thus, all children with ADHD with impairment in at least 1 setting were included in analyses because limiting the sample to only children with cross-situational impairment would have eliminated those who later exhibited cross-situational impairment.

Diagnosis of Depression in Children During Years 6 Through 14

Children were said to exhibit depression if 2 factors were present. Those factors were meeting diagnostic criteria for MDD or dysthymia according to the combined report of symptoms by parents and themselves using the "or" rule[31] and exhibiting func-

Table 1. Characteristics of the 248 Children Who Did and Did Not Meet Criteria for ADHD in Year 1 Who Were Assessed at Least Once in Years 6 Through 14[a]

Characteristic	ADHD in Year 1 (n=125)	No ADHD in Year 1 (n=123)
Age, mean (SD), y	5.2 (0.7)	5.2 (0.8)
Intelligence, mean (SD)[b]	91.7 (12.8)	104.3 (14.0)
Income, mean (SD), $[c]	38 340 (33 866)	48 294 (34 395)
Female, No. (%)[d]	18 (14.4)	23 (18.7)
Race/ethnicity, No. (%)[e]		
Non-Hispanic white	79 (63.2)	81 (65.8)
African American	38 (30.4)	36 (29.3)
Other	8 (6.4)	6 (4.9)
No. of inattention symptoms in wave 1, mean (SD)[f]	7.2 (2.0)	0.8 (1.4)
No. of HI symptoms in wave 1, mean (SD)[f]	7.6 (1.7)	1.4 (1.7)
No. of depression symptoms in wave 1, mean (SD)[g]	1.9 (1.8)	0.5 (1.0)

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; HI, hyperactivity-impulsivity symptoms.
[a] Percentages may not total 100 because of rounding.
[b] Intelligence indicates an estimated score based on the average of 2 administrations of the Short Form of the Stanford-Binet Intelligence Scale, Fourth Edition,[32] during the first 2 years.
[c] In 1995-1996 dollars.
[d] $P=.36$.
[e] $P=.84$.
[f] Reported by parents and teachers.
[g] Reported by parents.

tional impairment in at least 1 setting during assessment years 6 through 14.

Measures of Suicidal Behavior

In the Diagnostic Interview Schedule for Children, parents and children were asked in the year 9 assessment whether they had ever attempted suicide. In each subsequent assessment across years 6 through 14, they were asked whether their child (parent) or they themself (child) had attempted suicide. Suicide attempts were considered to have occurred at the age reported in the initial lifetime assessment or in the first year in which they were reported. Children were considered to have engaged in concrete suicidal ideation if the parent or child reported in an assessment that their child (parents) or they themself (child) had considered a specific suicidal plan during the past 6 months. Concrete ideation was considered to have occurred in the first year in which it was reported.

STATISTICAL ANALYSES

Primary tests of predictors of adverse outcomes were conducted using Cox proportional hazard models adjusted for relevant covariates because this method provides an effective solution to right-hand censoring. Supplemental longitudinal tests of time-varying correlates of the outcomes used longitudinal binomial regression in SAS GENMOD (SAS Institute Inc, Cary, North Carolina). Statistical tests used 1 *df* unless noted.

SAMPLE BIAS AND CENSORING

We tested whether the 248 included participants differed from the 11 who dropped out. Log-linear regression revealed that the included and excluded participants did not differ on family income ($P=.46$) or year 1 child ADHD ($P=.35$), depression ($P=.16$), or CD symptoms ($P=.10$). Demographic characteristics of the 248 participants are presented in **Table 1** and the numbers participating in each assessment are in **Table 2**.

Among these 248 participants, 8.1% completed 1 to 3 assessments, 32.2% completed 4 to 5 assessments, and 59.7% completed 6 to 7 assessments. The sample was censored because youth completed different numbers of assessments. Because approximately half the comparison children were dropped during years 12 through 14, Poisson regression showed that children with ADHD in year 1 (mean [SD], 5.6 [1.6]) were assessed more times during years 6 through 14 than comparison children (mean [SD], 4.9 [1.9]) ($\beta=0.121$, $\chi^2=13.02$, $P<.001$). Because children aged out of the study after their assessment at 18 years of age, younger children in wave 1 were assessed more times than older children (age of 4 years: mean [SD], 5.8 [1.5]; age of 5 years: mean [SD], 5.8 [1.5]; age of 6 years: mean [SD], 5.1 [1.4]; $\beta=-0.08$, $\chi^2=13.39$, $P<.001$). In addition, girls (mean [SD], 6.1 [1.1]) were assessed more times than boys (mean [SD], 5.4 [1.5]) ($\beta=0.15$, $\chi^2=13.98$, $P<.001$) and children from lower-income families were assessed more often ($\beta=-0.03$, $\chi^2=5.50$, $P=.02$).

