A 4-Year Follow-Up of Attention-Deficit/Hyperactivity Disorder in a Population Sample

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ABSTRACT

Background: Prior follow-up studies of attention-deficit/hyperactivity disorder (ADHD) ascertained ADHD cases in clinical samples mostly from North America but rarely from European countries. They have provided a good deal of information about the persistence of ADHD and its impairments, but the degree to which these results generalize to population samples and to other countries is not certain. Prior studies have also not assessed predictors of new-onset ADHD in youth without ADHD.

Method: At baseline, 7,912 of 18 million telephone numbers were randomly selected from throughout France from October 2, 2008, through December 11, 2008. Among 4,186 eligible families, 1,012 (24.2%) were successfully recruited at baseline, when a telephone interview was administered to all families about a child in the 6- to 12-year age range. Four years later, we attempted to recruit the entire sample to assess the persistence of ADHD and its impairments and the emergence of new associated conditions.

Results: 86.5% of the families assessed at baseline were followed-up (N = 875). Participants who were and were not interviewed at follow-up did not differ on any clinical or demographic features. At follow-up, the prevalence of full or subthreshold ADHD was 65.8% for ADHD participants and 9.8% for those not having ADHD at baseline. Among the children who were not diagnosed with ADHD at baseline, 3.4% were diagnosed with ADHD at follow-up. Both the persistence of ADHD and new onsets of ADHD were significantly predicted by several baseline clinical features and by having a family history of ADHD (all *P* values < .05).

Conclusions: We replicated prior predictors of ADHD's persistence and provide new data about predictors of new ADHD onsets in the population. Our data about subthreshold ADHD support a dimensional conceptualization of the disorder and address the potential clinical utility of a subthreshold diagnostic category.

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We know from decades of longitudinal research that a majority of patients with attention-deficit/hyperactivity disorder (ADHD) continue to be impaired by the disorder through adolescence into adulthood.[1–12] Indeed, although the persistence of ADHD had been questioned in the 1990s,[13] it is now widely accepted that ADHD persists in two-thirds of cases[14] and that this persistence increases the risk for substance use disorders,[15] psychiatric comorbidity,[6,16,17] poor work and social functioning,[18,19] emotional dysregulation,[20] executive dysfunction,[21,22] and criminality.[4]

Although most longitudinal studies of ADHD have focused on establishing the nature and severity of outcomes associated with the disorder, clinicians would benefit from knowing the degree to which clinical features in childhood predict later outcomes. Several studies have addressed this issue. The most consistent finding is that diagnoses of conduct disorder and measures of aggression predict a more persistent course of ADHD and its complications.[12,23–28] Other baseline clinical features found to be predictive of persistent ADHD from prospective, longitudinal studies are psychosocial adversity and psychiatric comorbidity,[29–32] functional impairments,[29,30] family and school functioning,[31] symptoms of hyperactivity,[32] and exposure to maternal psychopathology.[29] In a retrospective study[33] of adults with ADHD, childhood ADHD severity and childhood treatment significantly predicted persistence of ADHD.

Some evidence suggests that a family history of ADHD is associated with greater persistence of the disorder. In a prospective study of 140 ADHD boys and 120 boys without ADHD into mid-adolescence, 85% of the ADHD boys continued to have the disorder. The prevalence of ADHD was significantly higher among the relatives of persistent ADHD cases compared to relatives of remitted ADHD cases.[34] Parents of persistent ADHD cases were 20 times more likely to have ADHD than parents of controls, whereas parents of nonpersistent ADHD cases showed only a 5-fold increased risk. Similarly, siblings of persistent ADHD cases were 17 times more likely to have ADHD than siblings of controls, whereas siblings of nonpersistent ADHD cases showed only a 4-fold increased risk.[35] In the same sample, familial ADHD predicted persistence out to a 10 year follow-up.[29] A retrospective study[36] compared ADHD adolescents having retrospectively reported childhood-onset ADHD with ADHD children. The relatives of ADHD adolescents had higher rates of ADHD compared with the relatives of ADHD children.[36] A link between familial and persistent ADHD was also seen in a longitudinal study of velocardiofacial syndrome.[32] These data suggest that when

