Effect of Prior Stimulant Treatment for Attention-Deficit/Hyperactivity Disorder on Subsequent Risk for Cigarette Smoking and Alcohol and Drug Use Disorders in Adolescents

Timothy E. Wilens, MD; Joel Adamson, BA; Michael C. Monuteaux, ScD; Stephen V. Faraone, PhD; Mary Schillinger, BA; Diana Westerberg, BA; Joseph Biederman, MD

Objective: To examine the effects of early stimulant treatment on subsequent risk for cigarette smoking and substance use disorders (SUDs) in adolescents with attention-deficit/hyperactivity disorder (ADHD).

Design: Case-controlled, prospective, 5-year follow-up study.

Setting: Massachusetts General Hospital, Boston.

Participants: Adolescents with and without ADHD from psychiatric and pediatric sources. Blinded interviewers determined all diagnoses using structured interviews.

Intervention: Naturalistic treatment exposure with psychostimulants for ADHD.

Main Outcome Measures: We modeled time to onset of SUDs and smoking as a function of stimulant treatment.

Results: We ascertained 114 subjects with ADHD (mean age at follow-up, 16.2 years) having complete medication and SUD data; 94 of the subjects were treated with stimulants. There were no differences in SUD risk factors between naturally treated and untreated groups other than family history of ADHD. We found no increased risks for cigarette smoking or SUDs associated with stimulant therapy. We found significant protective effects of stimulant treatment on the development of any SUD (hazard ratio [HR], 0.27; 95% confidence interval [CI], 0.13-0.60; \( \chi^2 = 10.57, P = .001 \)) and cigarette smoking (HR, 0.28; 95% CI, 0.14-0.60; \( \chi^2 = 10.05, P = .001 \)) that were maintained when controlling for conduct disorder. We found no effects of time to onset or duration of stimulant therapy on subsequent SUDs or cigarette smoking in subjects with ADHD.

Conclusion: Stimulant therapy does not increase but rather reduces the risk for cigarette smoking and SUDs in adolescents with ADHD.

Arch Pediatr Adolesc Med. 2008;162(10):916-921
Despite the implications of the effects of early stimulant treatment on later SUDs, important limitations in the literature exist. For example, previous investigations have not generally examined the length of stimulant exposure and later SUD outcomes, severity of SUD outcomes, or co-morbidity with conduct disorder (CD). Moreover, differences may exist between boys with ADHD and ADHD may have substantially higher age-matched risk for cigarette smoking and SUDs in early adolescence. Moreover, differences may exist between boys and girls with ADHD in terms of SUD risk associated with prior stimulant treatment. For instance, Katusic et al reported a difference in SUD risk reduction associated with stimulant treatment in boys with ADHD but not in girls with ADHD.

The main objective of the present study was to examine the effects of early stimulant treatment on subsequent risk for cigarette smoking and SUDs in adolescents with ADHD. Based on previous work in a similarly aged sample of boys with ADHD, we hypothesized primarily that stimulants would be associated with a reduction in the risk for SUDs and cigarette smoking. Secondarily, we hypothesized that the duration of treatment would be directly related to the reduction in risk for SUDs.

SUBJECTS

Subjects were derived from a longitudinal case-control family study of adolescents with and without ADHD as described previously in detail. Briefly, the baseline study evaluated female subjects aged 6 to 18 years with ADHD (n=140) and without ADHD (n=122) ascertained from pediatric and psychiatric sources. Potential subjects were excluded if their nuclear family was unavailable for study, or if they had autism, psychosis, or blindness. All of the subjects with ADHD met full Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) (DSM-IV) criteria for ADHD at the time of the clinical referral, and at recruitment they all had active symptoms of the disorder. The present study reports on the 5-year follow-up of the subjects with ADHD. Parents and adult offspring provided written informed consent to participate, and parents gave consent for offspring younger than 18 years. Children and adolescents provided written assent to participate. The human research committee at Massachusetts General Hospital approved this study protocol.