SELECTION OF COVARIATES

We tested potential covariates to control confounding by including all potential covariates in simultaneous logistic regression models predicting each outcome without the diagnosis of ADHD or other hypothesized predictors (eg, year 1 CD symptoms). The potential covariates were a maternal history of major depression, demographic variables (age in year 1, sex, intelligence, race/ethnicity, and family income in year 1), and methodologic variables (site and cohort). All covariates significant at $P<.10$ were conservatively included as simultaneous predictors in final models, except that sex was always included as a covariate.

SENSITIVITY ANALYSES

Cox models were repeated excluding data from the 5 children with ADHD who never exhibited impairment in 2 or more settings as required by *DSM-IV* with virtually identical results. Because we would be interested in identifying predictors of the occurrence of adverse events at any time during adolescence, independent of variations in the *time* to those events (ie, survival), we also conducted parallel logistic regression analyses using ever experiencing the event (eg, diagnosis of depression) as the categorical response variable, controlling all relevant covariates and the number of years in which each child participated in assessments. These analyses yielded qualitatively identical results to the survival analyses for all predictors and outcomes.

RESULTS

VALIDATION OF DEPRESSION DIAGNOSES AND SUICIDE ATTEMPTS

To confirm that the depression diagnoses reflected clinically significant conditions, 2 external criteria were selected (inpatient psychiatric treatment and antidepressant medication) that reflect impairment and concern by families and treating physicians. Longitudinal binomial regressions with depression diagnoses as a time-varying covariate showed that youth with depression in each wave were more likely to take antidepressants in that year ($\beta=1.36$, $z=3.26$, $P<.001$). Averaged across years 6 through 14, 22.6% of children and adolescents with depression in each wave took antidepressants the same year compared with 3.7% of children and adolescents with-

Table 2. Numbers of Participants Who Were Assessed During Years 6 Through 14

	Year of Assessment of Depression[a]						
	6	7	8	9	12	13	14
ADHD in year 1	118	111	115	115	112	102	57
Comparison group	119	114	117	117	66	65	40
Total No.	**237**	**225**	**232**	**232**	**178**[b]	**167**[b]	**97**[b]

Abbreviation: ADHD, attention-deficit/hyperactivity disorder.
[a] There were no in-person assessments in years 10 and 11 owing to a gap in funding.
[b] The numbers of eligible comparison children and adolescents were reduced by approximately half during years 12 through 14, as described in the text, owing to reduced funding. In addition, the numbers of probands and comparison children and adolescents decreased in year 13, and especially in year 14, because many participants aged out of the study after 18 years of age.

out depression. Similarly, children and adolescents in each wave who were depressed were more likely to receive inpatient treatment in that year ($\beta = 1.56$, $z = 4.03$, $P < .001$). Averaged across years 6 through 14, 20.0% of children and adolescents with depression criteria in each wave received inpatient treatment that year compared with 2.8% for children and adolescents without depression.

Although suicidal behavior is a symptom of MDD, the validity of depression diagnoses would be questioned if suicide attempts were not more common among depressed children and adolescents. Among those who ever met criteria for depression, 32.2% attempted suicide at least once by assessment year 14 compared with 5.8% of those who never met depression criteria (adjusted odds ratio [OR], 6.95; 95% confidence interval [CI], 2.84-17.03). Across assessment years 6 through 14, 46.7% of those who had attempted suicide received inpatient mental health services at least once compared with 8.3% of those who had not made attempts (adjusted OR, 8.36; 95% CI, 3.21-21.78). Furthermore, in each assessment, 50.0% of children and adolescents who had made a suicide attempt in the past 6 months received inpatient treatment that year compared with 3.6% of those who had not ($\beta = 2.62$, $z = 5.33$, $P < .001$). When depression ($\beta = 1.37$, $z = 3.77$, $P < .001$) and suicide attempts ($\beta = 2.30$, $z = 5.10$, $P < .001$) were simultaneously entered as time-varying covariates, each independently predicted inpatient treatment in the same wave.