Clinical Points

- The ability to predict the prognosis of attention-deficit/hyperactivity disorder (ADHD) in patients is an important clinical tool because it helps clinicians focus scarce resources on efforts to monitor patients and prevent secondary disability. This study provides further evidence that persistence of ADHD is predicted by having a family history of ADHD, having ODD, and having higher levels of inattentive symptoms.
- Patients who have impairing ADHD symptoms but do not meet *DSM* criteria for ADHD are a diagnostic conundrum. This study shows that 14% of patients with subthreshold symptoms will convert to full diagnostic criteria over a 4-year period. Children with subthreshold ADHD symptoms may require close monitoring for worsening of the condition and also treatment depending on a clinical evaluation of the severity and pervasiveness of the impairing symptoms.

ADHD persists into adolescence and adulthood it is highly familial. Twin studies,[37] however, show that the heritability of ADHD is not greater in samples of adults compared with samples of children, which suggests that the familial effects of persistence are due to environmental risk factors.

In a systematic review, van Lieshout et al[38] assessed whether neuropsychological functioning predicted persistence of ADHD. They found 18 studies examining effortful and automatic neuropsychological tasks. None of these tasks reliably differentiated persistent from remitted cases of ADHD. In contrast to these negative results from studies of neuropsychological functioning, an emerging brain imaging literature has linked structural brain changes to the persistence of ADHD. Shaw et al[39] reported a 6-year longitudinal study of 163 children with ADHD and 166 controls without ADHD assessed with magnetic resonance imaging. Compared with persistent ADHD children, those with a good clinical outcome showed a normalization of cortical thickness over time in brain regions important for attentional control. Proal et al[40] imaged 59 adults, on average, 33 years after they had been diagnosed with ADHD as children. Consistent with Shaw and colleagues' study,[39] those with persistent ADHD had thinner cortices than those with remitting ADHD. They concluded that a compensatory maturation of prefrontal, cerebellar, and thalamic circuitry might lead to the remission of ADHD symptoms in ADHD patients. In a 16-year longitudinal study of persistent (n = 13) and remitted (n = 22) ADHD patients, Mattfeld et al[41] found that the positive functional correlation between 2 components of the default-mode network (posterior cingulate and medial prefrontal cortex) was reduced in patients with persistent ADHD.

Although these prior follow-up studies have yielded a wealth of valuable information about ADHD, nearly all ascertained ADHD cases were from clinical samples in North America. Thus, the degree to which these results generalize to population samples and to other countries is not certain. Prior studies have also not assessed predictors of new onsets of ADHD in youth without ADHD. The present study seeks to fill these gaps in the literature by reporting a 4-year follow-up study of a European population cohort. We hypothesized that new onsets of ADHD and persistence of ADHD would be predicted by baseline measures of conduct disorder, oppositional defiant disorder, and school difficulties.

METHOD

Ascertainment

Baseline. The baseline sample was selected from October 2, 2008, through December 11, 2008, by the survey company IDDEM (http://www.iddem.com/), which specializes in population-based epidemiologic telephone surveys.[42,43] Starting with 18 million French telephone numbers, 7,912 were randomly selected. When each phone number was called, we first asked for consent to proceed and then asked questions to determine the following demographic features: administrative region; size of the village, town, or city; marital status of the parents; and occupation of the head of household. Our goal was for the final distribution of our sample to match the distribution of the French population on each of these variables.

Of the 7,912 telephone numbers, 1,663 were no longer in service and 1,216 were not eligible because they did not have a child between the ages of 6 and 12 years. Among the 5,033 eligible families, 1,012 (20.1%) were successfully recruited. The remaining households were not recruited for the following reasons: telephone was not answered (892), telephone was busy (41), telephone would not accept anonymous calls (70), the person answering the phone refused to participate (1,342), the participant stopped the interview before completion (100), or we had achieved our target sample size (1,576). Families were usually called 6 times on different days before being classified as not answering or busy but, because some quota strata were more difficult to obtain than others, some families were called between 20 to 25 times before being classified as not answering or busy. If a family had more than 1 eligible child, we interviewed the parent about only 1 randomly selected child.

