Attention-Deficit/Hyperactivity Disorder in Young Children: Predictors of Diagnostic Stability

AUTHORS: Evelyn C. Law, MD,[a] Georgios D. Sideridis, PhD,[b,c] Lisa Albers Prock, MD, MPH,[a,c] and Margaret A. Sheridan, PhD[a,c,d]

[a]Division of Developmental Medicine, and [b]Clinical Research Center, Boston Children's Hospital, Boston, Massachusetts; [c]Harvard Medical School, Boston, Massachusetts; and [d]Harvard Center on the Developing Child, Harvard University, Cambridge, Massachusetts

WHAT'S KNOWN ON THIS SUBJECT: Approximately 50% of children diagnosed with attention-deficit/hyperactivity disorder (ADHD) at <7 years of age in the community do not meet criteria for ADHD over time. There is a need to examine predictors of diagnostic stability in young children with ADHD.

WHAT THIS STUDY ADDS: Predictors of diagnostic stability from early to middle childhood include child's baseline externalizing and internalizing symptoms, parental history of psychopathology, and socioeconomic status. These predictors may guide treatment planning at the time of ADHD diagnosis.

abstract

OBJECTIVES: The goals of this study were (1) to provide estimates of diagnostic stability for a sample of young children diagnosed with attention-deficit/hyperactivity disorder (ADHD) after undergoing comprehensive multidisciplinary assessments and (2) to identify baseline child and family characteristics that predict diagnostic stability over time.

METHODS: Children aged 3 to 6 years, 11 months consecutively diagnosed with ADHD after multidisciplinary consultations at a tertiary care clinic between 2003 and 2008 were recontacted in 2012 and 2013 (N = 120). At follow-up, the primary outcome was the proportion of children who continued to meet diagnostic criteria for ADHD. To identify predictors of diagnostic stability, logistic regression models were used. In addition, a latent class model was used to independently classify subjects into distinct clusters.

RESULTS: In this cohort, 70.4% of the children contacted at follow-up continued to meet diagnostic criteria for ADHD. Predictors of diagnostic stability included externalizing and internalizing symptoms at baseline, parental history of psychopathology, and family socioeconomic status. The latent class model independently identified 3 distinct profiles: (1) children who no longer met ADHD criteria; (2) children with persistent ADHD and high parental psychopathology; and (3) children with persistent ADHD and low family socioeconomic status.

CONCLUSIONS: Young children who underwent comprehensive developmental and psychological assessments before receiving an ADHD diagnosis, had higher rates of diagnostic stability than in previous studies of community samples. Child and family factors that predict diagnostic stability have the potential to guide treatment planning for children diagnosed with ADHD before 7 years of age. *Pediatrics* 2014;133:659–667

Attention-deficit/hyperactivity disorder (ADHD) is the most common neuro-behavioral disorder of childhood, occurring in 3% to 9.5% of children ages 4 to 17 years.[1–4] Diagnosis of ADHD in children aged <7 years presents significant challenges to clinicians because many behavioral manifestations of ADHD may be normative at such a young age.[5–8] Consequently, longitudinal studies exploring ADHD symptoms in preschool-aged children have demonstrated a wide range of estimates for diagnostic stability over time.[9–16] Previous research has defined "diagnostic stability" as the degree to which the original ADHD diagnosis is confirmed at the time of follow-up.

In studies that used community samples, diagnostic stability is ~50% for children aged <7 years after a ≥2-year period.[9–16] Most of these studies have used parent and/or teacher checklists to ascertain a diagnosis of ADHD; they lack comprehensive assessment to evaluate for alternative conditions, such as cognitive or language delays or sleep disorders. Studies using clinic-referred samples often use more rigorous ADHD diagnostic criteria and include some form of standardized assessment to rule out alternative diagnoses.[17–21] These studies demonstrate a higher percentage (65%–89%) of preschool-aged children continuing to meet ADHD criteria 3 to 8 years later. Thus, differences in patient populations and diagnostic strategies used across studies may influence the accuracy of the initial ADHD diagnosis and estimates of diagnostic stability. Another potential reason for variable rates of diagnostic stability is that behavioral profiles that are relatively stable later in childhood may be more malleable early. During early childhood, adversity, parental socioeconomic status (SES), and enriched environments have been shown to shift risk for psychiatric and developmental disorders, including ADHD.[22–30]

Predictors of ADHD stability among children diagnosed during preschool or kindergarten are poorly understood. In the studies available, children with persistent ADHD have higher psychiatric comorbidities, family history of psychopathology, and exposure to childhood adversity than children who no longer meet criteria for ADHD at follow-up.[14,15] However, in these studies, initial ADHD diagnoses have been assessed by using parent report of symptoms without in-depth evaluation of medical or developmental diagnoses that may mimic ADHD symptoms. To the best of our knowledge, the present study is the first study to identify predictors of diagnostic stability in children aged <7 years who received an ADHD diagnosis after medical, developmental, and psychological assessments.

METHODS

Subjects

Participants were 120 children ages 3 to 6 years, 11 months consecutively diagnosed with ADHD at the Developmental Medicine Center of Boston Children's Hospital between January 1, 2003, and December 31, 2008. These children were prospectively recontacted at a mean interval of 7 years (range: 5.6–9.5 years) after their initial diagnosis. Children who were adopted or had autism spectrum disorder (ASD), genetic syndromes, or brain injuries at the time of initial ADHD diagnosis were excluded. The Boston Children's Hospital institutional review board approved all study procedures.