A 3-stage ascertainment procedure was used to select subjects. In the first stage, psychiatric or pediatric clinics conducted screening and referred subjects. In the second stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the third stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the fourth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the fifth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the sixth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the seventh stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the eighth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the ninth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the tenth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the eleventh stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twelfth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the thirteenth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the fourteenth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the fifteenth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the sixteenth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the seventeenth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the eighteenth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the nineteenth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twentieth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twenty-first stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twenty-second stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twenty-third stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twenty-fourth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twenty-fifth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twenty-sixth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twenty-seventh stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twenty-eighth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the twenty-ninth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother. In the thirtieth stage, we confirmed screening by administering a telephone questionnaire to each subject’s mother.

STATISTICAL ANALYSIS

We compared subjects having ADHD with and without a lifetime history of stimulant medication use relative to follow-up demographic factors. We used the t test for age, Wilcoxon rank sum test for socioeconomic status, and Pearson product correlation coefficient was 0.98. Coefficients for individual diagnoses were 0.88 for ADHD, 1.0 for CD, 1.0 for major depression, 0.95 for mania, 1.0 for separation anxiety, 1.0 for agoraphobia, 0.95 for panic, 1.0 for SUD, and 0.89 for tics or Tourette syndrome.

SUBSTANCE USE MEASURES

Our diagnostic interviews collected data on the lifetime use of nicotine, alcohol, marijuana, and other drugs. All substances except for alcohol and nicotine are referred to as drugs. For every substance used by a given subject, we derived the age at first use, lifetime diagnosis of DSM-IV abuse or dependence, and age at onset from structured interview data. Cigarette smoking refers to age-appropriate diagnosis of DSM-IV smoking dependence.
We ascertained 114 subjects with ADHD having complete medication and SUD data. These subjects ranged in age from 10 to 24 years at the 5-year follow-up (mean age at follow-up, 16.2 years). One hundred eight subjects (94.7%) identified themselves as white and 5 (4.4%) as black. One subject (0.9%) was of unknown race/ethnicity. We found no differences between exposed and unexposed subjects in age, rates of CD, socioeconomic status, source of ascertainment, parental history of SUDs, frequency of family intactness, or severity of ADHD impairment (Table 1). We found that subjects with ADHD receiving stimulant treatment were significantly more likely to have parents with a lifetime history of ADHD; all further analyses controlled for parental history of ADHD.

**RESULTS**

**EXPOSURE TO STIMULANTS**

**Risk for SUDs**

We compared subjects having ADHD with and without exposure to stimulants on age-adjusted rates of developing SUDs. We failed to find any evidence of a significantly higher risk for any SUD among subjects exposed to stimulant medication. Instead, we found evidence for a significant protective effect of stimulant exposure on the subsequent development of any SUD (hazard ratio [HR], 0.27; 95% confidence interval [CI], 0.13-0.60; $\chi^2_{1,1.05} = 10.05$, $P = .001$) (Figure 1). Stimulant-exposed adolescents with ADHD were 73% less likely to manifest an SUD compared with adolescents who were not exposed to stimulants (Table 2).

We also failed to find any evidence for increases in the risks for class or severity of dependence associated with stimulant treatment. Instead, we found evidence of specific SUD risk reduction associated with prior stimulant treatment. More specifically, we found a significant protective effect of stimulant exposure on the age-adjusted rate of development of drug abuse (n = 112) and, although not statistically significant, a lesser effect of stimulant exposure on drug dependence (n = 112). Likewise, we found no significant effect of stimulant exposure on alcohol abuse (n = 114) or on alcohol dependence (n = 114).

**Risk for Cigarette Smoking**

We also evaluated stimulant exposure in relation to the development of cigarette smoking (dependence). We failed to find a significantly higher risk for cigarette smoking (dependence) and prior exposure to stimulant medication. Instead, we found a significant protective effect of stimulant exposure on the age-adjusted rate of smoking development in our sample (HR, 0.28; 95% CI, 0.14-0.60; $\chi^2_{1,1.05} = 10.05$, $P = .001$) (Figure 2). Subjects with ADHD who were previously treated with stimulants had a 72% lower risk and a later onset of cigarette smoking relative to subjects with ADHD without stimulant treatment.