ASSOCIATION OF ADHD AT 4 TO 6 YEARS OF AGE WITH FUTURE ADVERSE OUTCOMES

ADHD as a Predictor of Depression

As indicated in **Table 3** and **Figure 1**A, the Cox model revealed that children and adolescents with ADHD in year 1 (ages 4-6 years) were at greater risk for depression across assessment years 6 (ages 9-11 years) through 14 (ages 17-18 years) than comparison children and adolescents, even controlling for sex, intelligence, and the significant predictor of maternal depression. Notably, 25 of 59 children and adolescents who were ever depressed (42.4%) met depression criteria more than once during years 12 through 14. Supplemental logistic regression analysis including covariates revealed that recurrent depression (≥2 episodes) was markedly more common among children and adolescents with ADHD (18.4%) than among controls (1.6%) (adjusted OR, 12.15; 95% CI, 2.62-56.32).

Table 3. Results of Prospective Tests of the Hypotheses That ADHD at 4 to 6 Years of Age Predicts Time to Meeting Criteria for Depression and Engaging in Suicidal Behavior[a]

Predictor	χ^2	*P* Value	Hazard Ratio
Response Variable: Diagnosis of Major Depression or Dysthymia During Assessment Years 6-14			
ADHD in year 1	15.60	<.001	4.32
Sex (male=1, female=2)	2.99	.09	1.73
Intelligence[b]	0.72	.40	0.99
Maternal depression	7.65	.01	2.08
Response Variable: Concrete Suicidal Ideation Reported During Assessment Years 6-14			
ADHD in year 1	5.38	.03	5.79
Sex (male=1, female=2)	0.89	.35	1.72
Maternal depression	8.90	.005	4.94
Response Variable: Suicide Attempt Reported During Assessment Years 6-14			
ADHD in year 1	8.26	.005	3.60
Sex (male=1, female=2)	4.83	.03	2.44
Cohort	1.96	.16	0.60

Abbreviation: ADHD, attention-deficit/hyperactivity disorder.
[a] Tests were performed during follow-up assessments using Cox proportional hazard models, controlling sex and all methodologic and demographic covariates that empirically predict each outcome.
[b] Intelligence indicates an estimated score based on the average of 2 administrations of the Short Form of the Stanford-Binet Intelligence Scale, Fourth Edition,[32] during the first 2 years.

Diagnosis of ADHD as a Predictor of Suicidal Behavior

By assessment year 14, 17 of the 248 participants had reported a specific suicidal plan at least once during assessment years 6 through 14 (12.0% of children and adolescents with year 1 ADHD and 1.6% of comparison children and adolescents). As indicated in Table 3, Cox modeling revealed that children with ADHD in year 1 were at greater risk for concrete suicidal ideation across assessment years 6 through 14 (ages 9-18 years), even controlling for sex and the significant predictor of maternal depression. Logistic regression estimated that children and adolescents with ADHD had more than 550% greater odds of ever engaging in concrete suicidal ideation than controls, adjusting for relevant covariates.

A total of 18.4% of children and adolescents with ADHD and 5.7% of comparison children and adolescents made at least 1 suicide attempt by assessment year 14. As indicated