Identification of ADHD in Young Children at Time 1

At time 1, each child completed a multidisciplinary assessment in which developmental–behavioral pediatricians obtained a detailed medical and social history, and completed a physical examination on each child; pediatric psychologists assessed each child's

developmental skills by using cognitive, language, and early academic standardized tests, reviewed day care and school intake questionnaires, and obtained ratings of child behavior by using the Behavior Assessment System for Children.[31] The team of clinicians met subsequent to the assessment to review the child's diagnostic criteria for ADHD and to discuss alternative diagnoses and potential comorbid conditions; the clinicians then systematically recorded all findings in a formal report.

Determination of Psychiatric Disorders at Time 2

After families were recruited for the follow-up time 2 study, they were scheduled for a visit in which parents completed the Diagnostic Interview Schedule for Children–Version IV (DISC-IV), Vanderbilt ADHD Diagnostic Parent Rating Scales, the parent global assessment (PGA), and the Children with Special Health Care Needs CSHCN Screener.[32–40] The PGA is a 7-point scale ranging from 1 (no impairments) to 7 (needs 24-hour supervision due to severe impairments). For children who were being treated with stimulant medications, parents were asked to complete rating scales describing their child's behavior on and off medication (eg, before the medication took effect in the morning). Parents also completed the Conflict Tactic Scales, Revised, which provides information about psychological and physical aggression in the family,[41] and the Social Communication Questionnaire–Lifetime Form,[42] which screens for difficulties in social and communication functioning. Parents were also asked about duration and intensity of behavioral therapy, school services, and medication use since time 1. Lastly, the Family Interview for Genetic Studies[43] and demographic information not uniformly available from records (including time 1 parental education and income) were obtained. Teachers were also asked to complete the

Vanderbilt ADHD Diagnostic Teacher Rating Scale.[44]

ADHD Case Definition at Time 2

Children who did not meet DSM-IV-TR criteria on both the DISC-IV and the Vanderbilt ADHD Diagnostic Parent Rating Scale, had a PGA score <3 (ie, minimal impairments), and <6 symptoms on the Vanderbilt ADHD Diagnostic Teacher Rating Scale were classified as no longer meeting criteria for ADHD at time 2. Nine children received an intermediate diagnosis on the DISC-IV, which indicated that symptoms and impairments were present but did not meet full diagnostic criteria for ADHD. Review of these 9 children showed that all of them had at least 4 symptoms in either the inattentive and/or hyperactive/impulsive criteria on the DISC-IV and the Vanderbilt ADHD Diagnostic Parent Rating Scale, impairments in multiple settings on the DISC-IV, a PGA score >3 (ie, moderate to severe impairments), and >6 symptoms on the Vanderbilt ADHD Diagnostic Teacher Rating Scale. For the purpose of this research study, we classified these intermediate cases as ADHD at time 2.

Covariates of Interest

All covariates were child and family characteristics at time 1 when each child initially received his or her ADHD diagnosis.

Child-level covariates included: (1) age at initial diagnosis; (2) gender; (3) presence of comorbid developmental, behavioral, or mental health diagnoses; (4) race/ethnicity; (5) composite nonverbal cognitive score on one of the following measures: the Wechsler Intelligence Scale for Children, the Wechsler Preschool and Primary Scale of Intelligence, the Differential Ability Scale, and the Stanford-Binet Intelligence Scales; (6) severity of externalizing symptoms (ie, attention problems, hyperactivity, aggression); and (7) severity of internalizing

symptoms (ie, anxiety, depression, somatization). The severity of externalizing and internalizing symptoms was taken from the Behavior Assessment System for Children and stratified into a T score ≥70 and <70.

Family-level covariates included: (1) parental history of psychopathology; (2) parental education level; (3) income-to-needs ratio (a proxy for family economic resources); and (4) percentage of residents living below the poverty level based on the child's address. Parental education level was a categorical variable divided into high school or less, some college, and at least a college degree. Income-to-needs ratio was calculated by dividing the subject's household income by the US Census Bureau poverty threshold income for a family of that size.

Data Analysis

Statistical analyses were conducted by using SPSS version 21.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY [2012]) and Latent GOLD 4.5 (Statistical Innovations Inc, Belmont, MA [2008]). To compare means of continuous variables, t tests were used; χ^2 statistics were used to compare proportions of categorical variables.

Logistic Regression

A multivariate logistic regression model was implemented to predict the stability of ADHD diagnosis from a combination of child-level and family-level factors. These factors were chosen on the basis of information from previous literature and were initially included in separate logistic regression models. A best synthesis model followed and included predictors with coefficients significant at $P < .10$.

Latent Class Model

Data were analyzed by means of latent class mixture modeling in an effort to identify the presence of subgroups that shared similar levels across a combi-

nation of independent variables. The latent class models were developed initially for dichotomous variables[45] and were extended to include nominal[46] and, subsequently, continuous indicators.[47,48] Because the likelihood ratio χ^2 statistic had been shown to be sensitive to sparse data, bootstrapping P values by using 500 replicated data sets was used to test the improvement in fit between 2 models in this study.[49] The magnitude of R^2 values, correct classifications based on group membership (stable versus unstable diagnosis), significance of independent variables in defining cluster group membership, and a significant reduction in the likelihood ratio test (L^2) were all considered when comparing nested models.