Because comorbidity with CD is a potent predictor of subsequent risk for SUDs and cigarette smoking in subjects with ADHD,11 we repeated each analysis controlling for the effect of CD, which did not change any of the results. As expected, the effect of CD was significant for overall SUDs, drug abuse (112 subjects; HR, 3.61; 95% CI, 1.13-11.50; $P = .03$), and drug dependence (112 subjects; HR, 5.00; 95% CI, 1.41-17.50; $P = .01$).

**ONSET AND DURATION**

We found no effect of age at onset of stimulant therapy on the development of any SUD or smoking. Likewise, there was no effect of stimulant duration on the development of cigarette smoking (HR, 1.02; 95% CI, 0.87-

---

**Table 1. Demographic and Stimulant Treatment Characteristics of Adolescents With Attention-Deficit/Hyperactivity Disorder (ADHD) at 5-Year Follow-up**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Stimulant Therapy (n=20)</th>
<th>Stimulant Therapy (n=94)</th>
<th>Statistic</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>16.12 (3.55)</td>
<td>16.12 (3.55)</td>
<td>$t=0.48$</td>
<td>.60</td>
</tr>
<tr>
<td>Socioeconomic status, mean (SD)</td>
<td>1.89 (0.83)</td>
<td>1.97 (1.03)</td>
<td>$z=-0.03$</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Family intact, No. (%)</td>
<td>15 (75.0)</td>
<td>62 (66.0)</td>
<td>$\chi^2=6.28$</td>
<td>.04</td>
</tr>
<tr>
<td>Full conduct disorder, No. (%)</td>
<td>7 (35.0)</td>
<td>38 (40.4)</td>
<td>$\chi^2=0.20$</td>
<td>.70</td>
</tr>
<tr>
<td>Level of ADHD impairment, No. (%)</td>
<td>3 (15.0)</td>
<td>35 (37.2)</td>
<td>$\chi^2=3.67$</td>
<td>.06</td>
</tr>
<tr>
<td>Substance use disorder</td>
<td>11 (55.0)</td>
<td>65 (69.1)</td>
<td>$\chi^2=1.49$</td>
<td>.20</td>
</tr>
<tr>
<td>Source of ascertainment, No. (%)</td>
<td>5 (25.0)</td>
<td>41 (43.6)</td>
<td>$\chi^2=2.37$</td>
<td>.10</td>
</tr>
</tbody>
</table>

$a$ Test.

$b$ Wilcoxon rank sum test.

$c$ Pearson product moment correlation $\chi^2$ test.

$d$ As assessed on an ordinal scale by the subject about the effect on daily functioning.

$e$ The values do not sum to the subsample size because some data points are missing.
The protective effects of stimulants against the development of SUDs are particularly noteworthy considering that a greater proportion of our adolescents with ADHD were more fully into the age range at risk for SUDs compared with boys with ADHD when they were assessed. Furthermore, girls with ADHD have an almost 2-year earlier age at onset of SUDs relative to boys with ADHD (17 years vs 19 years). Investigations examining the effects of stimulant therapy on subsequent SUDs have generally shown more of a protective effect in adolescents and a neutral effect in adults, leading to the notion that stimulants may delay rather than protect against subsequent SUDs. More research is needed to understand this developmental effect of stimulants (eg, persistence of treatment vs underlying biologic effect) on subsequent substance use and to further clarify their protective mechanisms.

Our results are among the first to demonstrate a clinically and statistically significant reduction in the risk and delayed onset of cigarette smoking associated with stimulant treatment in adolescents with ADHD. Our present results are consistent with epidemiological evidence from Germany indicating delays in the onset of smoking and lower rates of smoking associated with stimulant treatment in subjects with ADHD. Our data are also consistent with a recent prospective study that found an association between stimulant therapy and diminished risk for cigarette smoking. However, our findings are in opposition to results of an older naturalistic study by Lambert and Hartsough that showed higher risk for tobacco dependence in treated subjects with ADHD; however, their stimulant-treated group had an overrepresentation of CD, a strong predictor of SUDs and cigarette smoking. Our data may be of further importance given prior work in boys with ADHD showing that early cigarette smoking in ADHD is related to a high risk for subsequent SUDs.

