# PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Positive Association Between Attention-Deficit/ Hyperactivity Disorder Medication Use and Academic Achievement During Elementary School Richard M. Scheffler, Timothy T. Brown, Brent D. Fulton, Stephen P. Hinshaw, Peter Levine and Susan Stone

Pediatrics 2009;123;1273

DOI: 10.1542/peds.2008-1597

The online version of this article, along with updated information and services, is located on the World Wide Web at: <a href="http://pediatrics.aappublications.org/content/123/5/1273.full.html">http://pediatrics.aappublications.org/content/123/5/1273.full.html</a>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2009 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.



## Positive Association Between Attention-Deficit/ Hyperactivity Disorder Medication Use and Academic **Achievement During Elementary School**

Richard M. Scheffler, PhDa, Timothy T. Brown, PhDa, Brent D. Fulton, PhDa, Stephen P. Hinshaw, PhDb, Peter Levine, MDc, Susan Stone, PhDd

aSchool of Public Health, Nicholas C. Petris Center on Health Care Markets and Consumer Welfare, Department of Psychology, and School of Social Welfare, University of California, Berkeley, California; Department of Pediatrics, Permanente Medical Group, Walnut Creek, California

The authors have indicated they have no financial relationships relevant to this article to disclose

#### What's Known on This Subject

Approximately 4.4 million children in the United States have been diagnosed with ADHD, and  $\sim$ 56% of affected children take prescription medications to treat the disorder. ADHD is strongly linked with low academic achievement.

#### What This Study Adds

This study shows that children who took prescription medication to treat ADHD had higher mathematics and reading test scores during elementary school, comparable with 0.19 and 0.29 school years, respectively, than their unmedicated peers with ADHD.

#### ABSTRACT -

OBJECTIVE. Approximately 4.4 million (7.8%) children in the United States have been diagnosed with attention-deficit/hyperactivity disorder, and 56% of affected children take prescription medications to treat the disorder. Attention-deficit/hyperactivity disorder is strongly linked with low academic achievement, but the association between medication use and academic achievement in school settings is largely unknown. Our objective was to determine if reported medication use for attentiondeficit/hyperactivity disorder is positively associated with academic achievement during elementary school.

METHOD. To estimate the association between reported medication use and standardized mathematics and reading achievement scores for a US sample of 594 children with attention-deficit/hyperactivity disorder, we used 5 survey waves between kindergarten and fifth grade from the nationally representative Early Childhood Longitudinal Study—Kindergarten Class of 1998-1999 to estimate a first-differenced regression model, which controlled for time-invariant confounding variables.

RESULTS. Medicated children had a mean mathematics score that was 2.9 points higher than the mean score of unmedicated peers with attention-deficit/hyperactivity disorder. Children who were medicated for a longer duration (at >2 waves) had a mean reading score that was 5.4 points higher than the mean score of unmedicated peers with attention-deficit/hyperactivity disorder. The medication-reading association was

www.pediatrics.org/cgi/doi/10.1542/ peds.2008-1597

doi:10.1542/peds.2008-1597

attention-deficit/hyperactivity disorder, prescription medication, children, academic achievement

#### Abbreviations

ADHD—attention-deficit/hyperactivity

ECLS-K—Early Childhood Longitudinal Study-Kindergarten Class of 1998 – 1999 IEP—individualized education program

Accepted for publication Sep 5, 2008

Address correspondence to Richard M. Scheffler, PhD, University of California, 50 University Hall, MC7360, Berkeley, CA 94720. E-mail: rscheff@berkeley.edu.

PEDIATRICS (ISSN Numbers: Print 0031-4005: Online, 1098-4275). Copyright © 2009 by the American Academy of Pediatrics

lower for children who had an individualized education program than for those without such educational accommodation.

CONCLUSIONS. The finding of a positive association between medication use and standardized mathematics and reading test scores is important, given the high prevalence of attention-deficit/hyperactivity disorder and its association with low academic achievement. The 2.9-point mathematics and 5.4-point reading score differences are comparable with score gains of 0.19 and 0.29 school years, respectively, but these gains are insufficient to eliminate the test-score gap between children with attention-deficit/hyperactivity disorder and those without the disorder. Long-term trials are needed to better understand the relationship between medication use and academic achievement. Pediatrics 2009; 123:1273-1279

TTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) is a prevalent childhood mental health condition affecting  $\sim$ 7.8% of the school-aged population. It is characterized by developmentally atypical levels of inattention, activity, and impulsivity.<sup>2</sup> A recent estimate reports that 56% of affected children are treated with prescription medication,1 which has proven to be efficacious for symptom reduction in a large number of trials.3