RESULTS

Study Participants

At time 1, a total of 330 children aged <7 years received an ADHD diagnosis in the Developmental Medicine Center of Boston Children's Hospital. Of these, 120 met inclusion criteria and were seen by the multidisciplinary teams described earlier (Fig 1). Longitudinal follow-up was possible for 88 children (73.3% of the cohort). Table 1 presents baseline characteristics of the cohort. Characteristics of children who were and were not followed up at time 2 were compared; there was no significant difference between the 2 groups in age of initial ADHD diagnosis, current age, gender, nonverbal cognitive score, and percent living below the poverty level.

Behavioral, Developmental, and Psychiatric Profiles of the Cohort

The cohort as a whole was found to have high rates of comorbid developmental disorders after multidisciplinary assessment as well as high rates of comorbid psychiatric disorders at follow-up (Table 2). After a mean interval of 7 years, 62 children (70.4% of
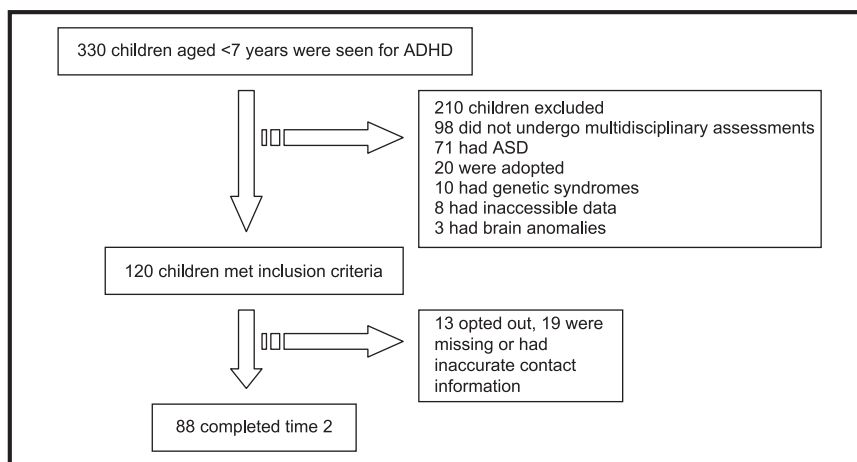
330 children aged <7 years were seen for ADHD

210 children excluded
98 did not undergo multidisciplinary assessments
71 had ASD
20 were adopted
10 had genetic syndromes
8 had inaccessible data
3 had brain anomalies

120 children met inclusion criteria

13 opted out, 19 were missing or had inaccurate contact information

88 completed time 2

FIGURE 1
Study population flow diagram.

TABLE 1 Characteristics of the Study Cohort

Characteristic	Entire Cohort		Children With ADHD at Time 2 (n = 62)		Children Without ADHD at Time 2 (n = 26)		P^a
	Mean	SD	Mean	SD	Mean	SD	
Age at diagnosis, mo	68.13	11.35	68.25	11.78	68.93	9.73	.778
Age at time 2, mo	150.89	24.36	150.20	24.74	153.04	24.19	.618
Percent living below poverty level	8.55	8.49	9.08	8.92	7.04	5.73	.202
Nonverbal cognitive composite	93.16	17.36	90.00	15.87	95.11	14.08	.154
Income-to-needs ratio	4.40	3.75	2.90	2.01	7.69	4.55	<.001***
	N	%	N	%	N	%	
Females	21/120	17.50	11/62	17.74	4/26	15.38	.788
Presence of comorbid condition	91/120	75.83	45/62	72.58	21/26	80.77	.418
At least 1 externalizing subscale with T score >70	59/120	49.20	39/62	62.90	6/26	23.08	.001**
At least 1 internalizing subscale with T score >70	19/120	15.80	12/62	19.35	2/26	7.69	.172
Race (non-Hispanic white)	64/88	72.73	42/62	67.74	22/26	84.62	.105
Maternal education (up to high school)	18/88	20.45	16/62	25.81	3/26	11.54	.138
Paternal education (up to high school)	27/88	30.68	26/62	41.94	4/26	15.38	.017*
Parental report of psychopathology	77/176	43.75	68/124	54.84	9/52	17.31	<.001***
Parental report of anxiety and/or depression	60/176	34.09	54/124	43.55	6/52	11.54	<.001***
Parental report of bipolar disorder	10/176	5.68	8/124	6.45	2/52	3.85	.496
Parental report of schizophrenia	7/176	3.98	6/124	4.84	1/52	1.92	.367
Parental report of substance abuse	24/176	13.64	16/124	12.90	8/52	15.38	.662
Parental report of ADHD	93/176	52.84	82/124	66.13	11/52	21.15	<.001***

* $P < .05$, ** $P < .01$, *** $P < .001$.
a To compare children with and without ADHD at time 2, t tests and χ^2 statistics were used.

the cohort) continued to meet diagnostic criteria for ADHD.

Prediction of Stable ADHD Diagnosis by Using Logistic Regression Analysis

Within the child-level model, significant predictors of ADHD stability included elevated externalizing symptoms (b = 2.21, $P < .01$; odds ratio [OR]: 9.0), elevated internalizing symptoms (B = 1.53, $P < .05$; OR: 4.6), and lower nonverbal composite score (B = −0.05, $P < .05$, OR: 0.94) (Table 3). Family-level predictors were positive parental history of psychopathology (B = 2.04, $P < .05$; OR: 7.6) and lower income-to-needs ratio (B = −0.57, $P < .001$; OR: 0.56). In the combined model, the significant predictors discussed earlier remained significant except for the child's nonverbal cognitive score. All results were in the same direction and were more pronounced.