Although the mechanism of risk reduction for SUDs and cigarette smoking remains unclear, some recent preclinical data may shed light on this important area. For instance, Augustyniak et al showed that prepubertal exposure of methylphenidate hydrochloride in an animal model of ADHD (spontaneous hypertensive rat) resulted in diminished sensitivity to the incentive proper-

### Table 2. Rates of Substance Use Disorders in Adolescents With Attention-Deficit/Hyperactivity Disorder at 5-Year Follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Stimulant Therapy (n=20)</th>
<th>Stimulant Therapy (n=94)</th>
<th>Hazard Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance use disorder abuse</td>
<td>5 (25.0)</td>
<td>11 (11.7)</td>
<td>0.61 (0.20-1.89)</td>
</tr>
<tr>
<td>Substance use disorder dependence</td>
<td>2 (10.0)</td>
<td>3 (3.2)</td>
<td>0.29 (0.05-1.80)</td>
</tr>
<tr>
<td>Substance use smoking (curves truncated at 18 years).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The present results replicate previous findings in boys with ADHD that suggest a protective effect of stimulant treatment against subsequent alcohol and drug use disorders. The present work adds to a growing body of literature showing general reductions in SUDs among stimulant-treated children with ADHD in their adolescent years. Our results documenting protective effects of stimulants in adolescents with ADHD are not entirely consistent with those of Katusic et al, who found that the protective effect of stimulants against SUDs was limited to boys with ADHD. The reasons for the discrepancy are probably related to the small sample size of girls studied by Katusic et al, which limited their power to detect meaningful differences.

In a longitudinal sample of adolescents with ADHD followed up for 5 years, we found strong evidence that prior treatment with stimulants was associated with a subsequent decreased risk for SUDs and cigarette smoking. We did not detect any significant association between age at onset or duration of stimulant treatment and subsequent risk of SUDs or cigarette smoking. Similarly, in those who developed SUDs, there was no relationship between stimulant treatment and the severity or duration of SUDs. Although limited by a small sample of adolescents who were unmedicated for their ADHD, our results extend to adolescents with ADHD the previously reported findings in boys with ADHD, suggesting that prior stimulant treatment does not increase the risk for subsequent SUDs and cigarette smoking and may instead have a protective effect on the development of SUDs and the start of cigarette smoking.

The present results replicate previous findings in boys with ADHD that suggest a protective effect of stimulant treatment against subsequent alcohol and drug use disorders. The present work adds to a growing body of literature showing general reductions in SUDs among stimulant-treated children with ADHD in their adolescent years.
ties of cocaine in adulthood without altering the responses of the mesolimbic dopamine system. Similarly, enduring effects of early exposure to methylphenidate among rat pups resulted in diminished subsequent behaviors among these animals that were synonymous with SUDs. Psychosocial considerations explaining the reduced risk of SUDs associated with stimulant treatment also need to be considered. For instance, decreased risk for SUDs may be related to those families who seek out appropriate treatment for their children. Alternatively, it may be that the necessary supervision and heightened monitoring of youth receiving stimulants are associated with the reduced SUDs. Clearly, more work is necessary to understand if the risk reduction for SUDs and cigarette smoking in adolescents with ADHD treated with stimulants is related to a biologic, psychosocial, or combined mechanism of action.

These results must be considered in light of the methodological limitations. Our naturalistic study design cannot provide evidence so compelling as that produced by a randomized controlled study of stimulant treatment. Because participating subjects were referred and were largely of white race/ethnicity, we do not know if our results will generalize to children with ADHD in the general population or of other racial/ethnic backgrounds. Furthermore, because the adolescents with ADHD in our sample were mostly adolescents, they had not yet fully transitioned through the age range at risk for SUDs and cigarette smoking. The small size of our sample of untreated adolescents with ADHD also limits our statistical power. Although our study was prospective, we depended on retrospectively (ie, within the intervals between assessments) reported ages of treatment and cigarette smoking and SUD onset to establish the temporal sequence. We relied on structured interview data and not on objective measures (eg, urine toxicologic screening results) to determine dependence on cigarette smoking or SUDs and may have underestimated lifetime rates of these disorders. However, recent findings suggest that structured interview–derived substance use data may be more sensitive than objective measures in determining past SUDs. We also did not examine the role of other treatment modalities and SUDs. However, previous work failed to find any relationship between psychotherapy and later SUDs outside of stimulant treatment.