Affected children also exhibit deficits in academic functioning.<sup>4</sup> Relative to their peers without the condition, children with ADHD earn lower grades<sup>5</sup> and lower mathematics and reading achievement scores<sup>6</sup>; they also experience higher rates of grade retention, special education placement, and school dropout.<sup>4,6,7</sup> A number of well-controlled studies show that stimulant treatment yields acute improvements on a variety of objective tests of accuracy and academic productivity,<sup>8</sup> such as sustained attention<sup>9</sup> and short-term memory<sup>10</sup>; task performance indexed by brief, repeated tests of school material<sup>11</sup>; note-taking quality, quiz scores, rates of homework completion<sup>12</sup>; and the average number of problems attempted and completed in mathematics and/or reading tests.<sup>13–15</sup> On the other hand, medication trials using the outcome of academic achievement, especially over the long run, are far rarer.<sup>8,16</sup> Notably, research regarding medication effects on academic outcomes has not consistently shown gains.<sup>3,17–20</sup>

Methodologic issues related to choice of outcome measures, small sample sizes, and short durations of medication treatment may all be relevant to explaining the inconclusive findings in the literature. Specifically, typically used "broadband," standardized achievement measures may be too insensitive to show gains.<sup>21</sup> The small samples involved in most studies provide limited power to estimate achievement growth, a key issue given the heterogeneity in achievement growth within children with ADHD, some of which is related to initial achievement levels.<sup>22</sup> In addition, the typical stimulant trial spans only a few weeks or months, an inadequate period of time for effects on growth in academic achievement to become evident.

In short, a major gap remains between relatively small-sample, short-term investigations of medication effects on various aspects of cognitive performance versus larger-sample, longer-term studies that estimate the relationship between medication use and academic achievement growth over time. We attempted to bridge that gap by using data from a US sample of 594 children diagnosed with ADHD who took 5 well-calibrated, standardized tests in both mathematics and reading between kindergarten and fifth grade. On the basis of existing findings of short-term symptomatic and cognitive enhancements from medication treatment, we hypothesized that children who were medicated for ADHD would demonstrate higher mathematics and reading achievement relative to their unmedicated peers with ADHD. We also conducted exploratory analyses to examine if the gender of the child or whether he or she received an individualized education program (IEP) would moderate any medication findings.

#### **METHODS**

#### Data

We used the Early Childhood Longitudinal Study—Kindergarten Class of 1998–1999 (ECLS-K) data set to test our hypotheses.<sup>23,24</sup> The ECLS-K tracks the academic progress of a large, nationally representative sample of children who attended kindergarten in the United States in 1998 to 1999. Parents also provided extensive information on child and family background characteristics at 5 data-collection waves between kindergarten and fifth grade.

This data set is particularly well suited for estimating the association between medication use and academic achievement: (1) it includes information about whether a child has been diagnosed with ADHD and whether he or she has been taking medication to treat the condition; (2) it collects repeated, standardized, and carefully calibrated measures of academic achievement across the elementary school years; and (3) its longitudinal structure enables us to control for time-invariant confounding variables. These key features present an unprecedented opportunity to supplement previous research generated from small-sample, short-term medication trials that typically use narrow academic achievement measures.

#### **Key Variables**

#### Mathematics and Reading Achievement

Mathematics and reading achievement tests were administered to each child at 5 waves: in the fall and spring of kindergarten and in the spring of the first, third, and fifth grades. The achievement tests were developed by ECLS-K staff from a combination of sources including published achievement tests and extensive consultation with educational experts.<sup>25</sup> These tests closely parallel the National Assessment of Educational Progress, a widely recognized national assessment system designed to gauge student progress on early mathematics and reading skills. Specific test items were constructed to capture the range of grade-appropriate and subject matter-specific proficiencies garnered between kindergarten and fifth grade (eg, from number recognition to word problems involving area and volume for mathematics; from letter recognition to textual extrapolation and evaluation for reading). To carefully calibrate student achievement, all children initially completed a "routing" test. On the basis of their individual results, children were then administered a second set of items closely matched to their respective ability levels. ECLS-K achievement tests have undergone extensive psychometric testing and were ultimately calibrated by using an item response theory analytic technique, thus allowing for direct comparison of scores from kindergarten through fifth grade.

#### ADHD Diagnosis

Parents were asked whether their child had been diagnosed with ADHD by a professional at 4 waves: the fall of kindergarten and the spring of first, third, and fifth grades. If the parent responded affirmatively at any of these waves, we considered the child to have a diagnosis of ADHD on the basis of evidence that ADHD is quite persistent over time.<sup>5,26,27</sup>

### ADHD Medication

At the fifth-grade-spring wave, parents of diagnosed children were asked whether the child was currently taking prescription medication to treat ADHD, and if so, the total time the child had taken the medication. Table 1 shows our coding of medication status at each wave based on the total time the child had taken medication. For children who were not currently taking medication, we assumed they did not take medication during the study time frame. For children who were currently taking medication (almost 90% of whom were taking a