Exploring the Presence of Subgroups Based on ADHD Diagnostic Stability By Using Latent Class Modeling

A set of ancillary analyses was conducted to evaluate whether specific clusters of individuals and profiles would explain the stability of ADHD

TABLE 2 Comorbid Diagnoses of the Cohort of Young Children Diagnosed With ADHD

Type of Comorbid Disorder[a]	Time Point		
	Before Initial Multidisciplinary Assessment ($N = 120$)	Time 1 ($N = 120$)	Time 2 ($n = 88$)
ADHD	2 (1.67%)	120 (100%)	62 (70.40%)
Behavioral disorders[b]	1 (0.82%)	4 (3.28%)	11 (12.50%)
Learning disorders	0	21 (17.50%)	31 (35.22%)
Tics disorder	0	0	6 (6.81%)
Mood disorders[c]	0	10 (8.33%)	34 (38.60%)
Developmental disabilities[d]	20 (16.67%)	78 (65.00%)	40 (45.45%)
Sleep disorders	2 (1.67%)	5 (4.17%)	5 (5.68%)

[a] Disorders are not mutually exclusive.

[b] Behavioral disorders include disruptive behavior disorder, oppositional defiant disorder, and conduct disorder.

[c] Mood disorders include anxiety, obsessive-compulsive disorder, depression, bipolar disorder, and mood disorder, not otherwise specified.

[d] Developmental disabilities include global developmental delay, intellectual disability, language/communication disorder, and motor/coordination disorder.

TABLE 3 Logistic Regression Analysis for the Prediction of Stability of an ADHD diagnosis From Child-Level, Family-Level, and Combined Model Predictors

Predictors	B	SE	P	OR	95% Confidence Interval	
					Lower Bound	Upper Bound
Child-level factors						
Gender (girls)	−0.672	0.918	.464	0.511	0.084	3.086
Current age	−0.012	0.014	.414	0.988	0.961	1.017
Nonverbal cognitive composite	−0.052	0.025	.034*	0.949	0.904	0.996
Elevated externalizing behaviors	2.21	0.711	.002**	9.094	2.257	36.639
Elevated internalizing behaviors	1.53	0.674	.023*	4.606	1.230	17.250
Age at initial diagnosis	0.027	0.031	.392	1.027	0.966	1.092
Race (white)	0.652	0.681	.338	1.920	0.505	7.292
Presence of comorbid diagnoses	−1.35	0.812	.097	0.260	0.053	1.276
Family-level factors						
Gender[a]	−0.622	0.888	.484	0.537	0.094	3.060
Current age[a]	0.013	0.014	.360	1.013	0.986	1.040
Parent history of psychopathology	2.04	0.952	.032*	7.683	0.413	0.773
Income-to-needs ratio	−0.572	0.160	<.001***	0.565	0.079	1.805
Parental education (up to high school)	−0.974	0.798	.222	0.377	1.190	49.611
Percent living in poverty	−0.021	0.048	.658	0.979	0.892	1.075
Combined model, including child-level and family-level factors						
Gender[a]	−1.17	1.325	.378	0.311	0.023	4.179
Current age[a]	0.018	0.017	.305	1.018	0.984	1.053
Nonverbal cognitive composite	−0.053	0.034	.121	0.948	0.886	1.014
Elevated externalizing behaviors	2.33	1.041	.025*	10.297	1.339	79.192
Elevated internalizing behaviors	2.33	1.157	.044*	10.319	1.069	99.621
Presence of comorbid diagnoses	−1.18	1.077	.275	0.309	0.037	2.551
Parental history of psychopathology	3.55	1.460	.015*	34.643	1.980	606.272
Income-to-needs ratio	−0.749	0.216	.001**	0.473	0.309	0.723

* $P < .05$, ** $P < .01$, *** $P < .001$.

[a] Gender and current age were forced into the model.

diagnosis (Table 4). A 1-class, baseline model was used as a reference point, and this model was compared with a 2-class model. The 2-class model provided a good fit to the data and suggested that the group of children with stable ADHD diagnosis had baseline characteristics different from the group of children with unstable ADHD diagnosis ($R^2 = 90.25\%$). Although the 2-class model provided a good fit to the data, examination of the bivariate residuals suggested that some were above the expected value of 1.0, and the probability of misfit was equal to 3.4%. Thus, on the basis of findings from previous research,[50,51] the model was fit with the addition of a 3-class model, in an attempt to minimize those residual covariations and to improve model fit. The difference between a 2-class and a 3-class model was evaluated by using the log-likelihood −2LL statistic based on the bootstrap distribution and 500 replications (Table 5), suggesting that a 3-class model provided significantly improved fit (−2LL$_{Diff}$ = 165.76, $P < .001$).

In the 3-class model, there were 2 classes of children that belonged to the stable ADHD group and 1 class of children that fit into the unstable ADHD group (Fig 2). Only 8.14% were considered misclassified cases. Class 1 represented children with a 99.5% probability of having a stable ADHD diagnosis. These were children with elevated internalizing and externalizing symptoms, had parents with a history of psychopathology and low educational level, and also came from families with low family economic resources. Class 2 described a cluster of children with an 82% probability of having a stable ADHD diagnosis. The major difference, however, was that children in class 2 tended to have parents with more psychopathology but a higher probability of attending college and higher income-to-needs ratio compared with class 1 children. Last, class 3 described children who no longer met criteria for ADHD. These children were characterized by relatively low levels of internalizing and externalizing symptoms during early childhood, came from families with higher economic resources, and had parents who were more likely to attend college.