Four years after the baseline assessment, we attempted to contact each family by telephone to request their participation in the follow-up study. To maximize the possibility of contact, calls were made throughout the day between 7 AM and 11 PM. If no one answered the telephone, we attempted to make contact via mail. If the phone number was not working, we searched for the parents' names in the telephone directory of other regions.

Assessment

Baseline. After a parent in the household gave verbal consent to participate, the interviewer administered a 2-part questionnaire. The first part, which was administered to all families, covered family living situation, school performance of the child, symptoms of ADHD, conduct disorder (CD), and oppositional defiant disorder (ODD). To reduce costs, the second part was administered to all families having

an ADHD child and to a randomly selected subset of half the children without ADHD. The second part of the questionnaire included questions about sleep disturbance, eating habits, use of iron as a supplement, and history of treatment for ADHD. Structured questions were used to inquire about family history of ADHD and other disorders. The interviewers were trained by one of the authors (M.L.). The questions about disorders were adapted from a version of the Kiddie-Schedule for Affective Disorders and Schizophrenia for School Age Children[44] updated with items addressing all *DSM-IV* criteria by coauthors M.L. and E.K. At both baseline and follow-up, diagnoses were made following *DSM-IV* criteria. Following prior reports,[45–47] we defined "subthreshold ADHD" by modifying *DSM-IV* criteria by requiring only 3 or more inattentive symptoms or 3 or more hyperactive-impulsive symptoms.

Follow-up. At follow-up, we repeated the first part of the questionnaire, including family living situation, school performance of the child, symptoms of ADHD, CD, and ODD, and administered it to the sample. Family history of ADHD was collected at follow-up by asking the parent if any other family members had been diagnosed with the disorder. Family history was not collected at baseline.

Statistical Analysis

We used Pearson χ^2 to test the association of categorical variables, logistic regression to predict binary outcomes from continuous predictors, and ordinal logistic regression to predict ordinal outcomes from continuous predictors. We used receiver operating characteristic (ROC) curve analysis to determine the potential for making accurate predictions of persistent ADHD and new onsets of ADHD at follow-up. The ROC analysis assesses the diagnostic efficiency of tests for diagnoses and to adjust cut points for clinical or research purposes[48] and has been widely applied to assessing the accuracy of diagnostic tests.[49–52] The ROC analysis summarizes diagnostic efficiency with the area under the curve (AUC) statistic.

We used logistic regression to predict binary outcomes from baseline variables that were predictive in our univariate analyses. For each participant, we then computed the predicted values, or logits, from the logistic regression model. For each successive point on the logit scale, we computed a sensitivity and specificity of the logit as a predictor of prodromal status by predicting those higher than the cut point to be prodromal and others not to be prodromal. This was then used to draw the ROC curve. On the ROC graph, the sensitivity (true-positive rate) of different cut points on the test are graphed on the y-axis along with 1 minus the specificity (the false-positive rate) of the cut points on the x-axis to determine the ability of the test to optimize both measures for each point on the test. The higher the graph extends toward the upper left corner of the graph, the higher the discriminatory power of the test. The ROC analysis summarizes diagnostic efficiency with the AUC statistic. The AUC ranges from 0.5 (for a diagnostically useless test) to 1.0 (for a diagnostic test that is a perfect predictor). The AUC has 2 useful properties. First, it is equivalent to the Mann-Whitney *U* statistic computed from a comparison of a continuous score between 2 groups.[53] Second, it equals the probability that a randomly selected persistent or new-onset case will have a more extreme logit score than a randomly selected member of the nonpersistent or non–new-onset group.[53,54] All analyses used STATA 12.0 (StataCorp LP).