TABLE 1 Medication Status of Children Diagnosed With ADHD at Each Survey Wave According to Medication Duration

Medication Duration Range	Midpoint of Medication Duration Range, y	n	Percent (Weighted)	Medication Status According to Survey Wave				
				K, Fall 1998	K, Spring 1999	First Grade, Spring 2000	Third Grade, Spring 2002	Fifth Grade, Spring 2004
Not currently taking medication	0.00	191	32.3	0	0	0	0	0
0 < years < 0.08	0.04	13	1.8	0	0	0	0	1
$0.08 \le y < 1$	0.54	69	10.3	0	0	0	0	1
$1 \le y < 2.5$	1.75	118	15.5	0	0	0	0	1
$2.5 \le y < 4.5$	3.50	131	23.7	0	0	0	1	1
≥4.5 y	5.00	72	16.4	0	1	1	1	1
Total		594	100.0					
No. of years between fifth-grade-spring and survey wave				5.5	5	4	2	0

Medication status according to medication indicates whether the child was taking medication at each wave (0, no; 1, yes). Medication status is 1 for a given wave if the midpoint of the medication duration range (see second column) is greater than or equal to the number of years between the fifth-grade-spring and the given wave (see last row). For example, for the 2.5  $\leq$  years < 4.5 duration row, the midpoint of the duration range is 3.5 years. Therefore, medication status is 0 in first-grade spring because 3.5 years (the number of years between fifth-grade spring and first-grade spring), but is 1 in third-grade spring because 3.5 years (the number of years between fifth-grade spring). Medication duration endpoints were based on the endpoints used by ECLS-K interviewers. Note that 0.08 years represents 1 month. n indicates number of observations; K, kindergarten.

stimulant), the possible responses for the total time taking medication included duration ranges (eg. 2.5-4.5 years). Therefore, we assumed that the child took medication for a duration equal to the midpoint of the range (eg, 3.5 years for the 2.5- to 4.5-year range) and did not have significant nonadherence gaps. For children who had taken medication for  $\geq 4.5$  years, we assumed that they had been taking medication in the spring of kindergarten but had not taken medication in the fall of kindergarten, as the onset of medication typically occurs when the child enters formal schooling.7 We estimated additional models that varied our medication coding assumptions. The medication rate of 67.7% (95% confidence interval: 61.1%-74.3%) in the spring of fifth grade is consistent with the 62.7% we found for 12year-old children with ADHD using the 2003 National Survey of Children's Health.<sup>28</sup>

#### Model

Our goal was to estimate the association between ADHD medication use and a child's academic achievement using a method that best controls for confounding variables. Because we repeatedly observed the same children, we were able to use a first-differenced regression model.<sup>29</sup> Importantly, this model controls for time-invariant characteristics, which include many potential confounders such as a child's demographic characteristics (eg, gender and race) and intelligence, as well as time-invariant components of parent, teacher, and school educational inputs to the child.

Although a first-differenced model regresses changes in the dependent variable on changes in the independent variables, the parameter estimates are interpreted by using a structural model, which is the model that is first differenced.<sup>30</sup> In the structural model, each child had a maximum of 5 observations; separate models were estimated for mathematics and reading scores. The dependent variable was the child's test score, and the key independent variable was whether the child was medicated. Each model also included the child's test date, a

dummy variable for each wave (except the first), the interaction between the test date and each wave, and a dummy variable for each child (except 1). Therefore, the medication parameter represents the mean test score difference between the test scores of children at waves when they were unmedicated and the test scores of children at waves when they were medicated, controlling for the time-varying variables as well as time-invariant characteristics.

To compare children who had been medicated at  $\geq 2$  waves with unmedicated children, we estimated additional models that included 2 medication variables: the first indicated at each wave whether the child was first medicated, and the second indicated at each wave whether the child had been medicated at  $\geq 2$  waves. The 2 medication parameters, respectively, represent the mean difference between the test scores of children at waves when they were unmedicated and the test scores of children (1) at waves when first medicated and (2) at waves when medicated for  $\geq 2$  waves.

All models were estimated by using SUDAAN 9.0.1. (Research Triangle Institute, Research Triangle Park, NC),<sup>31</sup> incorporated the complex survey design of the ECLS-K and allowed for the first-differenced error terms to have an exchangeable correlation structure.

#### Sample Size

The ECLS-K included 21 356 eligible children. Totals of 19 684, 20 578, 17 324, 15 305, and 11 820 children responded at the fall of kindergarten, spring of kindergarten, and the spring of the first-, third-, and fifth-grade waves, respectively.<sup>23</sup> Medication information was available for 783 of the 1195 children who had been diagnosed with ADHD; data were missing for the remainder mostly because they did not participate in the fifth-grade-spring wave. Missing weights reduced our analytic sample to 594 children who had at least 2 nonmissing test scores in adjacent waves, resulting in 2258 and 2226 first-differenced mathematics and reading scores, respectively.