Profiles of Children With Remitted ADHD

Of the 26 children who did not meet diagnostic criteria for ADHD at follow-up,

TABLE 4 Percentage of Sample Belonging to Each Class and Significance of Predictor

Fixed Effect	Class 1 Stable Diagnosis	Class 2 Stable Diagnosis	Class 3 Unstable Diagnosis	Z Test	P	$R^{2,a}$
Cluster size, n (%)	33 (38.4)	29 (33.7)	2 (27.9)			
Stability of ADHD diagnosis				3.009	.0047**	65.8%
Stable	99.5%	82.06%	8.71%			
Parental history of psychopathology				2.223	.08	8.92%
Present	91.09%	93.86%	69.86%			
Externalizing symptoms				2.360	.0096**	14.19%
T score >70 in ≥1 subscale	53.63%	42.82%	27.34%			
Internalizing symptoms				2.108	.11	9.30%
T score >70 in ≥1 subscale	22.52%	23.82%	5.63%			
Parents going to college				1.894	.011*	60.98%
Yes	4.65%	88.94%	78.38%			
Income-to-needs ratio				4.810	<.001***	55.83%
Income greater than expected for a family of that size	6.44%	20.89%	41.92%			

* $P < .05$, ** $P < .01$, *** $P < .001$.

a These values indicate amount of variance of each variable explained by using the 3-class solution.

TABLE 5 Nested Latent Class Models Suggesting the Superiority of a 3-Class Solution Over Competing 1- and 2-Class Models for Explaining Stability in ADHD Diagnosis

Model Tested	BIC$_{LL}$^{a}	LL	Class Error^b, P
1-class independence model	1278.330	−610.212	<.0001***
2-class	1199.742	−553.100	.039*
3-class	1183.840	−527.332	.732

* $P < .05$, *** $P < .001$.

a BIC$_{LL}$, Bayesian Information Criterion based on log-likelihood.

b A nonsignificant model indicates no difference between the hypothetical and obtained model.
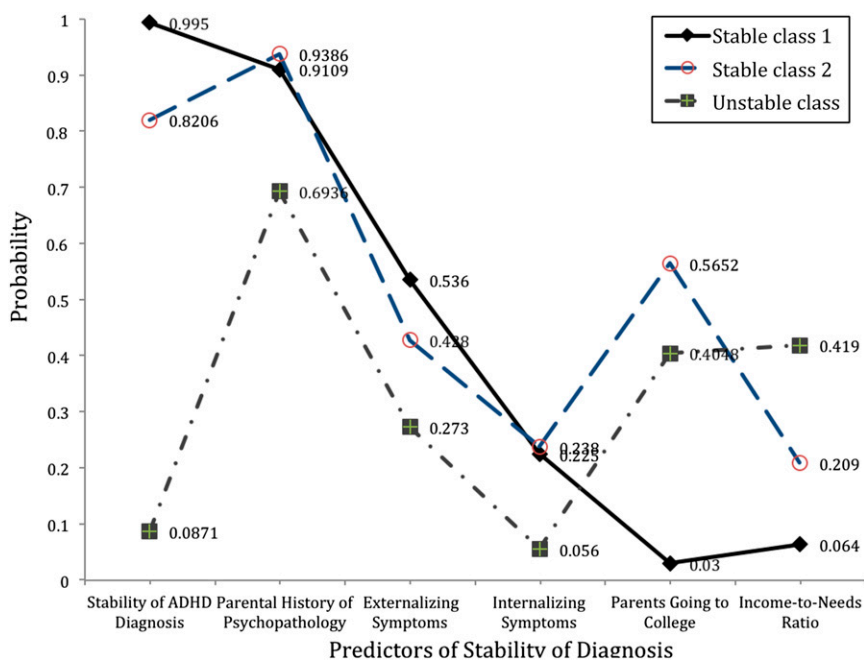
FIGURE 2
Latent class model displaying the presence of 2 stable diagnosis classes and 1 unstable diagnosis class.

LAW et al

new diagnoses emerged in 15 children. Specifically, 2 children met criteria for anxiety disorders, 10 had new diagnoses of ASD, and another 3 had new learning disorders. The remaining children did not meet diagnostic criteria for any developmental, learning, or behavioral disorder, including ADHD, and did not shift from one externalizing disorder to another, which suggests remittance of ADHD symptoms at time 2. For children who were reported to have new ASD by parents, psychological reports were available for the majority of these children. Their Social Communication Questionnaire total scores (median: 17.40 points) were significantly higher compared with those without a new ASD diagnosis (median: 5.93 points; $P < .001$).

DISCUSSION

Several important findings emerged from the present cohort study. First, ADHD stability over a 7-year period was 70% when young children underwent comprehensive developmental and psychological evaluations. Although diagnostic stability in this cohort was higher overall than previous studies of community samples[9–16], this study found that diagnosing ADHD in young children is not an easy task, even for professionals with expertise in the pediatric ADHD population. More than one-half of children who no longer met criteria for ADHD were later found to have alternative developmental diagnoses, including anxiety, ASD, and learning disorders. However, there was a group of children who no longer met criteria for ADHD and did not have any new onset of psychiatric disorders, suggesting ADHD remittance over time.