Despite these limitations, this study provides evidence for the first time (to our knowledge) that prior stimulant treatment does not increase the subsequent risk for and may have protective effects against the development of cigarette smoking and SUDs in adolescents with ADHD. These data add to a growing literature documenting that stimulant treatment of ADHD may diminish the risk for cigarette smoking and SUDs in adolescence. These results should allay lingering concerns among clinicians and families about future substance use problems when prescribing stimulants to a child with ADHD. Future research should focus on more salient predictors and moderators of SUDs in adolescents with ADHD, as well as on observing this group fully through the age range of SUD risk.

Accepted for Publication: February 29, 2008.
Correspondence: Timothy E. Wilens, MD, Pediatric Psychopharmacology Program, Massachusetts General Hospital, Harvard Medical School, 55 Parkman St, Yawkey 6A, Boston, MA 02114 (twilens@partners.org).

Author Contributions: Dr Wilens had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Faraone and Biederman. Acquisition of data: Wilens, Schillinger, Westerberg, and Biederman. Analysis and interpretation of data: Wilens, Adamson, Monuteaux, Faraone, and Biederman. Drafting of the manuscript: Adamson, Faraone, and Biederman. Critical revision of the manuscript for important intellectual content: Wilens, Monuteaux, Faraone, Schillinger, Westerberg, and Biederman. Statistical analysis: Adamson, Monuteaux, and Faraone. Obtained funding: Faraone and Biederman. Administrative, technical, and material support: Wilens, Schillinger, Westerberg, and Biederman. Study supervision: Wilens, Monuteaux, and Biederman.

Financial Disclosure: Dr Wilens receives grant support from Abbott, McNeil, Eli Lilly & Co, National Institutes of Health (National Institute on Drug Abuse), Merck, and Shire; is on the speaker’s bureau for Eli Lilly & Co, McNeil, Novartis, and Shire; and is a consultant for Abbott, McNeil, Eli Lilly & Co, National Institutes of Health (National Institute on Drug Abuse), Novartis, Merck, and Shire. Dr Faraone receives research support from, is on the speaker’s bureau for, and has had an advisory or consulting relationship with McNeil and Shire; he also has had an advisory or consulting relationship with Novartis and Eli Lilly & Co. Dr Biederman receives research support from Alza, AstraZeneca, Bristol Myers Squibb, Eli Lilly & Co, Janssen Pharmaceuticals Inc, McNeil, Merck, Organon, Otsuka, Shire, National Institute of Mental Health, and Eunice Kennedy Shriver National Institute of Child Health and Human Development; is a consultant or advisory board member for Janssen, McNeil, Novartis, and Shire; and is on the speaker’s bureau for Janssen, McNeil, Novartis, Shire, and UCB Pharma, Inc. Dr Biederman in previous years received research support, consultation fees, or speaker’s fees for and from the following additional sources: Abbott, AstraZeneca, Celltech, Cephalon, Eli Lilly & Co, Esai, Forest, Glaxo, Glatech, National Alliance for Research on Schizophrenia and Depression (NARSAD), National Institute on Drug Abuse, New River, Novartis, Noven, Neuroscience, Pfizer, Pharmacia, The Prechter Foundation, The Stanley Foundation, and Wyeth.

Funding/Support: This study was supported by grants DA R01 DA14419 and K24 DA016264 from the National Institutes of Health (Dr Wilens) and by the Lilly Foundation.

REFERENCES

20. Vitiello B. Long-term effects of stimulant medications on the brain: possible rel-

6. Weiss G, ed. Attention-Deficit Disorder: Child and Adolescent Psychiatric Clinic-


findings from a large group of girls ascertained from pediatric and psychiatric referral sources.

13. Molina BS, Pelham W. Childhood predictors of adolescent substance use in a

14. Molina BS, Flory K, Hinshaw SP, et al. Delinquent behavior and emerging sub-
stance use in the MTA at 36 months: prevalence, course, and treatment effects.

attention deficit hyperactivity disorder: findings from multiplex families. Am J Psychiatry.
2005;162(9):1621-1627.