TABLE 2 Descriptive Statistics of Full and Analytic Sample of ADHD-Diagnosed Children

Variable	Full Sample (N = 8370)	ADHD-Diagnosed Sample (N = 594)
Academic achievement tests, mean (SD)		
Mathematics scores		
Kindergarten, fall	22.7 (8.7)	19.3 (6.0)
Kindergarten, spring	32.9 (11.4)	28.1 (8.5)
First grade, spring	57.4 (16.5)	49.8 (13.1)
Third grade, spring	91.7 (21.6)	82.3 (19.1)
Fifth grade, spring	112.8 (21.8)	102.1 (20.9)
Reading scores		
Kindergarten, fall	29.3 (9.9)	25.4 (5.4)
Kindergarten, spring	40.7 (13.5)	35.1 (9.0)
First grade, spring	71.5 (22.3)	60.7 (17.4)
Third grade, spring	117.7 (25.3)	105.1 (23.3)
Fifth grade, spring	138.4 (23.3)	126.2 (22.0)
Test date, months from earliest test taken		
Kindergarten, fall	1.7 (0.6)	1.7 (0.5)
Kindergarten, spring	1.9 (0.5)	1.9 (0.5)
First grade, spring	1.7 (0.6)	1.7 (0.5)
Third grade, spring	1.5 (0.6)	1.6 (0.6)
Fifth grade, spring	1.8 (0.8)	1.7 (0.7)
Demographic characteristics		
Female, %	48.5	25.1
Race, %		
White	57.7	71.6
Black	16.1	12.2
Hispanic	18.9	11.0
Asian/Pacific Islander	3.5	1.4
Other	3.8	3.8
Age (Feb 2004), mean (SD), mo	143.0 (4.3)	143.6 (4.4)
IEP (at any wave), %	19.0	48.7
IEP (≥3 waves), %	3.2	11.9
Parents married (fifth-grade spring), %	66.6	55.6
Household size (fifth-grade spring), %		
2 to 3	20.6	26.1
4 to 5	60.8	57.2
≥6	18.5	16.7
Household income (fifth-grade spring), %		
≤\$25 000	26.6	31.8
\$25 001–50 000	29.6	30.3
\$50 001–75 000	17.6	16.9
>\$75 000	26.2	21.0
Mother's education (fifth-grade spring), %		
Less than high school	11.2	12.4
High school graduate (or equivalent)	25.9	30.6
Some college	36.7	35.8
College graduate	16.8	13.2
Some graduate school	9.4	8.0
ADHD diagnosis, %	9.4	

All statistics incorporate the complex survey design of the ECLS-K. The full sample was reduced from 11 820 children at the fifth-grade-spring wave to 8370 children primarily because of missing (or nonpositive) weights. Percentages may not add to 100 because of rounding.

#### **RESULTS**

#### **ECLS-K Sample Statistics**

Table 2 shows the standardized mathematics and reading test scores and the demographic characteristics of the full

TABLE 3 Regression Results for Mathematics and Reading Test Score Models

Variable	Mathe	matics	Reading		
	Model 1	Model 2	Model 3	Model 4	
Medication	2.9a (1.4)		2.4 (1.6)		
Medication (first wave)		2.9a (1.3)		2.6 (1.5)	
Medication (second + wave)		2.6 (1.9)		5.4 <sup>b</sup> (1.9)	
Test dates					
Test date	1.7 <sup>b</sup> (0.7)	1.7a (0.7)	3.2c (0.8)	3.1c (0.8)	
Test date $\times$ wave 2	0.8 (0.9)	0.8 (0.9)	0.2 (1.2)	0.2 (1.2)	
Test date $\times$ wave 3	2.0 (1.1)	2.0 (1.1)	0.3 (1.4)	0.2 (1.4)	
Test date $\times$ wave 4	-0.6(1.2)	-0.6(1.2)	-1.7(1.5)	-1.7(1.5)	
Test date $\times$ wave 5	-0.4(1.4)	-0.5(1.4)	-3.1a (1.5)	-2.9(1.5)	
Wave dummies					
Wave 2	6.5 <sup>c</sup> (1.7)	6.5 <sup>c</sup> (1.7)	8.3c (2.2)	8.3c (2.2)	
Wave 3	27.1 <sup>c</sup> (2.1)	27.1 <sup>c</sup> (2.1)	34.8c (2.4)	34.5c (2.4)	
Wave 4	63.2 <sup>c</sup> (2.6)	63.2 <sup>c</sup> (2.7)	81.6 <sup>c</sup> (3.3)	81.1c (3.3)	
Wave 5	82.0 <sup>c</sup> (3.8)	82.1c (3.8)	105.5c (2.9)	103.9c (2.9)	
n	2258	2258	2226	2226	
df	426	426	426	426	
R <sup>2</sup>	0.41	0.41	0.46	0.46	
F statistic	319 <sup>c</sup>	400c	846 <sup>c</sup>	734 <sup>c</sup>	