Clinicians caring for young children with ADHD symptoms, therefore, should be equipped to monitor learning, behavioral, and mood difficulties over time. Importantly, children with an early ADHD diagnosis should have continuity of care with clinicians who have expertise in

ADHD or should receive a comprehensive reevaluation during school age.

Although it is not surprising that elevated externalizing symptoms are associated with stability in ADHD diagnosis, we additionally observed that children with a greater risk of ADHD persistence had higher internalizing symptoms at a young age. This finding is consistent with previous literature on older children with ADHD,[52–54] and it points to the importance of screening for internalizing symptoms at initial diagnostic visits, even when parental concerns are about disruptions due to externalizing symptoms.

Finally, we observed that family factors, including parental history of psychopathology and family economic resources, are predictive of ADHD diagnostic stability. The idea that family contexts contribute to the maintenance of preschool-aged problem behaviors and long-term impairments is not new. Previous research studies have shown that variables of maternal psychopathology, family climate, and SES are predictive of stability of preschool psychiatric disorder.[14,15] Given the convergence of these findings in these previous samples and our own research, it seems that factors related to the family should be explored more explicitly in clinical settings. Furthermore, these findings indicate that parent-training programs may have a potentially important role in ADHD treatment in early childhood and may enhance child-specific treatments in this young age range. Evidence-based parent management training has been shown to help parents actively acquire parenting skills that target relationship building and improve parent–child interactions, as well as lower children's externalizing behaviors.[55,56] The American Academy of Pediatrics therefore recommends that primary care physicians prescribe such evidence-based therapy as a first line of treatment for preschool-aged children.[57]

Interestingly, parental education emerged in the latent class model as the most discriminating variable in the prediction of ADHD stability (R^2 = 60.98%). One possible explanation is that parents with different levels of education provide a different day-to-day environment for children and that these environmental factors mediate changes in the prefrontal cortex, decreasing ADHD symptoms over time. This speculation is bolstered by recent data pointing to the impact of early environments, particularly those linking the effects of SES on prefrontal cortex development and neurocognitive measures associated with ADHD symptoms.[23,24,58] Potential mediators of the relationships between low parental education and high ADHD persistence include differences in the quality of the home environment (eg, use of complex language, enrichment activities), quality of parent–child interactions, and degree of family conflicts. The influences of these variables on diagnostic stability in ADHD are beyond the scope of the present study but are of critical importance to explore in future studies.

Several limitations should be noted when interpreting our findings. One limitation is that this cohort consisted of children referred to a single tertiary care clinic. However, these children were not a convenience sample or recruited from advertisement. Our cohort consisted of every child aged <7 years diagnosed with ADHD in our specialty clinic in 2003 to 2008; almost all of them were referred to this clinic because pediatricians would not otherwise give a diagnosis of ADHD or start treatment at such a young age. Another limitation is that we were not able to recontact every child diagnosed at time 1. However, a comparison of demographic data indicated that subjects lost to follow-up did not differ from subjects with full participation. Lastly, families in this cohort had a higher mean income compared with the mean income of the US population, even when family size was considered. Use of a cohort with higher SES may have biased the study toward less severe cases and, consequently, may have produced more conservative results.

CONCLUSIONS

Although ADHD symptoms may improve in a subset of children, for many, ADHD symptoms are chronic and associated with many psychiatric comorbid conditions. Those with higher risk for long-term ADHD have more externalizing symptoms and internalizing symptoms at baseline, more parental psychopathology, and fewer family economic resources. This study adds to the growing literature demonstrating that: (1) child-specific therapies may not suffice as the only armamentarium for practitioners treating children with ADHD; and (2) the preschool years may serve as an important, sensitive period for intervention.

REFERENCES

1. Centers for Disease Control and Prevention (CDC). Mental health in the United States. Prevalence of diagnosis and medication treatment for attention-deficit/hyperactivity disorder—United States, 2003. *MMWR Morb Mortal Wkly Rep.* 2005;54(34):842–847

2. Centers for Disease Control and Prevention (CDC). Increasing prevalence of parent-reported attention-deficit/hyperactivity disorder among children—United States, 2003 and 2007. *MMWR Morb Mortal Wkly Rep.* 2010;59(44):1439–1443

3. Froehlich TE, Lanphear BP, Epstein JN, Barbaresi WJ, Katusic SK, Kahn RS. Prevalence, recognition, and treatment of attention-deficit/hyperactivity disorder in a national sample of US children. *Arch Pediatr Adolesc Med.* 2007;161(9):857–864

4. Centers for Disease Control and Prevention (CDC). Attention-deficit/hyperactivity disorder (ADHD). Data and statistics. Available at: www.cdc.gov/ncbddd/adhd/data.html. Accessed October 10, 2013

5. Kadesjö C, Kadesjö B, Hägglöf B, Gillberg C. ADHD in Swedish 3- to 7-year-old children. *J Am Acad Child Adolesc Psychiatry.* 2001;40(9):1021–1028

6. Pineda D, Ardila A, Rosselli M, et al. Prevalence of attention-deficit/hyperactivity disorder symptoms in 4- to 17-year-old children in the general population. *J Abnorm Child Psychol.* 1999;27(6):455–462

7. Smidts DP, Oosterlaan J. How common are symptoms of ADHD in typically developing preschoolers? A study on prevalence rates and prenatal/demographic risk factors. *Cortex.* 2007;43(6):710–717