Table 1. Demographics at Follow-Up

Item	ADHD (N = 36), n (%)	Not ADHD (n = 976), n (%)	χ^2	*df*	*P* Value
Sex			4.7	1	.03
Female	11 (31)	477 (49)			
Male	25 (69)	499 (51)			
Marital status			1.2	2	.5
Married	27 (84)	698 (83)			
Single	0 (0)	29 (3)			
Widowed	5 (16)	113 (14)			
Education of parent			13.3	3	.004
Elementary	2 (7)	8 (1)			
Secondary	10 (32)	196 (23)			
College	9 (29)	163 (19)			
Graduate	10 (32)	471 (32)			
Parent employed			3.0	1	.08
Yes	31 (97)	723 (86)			
No	1 (3)	116 (14)			

Abbreviation: ADHD = attention-deficit/hyperactivity disorder.

RESULTS

Eight hundred seventy-five of the 1,012 participants seen at baseline (86.5%) were successfully followed up at the 4-year assessment. Participants who were and were not seen at follow-up did not differ on diagnoses of ADHD, CD, ODD, subtype of ADHD, or the numbers of symptoms for these disorders (all *P* values > .05). They did not differ on age, sex, parental education, parental unemployment, or parental reports of school difficulties, or repeating a grade (all *P* values > .05).

Table 1 compares the demographics of the groups with and without ADHD at follow-up. It shows that the ADHD cases (as defined by parent reports) were significantly more likely to be male. Their parents had significantly higher levels of education and were nonsignificantly more likely to be unemployed. The mean ± SD age of the ADHD group (13.6 ± 1.7 years) did not differ from the group without ADHD (13.4 ± 1.8 years; $z = 0.9$; $P = .36$).

4-Year Outcome of ADHD

Of the children diagnosed with ADHD at baseline, 43.8% also met full criteria for ADHD at follow-up. An additional 22% met our criteria for subthreshold ADHD, yielding a persistence rate of 65.8%. Among the children who were not diagnosed with ADHD at baseline, 3.4% were diagnosed with ADHD at follow-up. An additional 6.4% met our criteria for subthreshold ADHD. The group difference in rates of full criteria ADHD was significant ($\chi_2^2 = 107.2$, $P < .001$), as was the group difference when subthreshold ADHD was included in the estimate of persistence ($\chi^2_3 = 123.4$, $P < .001$).

Table 2 presents rates of psychiatric disorders and school problems at follow-up stratified by baseline ADHD

Table 2. Psychiatric Disorders and School Problems at Follow-Up by Baseline Attention-Deficit/Hyperactivity Disorder (ADHD)

Variable	ADHD (n = 32), n (%)	Not ADHD (n = 843), n (%)	χ^2_1	*P* Value
Conduct disorder	8 (25.0)	70 (8.3)	10.6	.001
Oppositional defiant disorder	17 (53.1)	171 (20.2)	19.7	< .001
Alcohol use	5 (15.6)	91 (10.8)	0.7	.39
Tobacco use	2 (6.2)	26 (3.1)	1.0	.32
Cannabis use	0 (0)	10 (1.2)	0.4	.53
School difficulties	20 (62.5)	110 (13.1)	59.4	< .001
Repeat a grade	12 (38.7)	111 (13.2)	16.1	< .001

diagnosis. The ADHD youth showed significantly greater rates of CD, ODD, school difficulties, and repeated grades compared to the non-ADHD youth. The 2 groups did not differ in rates of tobacco use, alcohol use, or cannabis use.

Predictors of the Persistence of ADHD

We next compared participants diagnosed with ADHD at baseline who did and did not persist with ADHD at follow-up. We examined 3 strata of persistence: full criteria ADHD (n = 14), subthreshold ADHD (n = 7), and not ADHD (n = 11). Because these subgroups are small, our results must be cautiously interpreted. These persistence groups did not differ in baseline rates of CD, school difficulties, or repeated grades. Persistence of ADHD was significantly predicted by baseline oppositional defiant disorder, treatment for ADHD, and having a family history of ADHD.