Each variable in the table includes a parameter estimate followed by its standard error in parentheses. The dummy variables representing each child, which control for time-invariant characteristics, drop out of the first-differenced model and, therefore, are not shown. The model does not include a constant term because of first differencing. Wave 1 (reference wave) is kindergarten fall; wave 2 is kindergarten spring; wave 3 is first-grade spring; wave 4 is third-grade spring; and wave 5 is fifth-grade spring. n indicates number of observations; df, degrees of freedom. The parameter estimate was based on the following: n00; n00; n000 n001; and n0000 n001.

and ADHD-diagnosed samples. As of the fifth-grade-spring wave, 9.4% (95% confidence interval: 8.2%–10.6%) of all children had been diagnosed with ADHD, consistent with the 9.9% prevalence we found for 12-year-old children using the 2003 National Survey of Children's Health.<sup>28</sup>

## Model-Based Comparison of Diagnosed Children by Medication Status

Related to our hypotheses, Table 3 presents the results for the mathematics and reading regression models. Medicated children's mean mathematics score was 2.9 points higher (P = .04) than the mean score of unmedicated child's with the same time-invariant characteristics (see model 1). When medication was coded using 2 variables to indicate the first wave of medication and the second or subsequent wave of medication, respectively, the parameter estimates of 2.9 and 2.6 differed neither practically nor statistically from each other (see model 2). Among all children, the mean gain in mathematics scores between the fall of kindergarten and the spring of fifth grade was 90.2 points; therefore, the 2.9-point difference between medicated and unmedicated children is comparable with gains attained during 0.19 school years over this 6-year period.

For reading, only children medicated at  $\geq 2$  waves had a reading score that was significantly different (on average, 5.4 points higher [P < .01]) than those of their unmedicated peers (see models 3 and 4; note that the medication parameter estimate in model 3 does not

equal the average of the 2 medication parameter estimates in model 4, because the medication variables are correlated with other variables in the model). The 5.4point mean reading score difference is comparable with ~0.29 school years. When additional time-varying independent variables (parent's marital status, household size, household income, and mother's education) were added to the above models, the statistical significance of the results did not change.

We tested our medication coding assumptions as follows. The above models assumed that children with ADHD who were not taking medication at the fifthgrade-spring wave had never taken medication. When these children were excluded from the models, so that only children who took medication at ≥1 wave remained, the medication parameter estimate in model 1 slightly decreased to 2.8, whereas its standard error slightly increased to 1.6, resulting in a P value equal to .08; the reading result from model 4 remained significant. The original models also assumed no significant gaps in medication usage once a child began taking medication, which is often not the case.<sup>32</sup> To address this issue, we reestimated models 1 and 3 by removing a child's observations after the first wave of medication, when adherence may decrease, and the statistical significance of the results did not change.

To examine whether the medication parameter estimates varied among the subgroups of children, we reestimated the models in Table 3 by including the interaction between the medication variables and (1) the child's gender, (2) a variable indicating whether the child had an IEP at any wave, suggesting comorbid conditions or severe ADHD, or (3) a variable indicating whether the child had an IEP at  $\geq 3$  waves, indexing the degree of special education supports. In these models, the interaction-term parameters measure whether the association between medication and test scores differs between, for example, boys and girls. Because gender is time-invariant, we cannot estimate the medication association for boys and girls separately.29 We did not find a significant interaction with gender but did find that the medication parameter estimate indicating ≥2 waves of medication was significantly lower in reading for children who had an IEP and was significantly lower in both mathematics and reading for children who had an IEP at  $\geq 3$  waves.

#### DISCUSSION

The major finding from our analysis of the ECLS-K longitudinal data set is that medication use during elementary school is associated with higher mathematics test scores and is associated with higher reading test scores after ≥2 waves of medication. Such improvement is notable, as early academic success seems to be critical to later school progress.<sup>33,34</sup> The models controlled for all time-invariant differences between the unmedicated and medicated children. The 2.9-point difference in mathematics scores between medicated versus unmedicated children is comparable with the gains achieved during 0.19 school years; however, this gain does not eliminate the achievement gap between children with and without ADHD. Similarly, the 5.4-point difference

in reading scores between children medicated at  $\geq 2$ waves versus unmedicated children is comparable with 0.29 school years, but is not sufficient to eliminate the achievement gap during the elementary school years.

The finding that medication was associated with reading scores only for children medicated at  $\geq 2$  waves needs additional investigation. The different findings for mathematics versus reading may point to underlying differences in the process of knowledge acquisition as well as dynamics related to strategies of formal instructional input between these 2 subject areas. The finding that the association between ≥2 waves of medication and reading scores was lower for children who had an IEP also needs additional investigation to determine how medication may differentially affect children with comorbid conditions or severe levels of ADHD.