8. Campbell SB. Behavior problems in preschool children: a review of recent research. *J Child Psychol Psychiatry.* 1995;36(1):113–149

9. Campbell SB, Ewing LJ, Breaux AM, Szumowski EK. Parent-referred problem three-year-olds: follow-up at school entry. *J Child Psychol Psychiatry.* 1986;27(4):473–488

10. Campbell SB, Ewing LJ. Follow-up of hard-to-manage preschoolers: adjustment at age 9 and predictors of continuing symptoms. *J Child Psychol Psychiatry.* 1990;31(6):871–889

11. Pierce EW, Ewing LJ, Campbell SB. Diagnostic status and symptomatic behavior of hard-to-manage preschool children in middle childhood and early adolescence. *J Clin Child Psychol.* 1999;28(1):44–57

12. McGee R, Partridge F, Williams S, Silva PA. A twelve-year follow-up of preschool hyperactive children. *J Am Acad Child Adolesc Psychiatry.* 1991;30(2):224–232

13. Palfrey JS, Levine MD, Walker DK, Sullivan M. The emergence of attention deficits in early childhood: a prospective study. *J Dev Behav Pediatr.* 1985;6(6):339–348

14. Lavigne JV, Arend R, Rosenbaum D, Binns HJ, Christoffel KK, Gibbons RD. Psychiatric disorders with onset in the preschool years: II. Correlates and predictors of stable case status. *J Am Acad Child Adolesc Psychiatry.* 1998;37(12):1255–1261

15. Tandon M, Si X, Luby J. Preschool onset attention-deficit/hyperactivity disorder: course and predictors of stability over 24 months. *J Child Adolesc Psychopharmacol.* 2011;21(4):321–330

16. Harvey EA, Youngwirth SD, Thakar DA, Errazuriz PA. Predicting attention-deficit/hyperactivity disorder and oppositional defiant disorder from preschool diagnostic assessments. *J Consult Clin Psychol.* 2009;77(2):349–354

17. Lahey BB, Pelham WE, Stein MA, et al. Validity of DSM-IV attention-deficit/hyperactivity disorder for younger children. *J Am Acad Child Adolesc Psychiatry.* 1998;37(7):695–702

18. Lahey BB, Pelham WE, Loney J, et al. Three-year predictive validity of DSM-IV attention deficit hyperactivity disorder in children diagnosed at 4-6 years of age. *Am J Psychiatry.* 2004;161(11):2014–2020

19. Beitchman JH, Wekerle C, Hood J. Diagnostic continuity from preschool to middle childhood. *J Am Acad Child Adolesc Psychiatry.* 1987;26(5):694–699

20. 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

21. Riddle MA, Yershova K, Lazzaretto D, et al. The Preschool Attention-Deficit/Hyperactivity Disorder Treatment Study (PATS) 6-year follow-up. *J Am Acad Child Adolesc Psychiatry.* 2013;52(3):264–278.e2

22. Nelson CA, Sheridan MA. Lessons from neuroscience research for understanding causal links between family and neighborhood characteristics and educational outcomes. In: Duncan G, Murnane RJ, ed. *Whither Opportunity?: Rising Inequality, Schools, and Children's Life Chances.* New York, NY: Russell Sage Foundation; 2011

23. Sarsour K, Sheridan M, Jutte D, Nuru-Jeter A, Hinshaw S, Boyce WT. Family socioeconomic status and child executive functions: the roles of language, home environment, and single parenthood. *J Int Neuropsychol Soc.* 2011;17(1):120–132

24. Sheridan MA, Sarsour K, Jutte D, D'Esposito M, Boyce WT. The impact of social disparity on prefrontal function in childhood. *PLoS ONE.* 2012;7(4):e35744

25. Noble KG, Norman MF, Farah MJ. Neurocognitive correlates of socioeconomic status in kindergarten children. *Dev Sci.* 2005;8(1):74–87

26. Hackman DA, Farah MJ. Socioeconomic status and the developing brain. *Trends Cogn Sci.* 2009;13(2):65–73

27. Benjet C, Borges G, Medina-Mora ME. Chronic childhood adversity and onset of psychopathology during three life stages: childhood, adolescence and adulthood. *J Psychiatr Res.* 2010;44(11):732–740

28. Raizada RD, Kishiyama MM. Effects of socioeconomic status on brain development, and how cognitive neuroscience may contribute to levelling the playing field. *Front Hum Neurosci.* 2010;4:3

29. Galera C, Bouvard MP, Lagarde E, et al. Childhood attention problems and socioeconomic status in adulthood: 18-year follow-up. *Br J Psychiatry.* 2012;201(1):20–25

30. Poulton R, Caspi A, Milne BJ, et al. Association between children's experience of socioeconomic disadvantage and adult health: a life-course study. *Lancet.* 2002;360(9346):1640–1645

31. Reynolds CR, Kamphaus, RW. *The Clinician's Guide to the Behavior Assessment System for Children.* New York, NY: The Guildford Press; 2002

32. Schwab-Stone M, Fisher P, Piacentini J, Shaffer D, Davies M, Briggs M. The Diagnostic Interview Schedule for Children-Revised Version (DISC-R): II. Test-retest reliability. *J Am Acad Child Adolesc Psychiatry.* 1993;32(3):651–657

33. Schwab-Stone M, Fallon T, Briggs M, Crowther B. Reliability of diagnostic reporting for children aged 6-11 years: a test-retest study of the Diagnostic Interview Schedule for Children-Revised. *Am J Psychiatry.* 1994;151(7):1048–1054