The mean number of baseline inattentive symptoms was significantly greater for those with persistent full (6.6 ± 1.7) or subthreshold (6.0 ± 2.4) ADHD compared with those who did not have ADHD at follow-up (3.6 ± 2.6, $z = 2.6$, $P = .009$). In contrast, the mean number of baseline hyperactive-impulsive symptoms did not discriminate the 3 groups (full ADHD: 5.4 ± 2.4; subthreshold ADHD: 2.7 ± 2.8; not ADHD: 4.3 ± 3.1; $z = 1.2$, $P = .2$). The mean number of ODD symptoms was greater for those with persistent full (2.6 ± 1.9) or subthreshold (1.7 ± 2.4) ADHD compared with those who did not have ADHD at follow-up (0.4 ± 0.7; $z = 2.7$, $P = .006$). In contrast, the mean number of baseline CD symptoms did not discriminate the 3 groups (full ADHD: 0.9 ± 1.6; subthreshold ADHD: 0.4 ± 1.1; not ADHD: 1.4 ± 2.7; $z = 0.6$, $P = .5$). As Table 3 shows, persistence was not predicted by baseline diagnoses of CD or problems in school. In contrast, persistent ADHD was predicted by participants having been treated for ADHD at baseline and having a sibling with ADHD (Table 3).

To estimate the predictive accuracy of the significant predictors, we computed a multivariate logistic regression model with persistence status as the outcome and all significant baseline measure as predictors. This model included only participants who had full or subthreshold ADHD at baseline. They were defined as having persistent ADHD at follow-up if they had either full or subthreshold ADHD at follow-up. When the logit scores from this model were used as the predictor for a ROC analysis, the area under the curve was 0.91 (Figure 1).

Predictors of New Onsets of ADHD

We next assessed which baseline features predicted new onsets of ADHD among children who had not been diagnosed with ADHD at baseline. These results are in Table 4. Compared with those without ADHD onset (n = 760), new-onset cases of full ADHD (n = 29) at follow-up were significantly more likely to have had subthreshold ADHD at baseline. New onsets of full ADHD or subthreshold ADHD (n = 54) were significantly more likely to have had difficulties in school or ADHD treatment. New onsets of ADHD were not predicted by diagnoses of CD or ODD or by having repeated a grade in school. With the exception of age, baseline demographic variables did not predict new onsets of ADHD. New onsets of ADHD were significantly younger than others at baseline (full ADHD: 9.1 ± 1.6; subthreshold ADHD: 8.8 ± 1.7; not ADHD: 9.4 ± 1.8; $z = 2.4$, $P = .02$).

The mean number of baseline inattentive symptoms was greater for those with new-onset full (0.93 ± 1.6) or subthreshold (1.02 ± 1.6) ADHD compared with those who did not have ADHD at follow-up (30.27 ± 0.8, $z = 5.9$, $P < .001$). The same was true for the mean number of baseline hyperactive-impulsive symptoms (full ADHD: 0.86 ± 1.5; subthreshold ADHD: 0.61 ± 1.2; not ADHD: 0.24 ± 0.8; $z = 4.5$, $P < .001$). The mean number of ODD symptoms was greater for those with new-onset full (0.69 ± 1.1) or subthreshold (0.54 ± 1.0) ADHD compared with those who did not have ADHD at follow-up (0.31 ± 0.9, $z = 2.6$, $P = .009$). In contrast, the mean number of baseline CD symptoms did not discriminate the 3 groups (full ADHD: 0.31 ± 0.9; subthreshold ADHD: 0.24 ± 0.9; not ADHD: 0.23 ± 0.8; $z = 0.4$, $P = .7$).

To estimate the predictive accuracy of the significant predictors, we computed a multivariate logistic regression model with new onset of full or subthreshold ADHD as the outcome and all significant baseline measures as predictors. This model included only participants who did not have either full or subthreshold ADHD at baseline. In this analysis, the area under the ROC curve was 0.68 (Figure 2).

DISCUSSION

Our 4-year follow-up of a population sample confirms prior reports of the persistence of ADHD and the morbid course of the disorder when assessed via parent reports. We replicated prior predictors of ADHD's persistence and provide new data about predictors of new ADHD onsets in the population. Our data also address the validity of cases of ADHD that meet only subthreshold symptom criteria, which is an understudied area. Our evaluation of predictive accuracy suggests that persistence of ADHD may be predictable but that new onsets of ADHD will be more difficult to predict.