The first-differenced regression model is a powerful design that controls for all time-invariant differences between unmedicated and medicated children. However, the parameter estimates may be biased if test scores influenced which children were medicated (also known as simultaneity) or if omitted variables associated with medication and test scores changed over time. Yet here, simultaneity would seem to understate the medication association with achievement, under the assumption that parents may be more likely to medicate an academically underperforming child. Omitted educational input variables that may change over time, such as parent, teacher, and school inputs, may cause the results to be understated (eg, if a parent substitutes medication for his or her time) or overstated (eg, if a parent complements medication with additional time). Also noteworthy is that improvements in behavior may indirectly lead to test score gains related to receipt of more educational inputs from a teacher.<sup>35</sup> The educational input variables were not included in the models, because they are endogenous (ie, the level of the input may be related to the child's academic achievement); hence, their inclusion may bias the other parameter estimates. Overall, the direction of the potential bias is inconclusive, but the arguments above suggest that any bias may underestimate the true medication-achievement linkage.

Key data limitations included missing or incomplete data from planned and unplanned attrition, other types of nonresponse, missing sampling weights, and imprecision in ADHD diagnostic and medication-duration measures. Overall, we contend that these limitations do not significantly affect the results. Most of the attrition was planned because the ECLS-K sampled only a subset of children who moved. Regression results showed that the sampling weights were statistically higher for children with lower kindergarten-fall test scores, the same children who were more likely to have missing data at subsequent waves. Hence, the weighting scheme did account for nonresponse in this dimension, reducing or eliminating the potential bias.

We note that the ECLS-K provided several sets of design variables (sampling weights, sampling unit identifiers, and strata identifiers) to aid with analysis of the data.<sup>23</sup> The recommended set for our analysis omitted some sampling weights. Therefore, we reestimated each model using the set of design variables provided by the ECLS-K to analyze fifth-grade, cross-sectional data, because this set included weights for all 783 diagnosed children with medication information. The statistical significance of the main results did not change.

Finally, information on both ADHD diagnosis and medication status was determined by parent reports, and the survey did not collect information on potential medication adherence gaps or medication dosage-level information. Although these are critical limitations, the ECLS-K is the best nationally representative data set available to complement small-sample, short-term medication trials that typically use narrow academic performance measures. Moreover, if our medication coding had random errors, including not accounting for medication adherence gaps, this would bias estimated medication-academic achievement associations toward zero, whether medication actually improved or degraded academic achievement.<sup>30</sup>

#### CONCLUSIONS

Some 4.4 million children in the United States have been diagnosed with ADHD, a condition that is strongly associated with low academic achievement. We have shown that medicated children with ADHD scored higher on the ECLS-K standardized mathematics and reading achievement tests compared with unmedicated peers; the score differences are comparable with 0.19 and 0.29 school years, respectively, during the primary schooling years. With nearly 60% of diagnosed children taking prescription medications to treat the disorder,1 at a cost of \$2.2 billion in 2003,36 the current findings have the potential for wide applicability, particularly because diagnostic prevalence and medication rates differ among demographic groups.<sup>37,38</sup> Our research supports the need for long-term trials to better understand the relationship between medication use and academic achievement in children with ADHD.

#### **ACKNOWLEDGMENTS**

This study was funded by National Institute of Mental Health grant R01-MH067084. The National Institute of Mental Health did not participate in the design or conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript.

We are grateful to Teh-wei Hu, PhD (University of California, Berkeley, CA) for participation and technical contributions to our study group. We thank Glen Elliott, PhD, MD (Children's Health Council, Palo Alto, CA), Richard Frank, PhD (Harvard University, Boston, MA), and David Salkever, PhD (University of Maryland, Baltimore County, MD) for thoughtful comments on early versions of this manuscript (none received financial compensation) and Sepideh Modrek (predoctoral fellow, University of California, Berkeley) for helping with merging and preparing the data. We also thank Elvira Germino Hausken, EdD, and Gail Mulligan, PhD (National Center for Education Statistics), for providing helpful information about the details of the ECLS-K survey and data set.