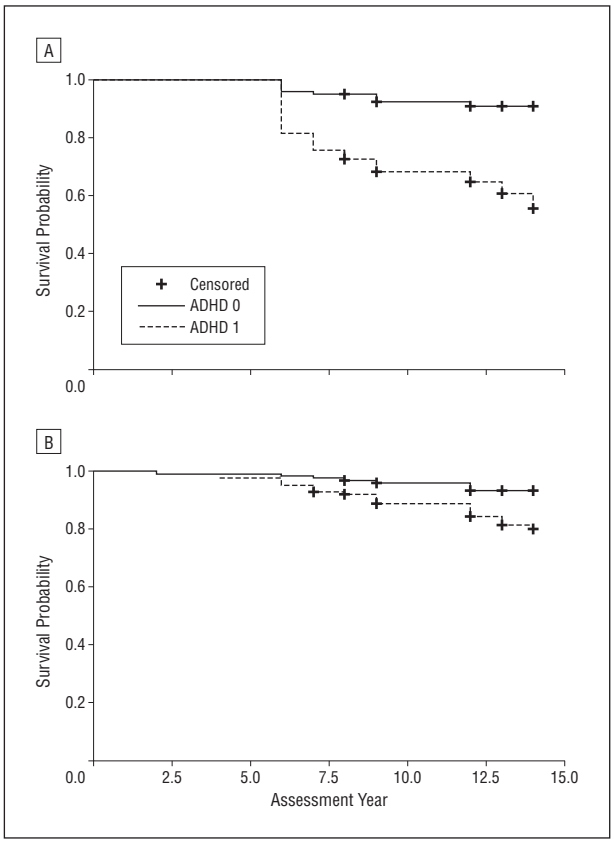

Figure 1. Survival probabilities for (A) the diagnosis of major depression and/or dysthymia and (B) suicide attempts during assessment years 6 through 14 (spanning 9-18 years of age) among 125 children and adolescents with attention-deficit/hyperactivity disorder (ADHD) in year 1 and 123 comparison children and adolescents.

in Table 3 and Figure 1B, Cox modeling revealed that children with ADHD in year 1 were at greater risk for suicide attempts across assessment years 6 through 14 (ages 9-18 years), even controlling for cohort and the significant effect of sex (ie, more common in girls). A supplemental logistic regression estimated that children and adolescents with ADHD had more than 200% greater odds of attempting suicide than controls, adjusting for relevant covariates. Methods of suicide attempts are summarized in **Table 4**.

PREDICTORS OF DEPRESSION AND SUICIDE ATTEMPTS AMONG CHILDREN WITH ADHD AT 4 TO 6 YEARS OF AGE

The association of ADHD with future depression reflects high sensitivity (83.0%) but modest specificity (60.0%). That is, although the great majority of children who developed depression had ADHD in year 1 (true positives), a substantial number of children and adolescents with ADHD had not developed depression by year 14 (false positives). Therefore, it is important to refine the prediction of adverse outcomes among young children with ADHD.

SUBTYPES OF ADHD AND RISK FOR DEPRESSION AND SUICIDE ATTEMPTS

Although the subtypes of ADHD are not stable over time,[20] it is still important to determine (1) whether each subtype of ADHD in early childhood predicts adverse outcomes in adolescence and (2) whether significant differences can be identified among the subtypes that would improve prediction of which young children with ADHD experience adverse outcomes. As shown in **Figure 2**A, Cox models showed that children with the combined subtype (ADHD-CT; n=85; χ^2=19.73, $P<.001$; hazard ratio, 5.59) or the predominantly inattentive subtype (ADHD-I; n=27; χ^2=6.49, $P<.02$; hazard ratio, 4.23) in year 1 were at greater risk for depression than controls (n=119), but the predominantly hyperactive-impulsive subtype (ADHD-HI; n=13) was not (P=.20), controlling for sex and maternal depression.

Cox models showed that children with the ADHD-CT subtype (χ^2=6.52, $P<.02$; hazard ratio, 7.19) in year 1 were at greater risk for concrete suicidal ideation than controls, but the children with the ADHD-HI ($P<.06$) and AHDH-I subtypes (P=.99) were not, controlling for sex, cohort, and the significant effect of maternal depression (χ^2=9.27, $P<.005$; hazard ratio, 5.11). As shown in Figure 2B, Cox models showed that children with the ADHD-CT subtype (χ^2=6.42, $P<.02$; hazard ratio, 3.20) or the AHDH-HI subtype (χ^2=4.12, $P<.05$; hazard ratio, 3.37) in year 1 were at greater risk for suicide attempts than controls, but the children with the ADHD-I subtype were not (P=.99), controlling for race/ethnicity and the significant effect of sex (χ^2=5.17, $P<.03$; hazard ratio, 2.54). No significant differences were found among the 3 subtypes at the $P<.05$ level for any of these 3 adverse outcomes, however.