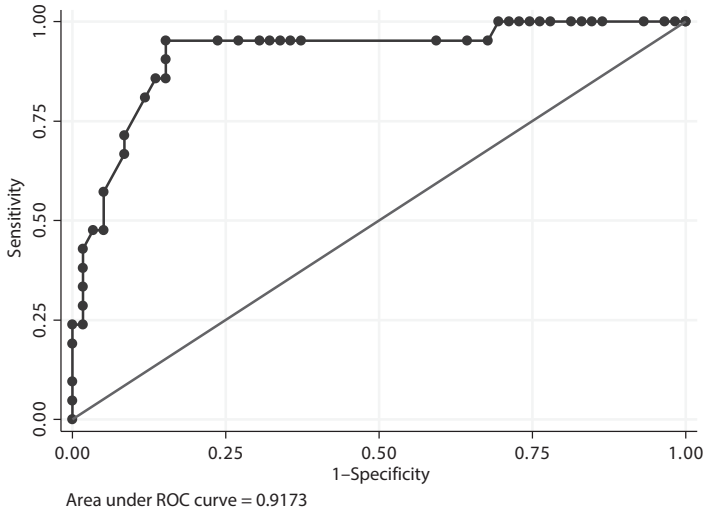
At a mean age of 13.6 years old, 65.8% of the ADHD group continued to show impairing symptoms of the disorder. This rate of persistence is somewhat lower than prior follow-up studies of ADHD into adolescence. It is somewhat lower than the 85% rate of persistence of full or

Table 3. Association of Baseline Clinical Features and Family History With Persistence of Attention-Deficit/Hyperactivity Disorder (ADHD)[a]

Variable	Follow-Up ADHD Diagnosis: ADHD (n = 14), n (%)	Subthreshold ADHD (n = 7), n (%)	Not ADHD (n = 11), n (%)	χ^2_2	*P* Value
Conduct disorder	2 (14.3)	1 (14.3)	2 (18.2)	0.08	1.0
Oppositional defiant disorder	7 (50.0)	2 (28.6)	0 (0)	7.6	.02
School difficulties	9 (64.3)	3 (42.9)	6 (54.6)	0.89	.64
Repeated a grade	5 (35.7)	1 (14.3)	3 (27.3)	1.1	.6
ADHD treatment	10 (71.4)	0 (0)	3 (27.3)	11.1	.004
Sibling ADHD diagnosis	6 (42.9)	0 (0)	0 (0)	9.5	.009
Family history of adult ADHD[b]	4 (28.6)	0 (0)	0 (0)	5.9	.05

[a]This table only includes subjects who had been diagnosed with ADHD at baseline.
[b]Family history was assessed at follow-up only.

Figure 1. Diagnostic Accuracy of Predicting Persistent Attention-Deficit/Hyperactivity Disorder[a]



[a]On the ROC graph, the sensitivity (true-positive rate) of different cut points on the predictor is graphed on the y-axis along with 1 minus the specificity (the false-positive rate) of the cut points on the x-axis to determine the ability of the test to optimize both measures for each point on the test. The higher the graph extends toward the upper left corner of the graph, the higher the discriminatory power of the test.
Abbreviation: ROC = receiver operating characteristic.

subthreshold ADHD computed in the data from Faraone et al[14] for the 3 studies[55–57] from US populations that followed ADHD from youth to ages between 12 and 15 years. Although we cannot determine if this lower rate of persistence is due to our use of a population sample or to the site of ascertainment being France rather than the United States, it seems likely that the lower severity of disorder in a nonreferred population would lead to a lower level of persistence. This is especially true given that our data and others indicate that increasing ADHD severity predicts greater persistence.[4,6,15–18,20–22] Like prior follow-up studies, we found that the magnitude of ADHD's persistence depended upon how we defined remission.[30,31,34]

At follow-up, the ADHD group had elevated rates of CD, ODD, school difficulties, and repeated grades, which show the continuing morbidity of the disorder. We did not, however, find significant differences in substance use disorders, which have been observed in other studies[15] that followed ADHD children into adolescence. Subsequent studies of this sample at older ages might see an emergence of these disorders.