#### **REFERENCES**

- Centers for Disease Control and Prevention. 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
- American Psychiatric Association. *Diagnostic and Statistical Man*ual of Mental Disorders. 4th ed. Text revision. Washington, DC: American Psychiatric Association; 2000
- 3. MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for ADHD. *Arch Gen Psychiatry*. 1999; 56(12):1073–1086
- 4. Hinshaw SP. Is ADHD an impairing condition in childhood and adolescence? In: Jensen PS, Cooper JR, eds. *Attention-Deficit Hyperactivity Disorder: State of the Science, Best Practices.* Kingston, NJ: Civic Research Institute; 2002:5–21
- Barkley RA, Fischer M, Edelbrock C, 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):546–587
- Currie J, Stabile M. Child mental health and human capital accumulation: the case of ADHD. J Health Econ. 2006;25(6): 1094–1118
- Barkley RA. Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment. 3rd ed. New York, NY: Guilford Press: 2006
- 8. Connor DF. Stimulants. In: Barkley RA. Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment. 3rd ed. New York, NY: Guilford Press; 2006
- Douglas VI. Cognitive control processes in attention-deficit/ hyperactivity disorder. In: Quay HC, Hogan AE, eds. Handbook of Disruptive Behavior Disorders. New York, NY: Plenum Press; 1999
- Bedard A, Jain U, Johnson SH, Tannock R. Effects of methylphenidate on working memory components: influence of measurement. J Child Psychol Psychiatry. 2007;48(9):872–880
- 11. Pelham WE, Carlson C, Sams SE, Vallano G, Dixon MJ, Hoza B. Separate and combined effects of methylphenidate and behavior modification on boys with attention deficit-hyperactivity disorder in the classroom. *J Consult Clin Psychol.* 1993;61(3): 506–515
- 12. Evans SW, Pelham WE, Smith BH, et al. Dose-response effects of methylphenidate on ecologically valid measures of academic performance and classroom behavior in adolescents with ADHD. *Exp Clin Psychopharmacol*. 2001;9(2):163–175
- McGough JJ, Wigal SB, Abikoff H, Turnbow JM, Posner K, Moon E. A randomized, double-blind, placebo-controlled, laboratory classroom assessment of methylphenidate transdermal system in children with ADHD. *J Atten Disord*. 2006;9(3): 476–485
- James RS, Sharp WS, Bastain TM, et al. Double-blind, placebocontrolled study of single-dose amphetamine formulations in ADHD. *J Am Acad Child Adolesc Psychiatry*. 2001;40(11): 1268–1276
- 15. Elia J, Welsh PA, Gullotta CS, Rapoport J. Classroom academic performance: improvement with both methylphenidate and dextroamphetamine in ADHD boys. *J Child Psychol Psychiatry*. 1993;34(5):785–804
- Hechtman L. Long-term treatment of children and adolescents with attention-deficit/hyperactivity disorder (ADHD). Curr Psychiatry Rep. 2006;8(5):398–408
- 17. MTA Cooperative Group. National Institute of Mental Health Multimodal Treatment Study of ADHD follow-up: changes in effectiveness and growth after the end of treatment. *Pediatrics*. 2004;113(4):762–769
- 18. Barbaresi WJ, Katusic SK, Colligan SC, et al. Modifiers of long-term school outcomes for children with attention-deficit/

- hyperactivity disorder: does treatment with stimulant medication make a difference? Results from a population-based study. J Dev Behav Pediatr. 2007;28(4):274-287
- 19. Paykina N, Greenhill LL. Pharmacological treatments for attention-deficit/hyperactivity disorder. In: Nathan PE, Gorman JM, eds. A Guide to Treatments That Work. New York, NY: Oxford University Press; 2007:29-70
- 20. Loe IM, Feldman HM. Academic and educational outcomes of children with ADHD. Ambul Pediatr. 2007;7(suppl 1):82-90
- 21. Reynolds CR, Kamphaus RW. Handbook of Psychological and Educational Assessment of Children. 2nd ed. New York, NY: Guilford Press; 2003
- 22. Rapport MD, Scanlan S, Denney CB. Attention-deficit/ hyperactivity disorder and scholastic achievement: a model of dual developmental pathways. J Child Psychol Psychiatry. 1999; 40(8):1169-1183
- 23. Tourangeau K, Nord C, Le T, Pollack JM, Atkins-Burnett S. Early Childhood Longitudinal Study, Kindergarten Class of 1998–99 (ECLS-K), Combined User's Manual for the ECLS-K Fifth-Grade Data Files and Electronic Codebooks. US Department of Education. Washington, DC: National Center for Education Statistics; 2006. NCES 2006-032
- 24. Tourangeau K, Le T, Nord C. Early Childhood Longitudinal Study, Kindergarten Class of 1998–99 (ECLS-K), Fifth-Grade Methodology Report. US Department of Education. Washington, DC: National Center for Education Statistics; 2005. NCES 2006-037
- 25. Pollack JM, Atkins-Burnett S, Najarian M, Rock DA. Early Childhood Longitudinal Study, Kindergarten Class of 1998-99 (ECLS-K). Psychometric Report for the Fifth Grade. US Department of Education. Washington, DC: National Center for Education Statistics; 2005. NCES 2006-036
- 26. 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
- 27. Biederman J, Faraone S, Milberger S, et al. Predictors of persistence and remission of ADHD into adolescence: results from