Table 4. Methods of Attempted Suicide Used in Single or Multiple Attempts by Children and Adolescents With at Least 1 Reported Suicide Attempt by Assessment Year 14

Method of Attempt	Children With ADHD at 4-6 Years, No. (n=23)	Comparison Children, No. (n=7)
Knife, slashing wrists, stabbing	6	1
Knife, slashing wrists, stabbing, drug overdose	3	0
Knife, slashing wrists, stabbing, hanging	1	1
Knife, slashing wrists, stabbing, drug overdose, firearm	1	0
Knife, slashing wrists, stabbing, drug overdose, hanging, toxic ingestion	1	0
Hanging	4	0
Hanging, firearm, jumping, drug overdose	1	0
Drug overdose	2	2
Jumping	1	1
Walking on railroad tracks	1	0
Unknown/refused	2	2

Abbreviation: ADHD, attention-deficit/hyperactivity disorder.

CHILD AND MATERNAL PREDICTORS OF FUTURE DEPRESSION AMONG PROBANDS

As shown in **Figure 3**A, among the 125 children with ADHD in wave 1, Cox modeling revealed that girls with ADHD were at greater risk for depression than boys

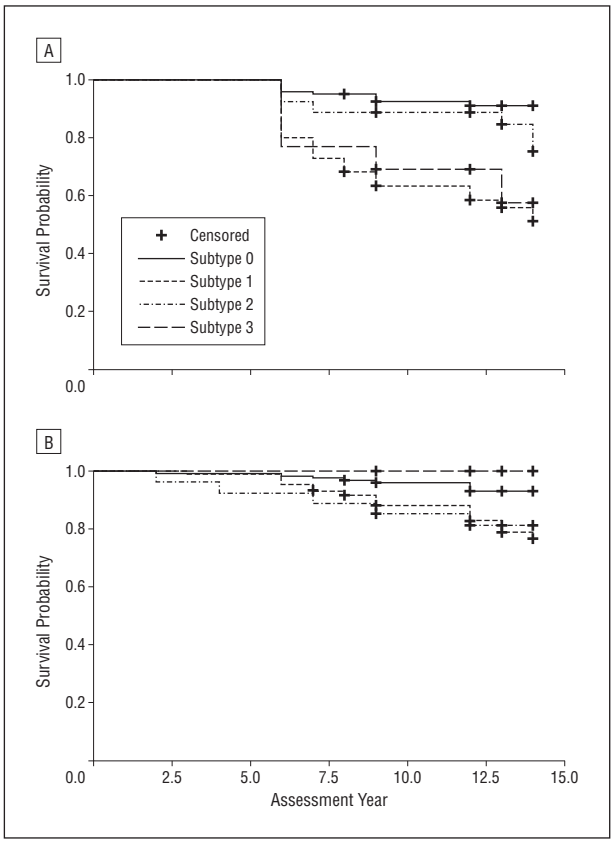

Figure 2. Survival probabilities for (A) the diagnosis of major depression and/or dysthymia and (B) suicide attempts during assessment years 6 through 14 (spanning 9-18 years of age) among comparison children and adolescents (n=123; 0) and children and adolescents who met criteria for the combined (n=85; 1), predominantly hyperactive-impulsive (n=27; 2), or predominantly inattentive (n=13; 3) subtypes of attention-deficit/hyperactivity disorder in year 1.