Persistence of ADHD was significantly predicted by baseline ODD, treatment for ADHD, and having a family history of ADHD, which is consistent with prior studies.[29,32,34–36] In contrast, we did not replicate prior reports that the persistence of ADHD could be predicted from CD, school difficulties or repeated grades. Our ROC analyses suggest that it may be possible to accurately predict persistence, but these findings should be viewed cautiously because of the small number of ADHD youth in the baseline sample.

If the consistent findings about familial ADHD predicting persistence were due to genetic effects, one would expect that twin studies of adults would yield higher heritabilities than twin studies of children. But this is not the case.[37] This suggests that some familial environmental effect underlies the association between familiarity and persistence. From our data, we cannot tell if this is a confounding effect, such as a parental bias in ratings, or if it is an environmental risk factor yet to be determined.

Our data about new onsets of ADHD are novel. We know of no other studies that have assessed new onsets of ADHD longitudinally from childhood into adolescence. New-onset cases of full ADHD were significantly more likely to have had subthreshold ADHD at baseline. New onsets of full ADHD or subthreshold ADHD were predicted by baseline measures of inattentive symptoms, hyperactive-impulsive symptoms, oppositional defiant symptoms, school difficulties, and ADHD treatment or having a family history of ADHD. As one might expect, new onsets of ADHD were younger than those without ADHD at baseline. Although many predictors were significant, the accuracy of prediction was low as indicated by the AUC of 0.68. Future work using a larger assessment battery may be needed to improve diagnostic accuracy.

As has been seen in other epidemiologic studies,[58] it is not possible to confirm diagnoses of ADHD for some children whose parents report they had received treatment for the disorder. This could have been due to inappropriate treatment or the treatment of subthreshold symptoms. The latter interpretation is suggested by our finding that prior treatment for ADHD was a predictor of a new-onset ADHD diagnosis. It is also possible that children were prescribed methylphenidate for problems with low alertness/vigilance rather than for ADHD.

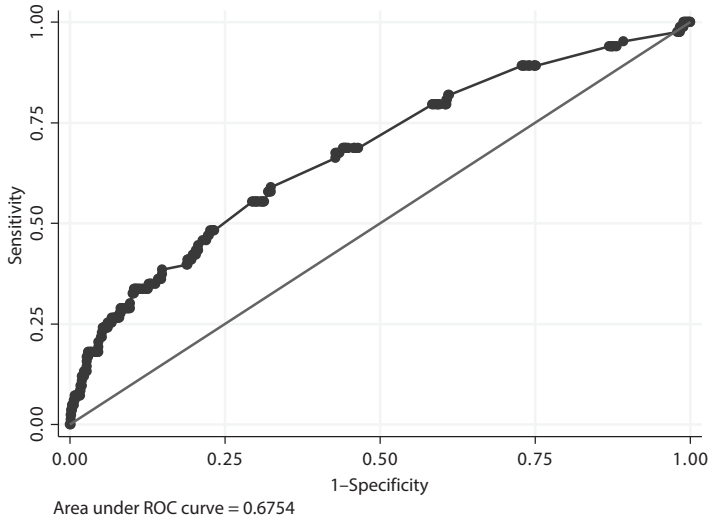
Our findings regarding subthreshold ADHD suggest that subthreshold symptoms of the disorder

Table 4. Association of Baseline Clinical Features and Family History With New Onsets of Attention-Deficit/Hyperactivity Disorder (ADHD)[a]

	New-Onset ADHD at Follow-Up				
Variable	ADHD (n = 29), n (%)	Subthreshold ADHD (n = 54), n (%)	Not ADHD (n = 760), n (%)	χ^2_2	*P* Value
Subthreshold ADHD	5 (17.2)	8 (14.8)	24 (3.2)	28.1	<.001
Conduct disorder	3 (10.3)	3 (5.6)	47 (6.2)	0.9	.6
Oppositional defiant disorder	0 (0)	1 (1.9)	17 (2.2)	0.7	.7
Difficulties in school	5 (17.2)	16 (29.6)	6 (0.8)	34.1	<.001
Repeat a grade	2 (6.9)	5 (9.3)	35 (4.6)	2.5	.3
ADHD treatment	2 (6.9)	5 (9.3)	12 (1.6)	16.4	<.001
Sibling with ADHD	6 (20.7)	10 (18.5)	46 (6.0)	19.3	<.001
Family history of adult ADHD[b]	2 (6.9)	6 (11.1)	34 (4.5)	4.9	.09

[a]This table only includes subjects who had not been diagnosed with ADHD at baseline.
[b]Family history was assessed at follow-up only.