- a four-year prospective follow-up study. J Am Acad Child Adolesc Psychiatry. 1996;35(3):343-351
- 28. Blumberg SJ, Olson L, Frankel MR, et al. Design and operation of the National Survey of Children's Health, 2003. Vital Health Stat 1. 2005;(43):1-24
- 29. Wooldridge JM. Introductory Econometrics: A Modern Approach. 2nd ed. Mason, OH: Thomson South-Western; 2003
- 30. Wooldridge JM. Econometric Analysis of Cross Section and Panel Data. Cambridge, MA: MIT Press; 2002
- 31. Research Triangle Institute. SUDAAN Language Manual, Release 9.0. Research Triangle Park, NC: Research Triangle Institute; 2004
- 32. Bokhari AS, Heiland F, Levine P, Ray GT. Risk factors for discontinuing drug therapy among children with ADHD. Health Serv Outcomes Res Methodol. 2008;8(3):134-158
- 33. Hinshaw SP. Externalizing behavior problems and academic underachievement in childhood and adolescence: causal relationships and underlying mechanisms. Psychol Bull. 1992; 111(1):127-155
- 34. Lee VE, Burkham DT. Inequality at the Starting Gate. Washington, DC: Economic Policy Institute; 2002
- 35. Spira EG, Fischel JE. The impact of preschool inattention, hyperactivity, and impulsivity on social and academic development: a review. J Child Psychol Psychiatry. 2005;46(7):
- 36. Scheffler RM, Hinshaw SP, Modrek S, Levine P. The global market for ADHD medications. Health Aff (Millwood). 2007; 26(2):450-457
- 37. Visser SN, Lesesne CA, Perou R. National estimates and factors associated with medication treatment for childhood attentiondeficit/hyperactivity disorder. Pediatrics. 2007;119(suppl 1): S99-S106
- 38. Schneider H, Eisenberg D. Who receives a diagnosis of attention-deficit/hyperactivity disorder in the United States elementary school population? Pediatrics. 2006;117(4): 601-609

#### THE ART OF MEDICINE: LORENZO ODONE AND MEDICAL MIRACLES

"There is no question that Lorenzo Odone lived until the age of 30 years because his parents, Augusto and Michaela Odone, defied doctors and developed a mixture of 2 cooking oils as a possible treatment for their son's devastating disease. The 1992 film Lorenzo's Oil, which commemorated this heroic effort, became an inspirational saga for other patients and families dealing with incurable conditions. Yet Lorenzo's story tells us as much about the limitations of medical research as it does about its triumphs. Not surprisingly, the movie outraged scientists and families affected by ALD (adrenoleukodystrophy), both of whom believed the film played with people's hopes. But the Odones had the last laugh. When the late Hugo Moser, the world's expert on ALD and one of Lorenzo's physicians, finally published data in 2005, it became clear that although the oil did little for already sick boys, it prevented the onset of ALD in two-thirds of susceptible boys who otherwise would surely have died from the disease. It was a breathtaking scientific achievement spearheaded by 2 laypeople."

> Lerner BH. www.thelancet.com; vol 373. March 14, 2009 Noted by JFL, MD

## Positive Association Between Attention-Deficit/ Hyperactivity Disorder Medication Use and Academic Achievement During Elementary School

Richard M. Scheffler, Timothy T. Brown, Brent D. Fulton, Stephen P. Hinshaw, Peter

Levine and Susan Stone *Pediatrics* 2009;123;1273 DOI: 10.1542/peds.2008-1597

**Updated Information &** including high resolution figures, can be found at:

Services http://pediatrics.aappublications.org/content/123/5/1273.full.h

tmÎ

**References** This article cites 24 articles, 4 of which can be accessed free

at:

http://pediatrics.aappublications.org/content/123/5/1273.full.h

tml#ref-list-1

Citations This article has been cited by 7 HighWire-hosted articles:

http://pediatrics.aappublications.org/content/123/5/1273.full.h

tml#related-urls

**Post-Publication** 3 P<sup>3</sup>Rs have been posted to this article

Peer Reviews (P<sup>3</sup>Rs) http://pediatrics.aappublications.org/cgi/eletters/123/5/1273

**Subspecialty Collections** This article, along with others on similar topics, appears in

the following collection(s): **Development/Behavioral Issues** 

http://pediatrics.aappublications.org/cgi/collection/developme

nt:behavioral issues sub

**Attention-Deficit/Hyperactivity Disorder (ADHD)** 

http://pediatrics.aappublications.org/cgi/collection/attention-d

eficit:hyperactivity\_disorder\_adhd\_sub

**Permissions & Licensing** Information about reproducing this article in parts (figures,

tables) or in its entirety can be found online at:

http://pediatrics.aappublications.org/site/misc/Permissions.xht

ml

**Reprints** Information about ordering reprints can be found online:

http://pediatrics.aappublications.org/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2009 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