16. Greenhill LL, Pliszka S, Dulcan MK, et al; American Academy of Child and Ade-
olescent Psychiatry. Practice parameter for the use of stimulant medications in
2004;43(2) suppl: 205-405.

17. American Academy of Pediatrics, Subcommittee on Attention-Deficit/ Hyperac-
tiy Disorder and Committee on Quality Improvement. Clinical prac-
tice guideline: treatment of the school-aged child with attention-deficit/hyperac-

18. Biederman J, Wilens T, Mick E, Milberger S, Spencer TJ, Faraone SV. Psycho-
active substance use disorders in adults with attention deficit hyperactivity dis-

19. Kollins SH, MacDonald EK, Cushman CR. Assessing the abuse potential of methyl-
phenidate in nonhuman and human subjects: a review. Pharmacol Biochem Behav.
2001;68(3):611-627.

20. Vitiello B. Long-term effects of stimulant medications on the brain: possible rel-
extension to the treatment of attention deficit hyperactivity disorder. J Child A-

21. Lambert NM, Hartsoog CS. Prospective study of tobacco smoking and sub-

22. Barkley RA, Fischer M, Smallish L, Fletcher K. Does the treatment of ADHD with
stimulant medication contribute to illicit drug use/abuse? a 13-year prospective study.

23. Biederman J, Wilens T, Mick E, Spencer T, Faraone SV. Pharmacotherapy of
attention-deficit/hyperactivity disorder reduces risk for substance use disorder.
Pediatrics. 1999;104(2):e20 http://pediatrics.aappublications.org/cgi/content/

24. Katusic SK, Barbaresi WJ, Colligan RC, Weaver AL, Leibson CL, Jacobsen SJ.
Psychostimulant treatment and risk for substance abuse among young adults
with a history of attention-deficit/hyperactivity disorder: a population-based, birth

25. Huss M. ADHD and substance abuse. In: IX Annual European Congress of Psy-

26. Wilens TE, Faraone SV, Biederman J, Gunawardene S. Does stimulant therapy
of attention-deficit/hyperactivity disorder increase later substance abuse: a meta-

27. Milberger S, Biederman J, Faraone SV, Wilens T, Chu MP. Associations between
ADHD and psychoactive substance use disorders: findings from a longitudinal study

findings from a large group of girls ascertained from pediatric and psychiatric referral sources.

29. Disney ER, Elkins JJ, McGuire M, Iacono WG. Effects of ADHD, conduct disorder,
156(10):1515-1521.

30. Huss M, Lehmkullu U. Methylphenidate and substance abuse: a review of pharma-

31. Manzucca S, Klein RG, Bessler A, Mallya P, LaPadula M. Adult outcome of hy-
peractive boys: educational achievement, occupational rank, and psychiatric status.
Arch Gen Psychiatry. 1993;50(7):565-576.

32. Milberger S, Faraone SV, Biederman J, Chu MP, Wilens T. Familial risk analysis of
the association between attention-deficit/hyperactivity disorder and psychoactive

33. Wilens T. Attention-deficit/hyperactivity disorder and the substance use disor-
ders: the nature of the relationship, subtypes at risk and treatment issues. In:
ders Co; 2004:283-301.

34. Monuteaux MC, Spencer TJ, Faraone SV, Wilson AM, Biederman J. A random-
ized, placebo-controlled clinical trial of bupropion for the prevention of smoking in
2007;68(7):1094-1101.


to subsequent alcohol and illicit drug use disorders? a controlled study of youths

37. Augustyniak PN, Koutrich S, Rezzadeh SM, Stewart J, Arvanitogiannis A. Dif-
ferential behavioral and neurochemical effects of cocaine after early exposure to
methylphenidate in an animal model of attention deficit hyperactivity disorder.
Behav Brain Res. 2006;167(2):379-382.

38. Carlezon WA, Mague SD, Anderson SL. Enduring behavioral effects of early ex-

39. Gignac M, Wilens TE, Biederman J, Kwon A, Mick E, Sweeney A. Assessing can-
nabis use in adolescents and young adults: what do urine screen and parental