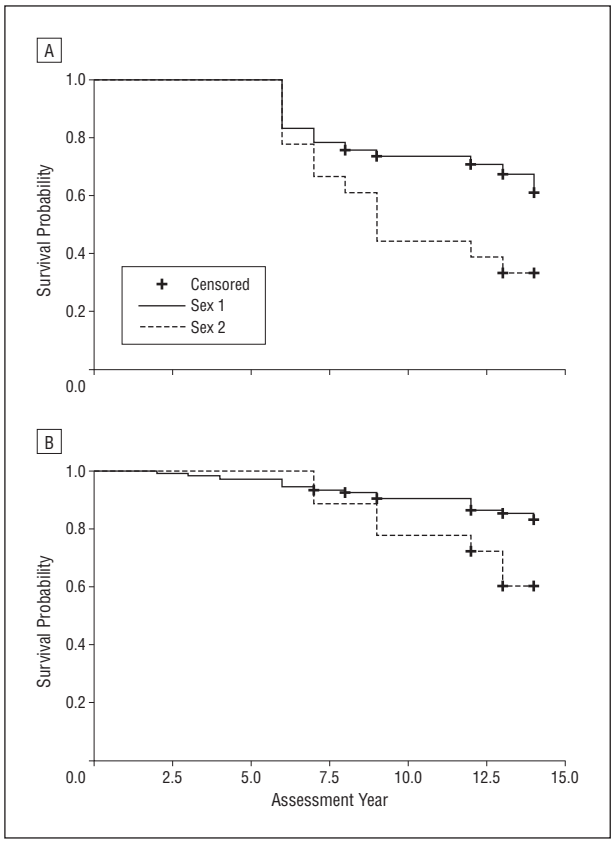

Figure 3. Survival probabilities for (A) the diagnosis of major depression and/or dysthymia and (B) suicide attempts during assessment years 6 through 14 (spanning 9-18 years of age) among boys (n=107) (1) and girls (n=18) (2) with attention-deficit/hyperactivity disorder in year 1.

with ADHD during assessment years 6 through 14 (χ^2=3.97, $P<.05$; hazard ratio, 1.96). In the same model, children with ADHD with depressed mothers (χ^2=3.95, $P<.05$; hazard ratio, 1.77) and older children and adolescents in year 1 (χ^2=5.00, $P<.03$; hazard ratio, 1.66) were at greater risk for depression. There was not a significant sex difference in the Cox model for the outcome of depression among children who did not meet criteria for ADHD in year 1 (χ^2=0.58, P=.45; hazard ratio, 0.45); indeed, adolescent depression was slightly more common in boys among children without ADHD in year 1.

A series of 4 separate longitudinal binomial regression analyses tested other child factors measured at ages 4 to 6 years, one at a time, to determine whether they predict future diagnoses of major depression or dysthymia among children with ADHD. The number of mother-reported child depression symptoms in assessment year 1 predicted future depression diagnoses (β=0.20, z=2.57, P=.01). In a separate model, mother-reported year 1 child anxiety symptoms predicted future depression (β=3.24, z=2.27, $P<.03$). In a third separate model, the number of mother-reported year 1 symptoms of child CD predicted future depression (β=0.22, z=2.57, $P<.02$). In a fourth model, the number of mother-reported year 1 symptoms of child oppositional defiant disorder did not significantly predict future depression (β=0.13, z=1.76, P=.08).

When all 4 child predictors were entered simultaneously, none was significant at $P<.05$. Because this is a substantive finding indicating that these correlated predictors accounted for overlapping variance in future depression (ie, collinear), the grand sum of the 4 kinds of mother-reported symptoms was tested as a predictor. The total number of these year 1 child emotional and disruptive symptoms significantly predicted future depression in longitudinal binomial regression (β=0.10, z=2.62, $P<.01$) (**Figure 4**). The interaction between the child's sex and the total number of year 1 child symptoms was not significant at $P<.05$. The adjusted OR estimated in logistic regression (OR, 1.15; 95% CI, 1.05-1.26) indicated that *each* additional child symptom in assessment year 1 (observed range, 0-17) was associated with 15.0% greater adjusted odds of meeting depression criteria at least once during waves 6 through 14.

CHILD AND MATERNAL PREDICTORS OF FUTURE SUICIDAL BEHAVIOR

Among the 125 children who met criteria for ADHD during year 1, Cox modeling revealed that girls were not at greater risk for later concrete suicidal ideation than boys (P=.17), but maternal depression placed children with ADHD at greater risk for concrete ideation (χ^2=9.55, $P<.001$; hazard ratio, 7.37). In contrast, Cox modeling revealed that girls with ADHD were at greater risk for sui-

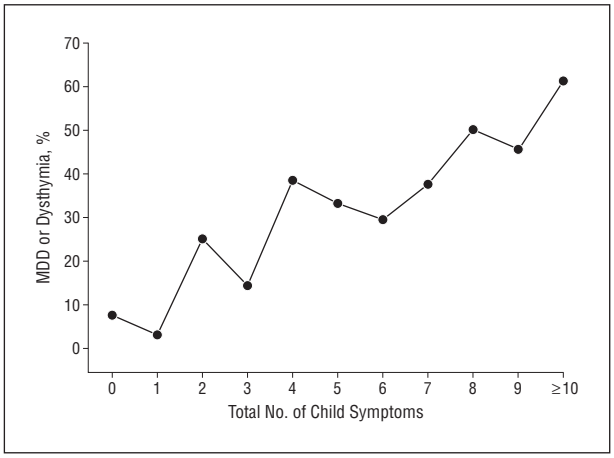

Figure 4. Association between the total number of depression, anxiety, oppositional defiant disorder, and conduct disorder symptoms in assessment year 1 and their meeting diagnostic criteria for depression at least once during assessment years 6 through 14 among the 125 children who met criteria for attention-deficit/hyperactivity disorder in year 1. MDD indicates major depressive disorder.

cide attempts than boys with ADHD ($\chi^2 = 3.89$, $P < .05$; hazard ratio, 2.57), controlling for cohort and age in year 1 (Figure 3B).