34. Shaffer D, Fisher P, Lucas CP, Dulcan MK, Schwab-Stone ME. NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): description, differences from previous versions, and reliability of some common diagnoses. *J Am Acad Child Adolesc Psychiatry.* 2000;39(1):28–38

35. Wolraich ML, Lambert W, Doffing MA, Bickman L, Simmons T, Worley K. Psychometric properties of the Vanderbilt ADHD diagnostic parent rating scale in a referred population. *J Pediatr Psychol.* 2003;28(8):559–567

36. Biederman J, Melmed RD, Patel A, et al; SPD503 Study Group. A randomized, double-blind, placebo-controlled study of guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder. *Pediatrics.* 2008;121(1). Available at: www.pediatrics.org/cgi/content/full/121/1/e73

37. Kollins SH, Jain R, Brams M, et al. Clonidine extended-release tablets as add-on therapy to psychostimulants in children and adolescents with ADHD. *Pediatrics.* 2011;127(6): Available at: www.pediatrics.org/cgi/content/full/127/6/e1406

38. Belhassan M, Zeitoun JD, Lefevre JH, et al. Infliximab infusion time in patients with inflammatory bowel diseases: is longer really safer? *Clin Res Hepatol Gastroenterol.* 2013;37(2):189–192

39. Bethell CD, Read D, Stein RE, Blumberg SJ, Wells N, Newacheck PW. Identifying children with special health care needs: development and evaluation of a short screening instrument. *Ambul Pediatr.* 2002;2(1):38–48

40. van Dyck P, Kogan MD, Heppel D, Blumberg SJ, Cynamon ML, Newacheck PW. The National Survey of Children's Health: a new data resource. *Matern Child Health J.* 2004; 8(3):183–188

41. Straus MA. Conflict tactics scales. In: Jackson NA, ed. *Encyclopedia of Domestic Violence.* New York: NY: Routledge, Taylor & Francis Group; 2007:190–197

42. Chandler S, Charman T, Baird G, et al. Validation of the social communication questionnaire in a population cohort of children with autism spectrum disorders. *J Am Acad Child Adolesc Psychiatry.* 2007;46(10):1324–1332

43. Maxwell E. *Manual for the FIGS.* Bethesda, MA: National Institute of Mental Health, Clinical Neurogenetics Branch; 1992

44. Wolraich ML, Feurer ID, Hannah JN, Baumgaertel A, Pinnock TY. Obtaining systematic teacher reports of disruptive behavior disorders utilizing DSM-IV. *J Abnorm Child Psychol.* 1998;26(2):141–152

45. Lazarsfeld PF, Henry NW. *Latent Structure Analysis.* New York, NY: Houghton; 1968

46. Goodman LA. Exploratory latent structure analysis using both identifiable and unidentifiable models. *Biometrika.* 1974;61(2): 215–231

47. Moustaki I. A latent trait and a latent class model for mixed observed variables. *Br J Math Stat Psychol.* 1996;49(2):313–334

48. Wolfe JH. Pattern clustering by multivariate cluster analysis. *Multivariate Behav Res.* 1970;5:329–350

49. von Davier, M. Bootstrapping goodness-of-fit statistics for sparse categorical data results of a Monte Carlo study. *Methods of Psychological Research Online.* 1997;2(2):29–48

50. Magidson J, Vermunt, JK. Latent class models for clustering: a comparison with K-means. *Can J Marketing Res.* 2002;20:37–44

51. Magidson JV. J. K. Latent class factor and cluster models, bi-plots and related graphical displays. *Sociol Methodol.* 2001; 31:223–264

52. Barkley RA, Anastopoulos AD, Guevremont DC, Fletcher KE. Adolescents with ADHD: patterns of behavioral adjustment, academic functioning, and treatment utilization. *J Am Acad Child Adolesc Psychiatry.* 1991;30(5):752–761

53. Fischer M, Barkley RA, Fletcher KE, Smallish L. The adolescent outcome of hyperactive children: predictors of psychiatric, academic, social, and emotional adjustment. *J Am Acad Child Adolesc Psychiatry.* 1993;32 (2):324–332

54. Yoshimasu K, Barbaresi WJ, Colligan RC, et al. Childhood ADHD is strongly associated with a broad range of psychiatric disorders during adolescence: a population-based birth cohort study. *J Child Psychol Psychiatry.* 2012;53(10):1036–1043

55. Bajwa J, Charach M, Duclos D. Adverse effects of rifampicin in dogs and serum alanine aminotransferase monitoring recommendations based on a retrospective study of 344 dogs. *Vet Dermatol.* 2013;Oct 28

56. Charach A, Carson P, Fox S, Ali MU, Beckett J, Lim CG. Interventions for preschool children at high risk for ADHD: a comparative effectiveness review. *Pediatrics.* 2013; 131(5). Available at: www.pediatrics.org/cgi/content/full/131/5/e1584

57. Wolraich M, Brown L, Brown RT, et al; Subcommittee on Attention-Deficit/Hyperactivity Disorder; Steering Committee on Quality Improvement and Management. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics.* 2011;128(5): 1007–1022

58. Shonkoff JP, Boyce WT, McEwen BS. Neuroscience, molecular biology, and the childhood roots of health disparities: building a new framework for health promotion and disease prevention. *JAMA.* 2009;301(21): 2252–2259