Figure 2. Diagnostic Accuracy of Predicting New-Onset Attention-Deficit/Hyperactivity Disorder[a]



[a]On the ROC graph, the sensitivity (true-positive rate) of different cut points on the predictor is graphed on the y-axis along with 1 minus the specificity (the false-positive rate) of the cut points on the x-axis to determine the ability of the test to optimize both measures for each point on the test. The higher the graph extends toward the upper left corner of the graph, the higher the discriminatory power of the test.
Abbreviation: ROC = receiver operating characteristic.

may be a harbinger of the future onset of the full ADHD syndrome. From a clinical perspective, this is important because it suggests that children with subthreshold symptoms should be monitored for future onset of the disorder. Such monitoring would allow for early treatment and, perhaps, preventive interventions in youth showing other correlates of the disorder. Our results are consistent with the idea that ADHD is a dimensional syndrome[59] and that the clinical diagnosis corresponds to a cut point on that dimensional continuum. From this perspective, the category of subthreshold ADHD is analogous to borderline hypertension. Yet clinicians should be careful in treating these borderline cases as that would greatly increase the prevalence. In our follow-up sample, the prevalence of *DSM-IV* ADHD was 3.0% but when we add subthreshold cases, the prevalence climbs to 9.5%. A similar pattern of findings was seen in a family study of adult ADHD: subthreshold ADHD showed much evidence for validity, but its prevalence was too high to justify clinical utility.[45,46,60,61] More work is needed to better understand this subthreshold category.

Our work should be viewed in the context of several methodological limitations. We conducted phone interviews with a parent rather than using an in-person psychiatric interview. Although in-person interviews are desirable, prior work suggests that telephone interviews are valid. Biederman et al[28] found that telephone interviews had high reliability ($\kappa = 0.93$, $P < .0001$), high sensitivity (95%), and high specificity (98%) when in-person interviews with the mother were used as the gold-standard diagnosis. Telephone interviews used in a population survey of 1,000 adults to estimate the prevalence of ADHD[62] were replicated in work using in-person interviews,[63] and telephone interviews assessing functional impairments associated with ADHD[64] replicated our prior work using in-person interviews.[65] Others studies[66–73] have documented the validity of telephone interviews for many psychiatric disorders.

Another limitation of our work is that we used only one informant (a parent) to collect information about the child. Others have shown that the estimated prevalence of ADHD is sensitive to the choice of informants and the number of informants.[74,75] In addition, many psychiatric disorders were not assessed, so we could not comment on other comorbidities.

Another limitation is that only 24% of eligible patients agreed to participate at baseline, and 86.5% of these agreed to participate at follow-up. Thus, any psychiatric phenomena due to nonparticipation could have skewed our results. Such biases, however, were not evident at follow-up based on comparisons of those lost and not lost to follow-up. Researchers who attempt to replicate this work must consider that many more people than 7,900 will need to be screened to end up with enough people willing to participate over 4 years and to conduct multivariate regression analyses. Moreover, because we had small numbers in our 3 strata of persistence results, those results must be cautiously interpreted. Due to cost issues, we could not assess other factors that have been associated with persistence in prior studies.[34]

Despite these limitations, our work extends prior follow-up studies of ADHD from clinical samples to the general population and from North America to France. Our results regarding persistence are consistent with the prior literature, and we have also provided novel data about new onsets of ADHD in adolescence. These data suggest that youth without ADHD with warning

signs should be monitored for the potential emergence of the disorder in adolescence. It is the task of future work to improve our ability to predict new onsets and confirm our finding that persistence of ADHD can be predicted with substantial accuracy.

Drug names: methylphenidate (Ritalin and others).

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