COMMENT

We tested the hypothesis that ADHD in early childhood predicts future depression and the key symptoms of concrete suicidal ideation and suicide attempts. The 7 diagnostic assessments conducted during assessment years 6 through 14 provided a strong evaluation of these outcomes over time and a sensitive test of the hypothesis. Our findings indicate that young children with ADHD are at high risk for both single and recurrent episodes of adolescent depression and for suicidal behavior, even controlling for a history of major depression in their mothers and other demographic and methodologic predictors of these outcomes. It is possible that findings of previous studies were inconsistent regarding the emergence of adolescent depression in children and adolescents with ADHD because they only assessed these episodic outcomes at a single point in time and perhaps because many samples included only boys. It is also possible that the children in the present study, who were referred at earlier ages than children in any previous study, to our knowledge, had a particularly severe form of ADHD that is strongly associated with adverse outcomes.

This is the first study, to our knowledge, to identify early child and family factors (measured at 4-6 years of age) that predict the later onset of depression among children with ADHD. There was not a sex difference in future concrete suicidal ideation among children with ADHD, but girls with ADHD were at greater risk for depression and suicide attempts than boys with ADHD. The small number of girls with ADHD is a limitation of the present study because we might have found that sex predicted other outcomes had we had greater statistical power. Nonetheless, the present study provides a rare long-term view of the clinical significance of ADHD in boys and girls and generates important hypotheses regarding sex differences in the outcomes of children with ADHD for future studies.

No significant sex difference was found in the risk for ever meeting criteria for adolescent depression by assessment year 14 among children who did not meet criteria for ADHD in year 1 (boys, 98 [9.2%]; girls, 21 [4.8%]). Given the small number of girls in the present sample one can only speculate, but this finding raises the important possibility that the greater increase in the prevalence of depression among girls beginning in early adolescence is found predominantly in children with a history of childhood ADHD.

Each diagnostic subtype of ADHD predicted important adverse outcomes, but they predicted somewhat different outcomes: ADHD-CT and ADHD-I predicted depression compared with controls, and ADHD-CT and ADHD-HI predicted suicide attempts. The latter finding may reflect the role of impulsivity in suicidal behavior.[33] Again, these conclusions are limited by the small number of children with ADHD-I and ADHD-HI at baseline because we may have found significant differences among the subtypes in outcomes had we had a larger sample. Nonetheless, this study provides the first long-term data regarding children with the *DSM-IV* subtypes of ADHD.

In addition, greater numbers of depression, anxiety, oppositional defiant disorder, and CD symptoms at ages 4 to 6 years among children with ADHD robustly predicted risk for depression during adolescence. Children with uncomplicated ADHD with few concurrent symptoms of other disorders were at low risk for depression, but children with many concurrent symptoms were at very high risk. In contrast, only CD symptoms at ages 4 to 6 years predicted suicide attempts. Although previous research[34] has shown that CD in middle childhood predicts future depression, but only if CD leads to social failure, this is the first study, to our knowledge, to show that early CD symptoms predict the specific symptom of attempted suicide. These findings suggest that it is possible to identify children with ADHD at very young ages who are at very high risk for later depression and suicidal behavior.

Considered in light of what is already known about the antisocial outcomes of childhood ADHD[35,36] and their risk for unintentional injury,[37] it would not be premature to test early prevention programs designed to reduce *both* serious behavioral and affective sequelae of ADHD in early childhood. Specific at-risk children could be identified on the basis of ADHD, maternal depression, and other predictors using recursive receiver operating characteristic curve–based methods that balance positive and negative predictive power.[38] Future research also should identify the mechanisms mediating these adverse outcomes among children with ADHD (eg, shared genetic risk or academic and social failure associated with ADHD fostering depression).

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