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Age of Onset, Duration, and Type of Medication Therapy for Attention-Deficit/Hyperactivity Disorder (ADHD) and Substance Use During Adolescence: A Multi-Cohort National Study

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Abstract

Objective—To examine whether age of onset, duration, or type of medication therapy for attention-deficit/hyperactivity disorder (ADHD) is associated with substance use during adolescence.

Method—Nationally representative samples of high school seniors were surveyed via self-administered questionnaires. The sample consisted of 40,358 individuals from ten independent cohorts (2005-2014) and represented a population that was 52% female, 62% White, 10% African-American, 14% Hispanic, and 14% other. Design-based logistic regression analyses were used to test the associations between age of onset, duration, and type of ADHD medication therapy and recent substance use, controlling for potential confounding factors.

Results—Individuals who initiated stimulant medication therapy for ADHD later (ages 10-14 and 15 years and older) and for shorter duration (2 years or less and 3-5 years) as well as those

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who reported only non-stimulant medication therapy for ADHD had significantly greater odds of substance use in adolescence relative to individuals who initiated stimulant medication therapy for ADHD earlier (aged 9 or less) and for longer duration (6 or more years). The odds of substance use generally did not differ between population controls (youth without ADHD and unmedicated youth with ADHD) and individuals who initiated stimulant medication for ADHD early (aged 9 or less) and for longer duration (6 or more years).

Conclusion—Relative to later onset and shorter duration of stimulant treatment for ADHD, early onset and longer duration of stimulant treatment for ADHD was associated with a risk of substance use during adolescence that is lower and similar to that in the general population.

Keywords

Attention-deficit/hyperactivity disorder; stimulant medication therapy; non-stimulant medication therapy; epidemiology; adolescent substance use

Introduction

The prescribing and medical use of prescription stimulants for attention-deficit/hyperactivity disorder (ADHD) has increased significantly among U.S. children and adolescents over the past two decades.[1-4] More than one in every ten U.S. children and adolescents aged 4 to 17 has ever received an ADHD diagnosis (6.4 million children), and over 80% of those were reported as currently having ADHD, with nearly three-fourths taking medication therapy for ADHD.[3,5] Children with ADHD are at heightened risk for initiating substance use and developing substance use disorders (SUDs).[6-11] Although clinical evidence suggests that childhood stimulant therapy for ADHD does not increase the subsequent risk for substance use and SUDs,[12-18] these studies suffer from some limitations such as small homogeneous samples, non-random sampling, and lack of attention toward potential sex differences and the role of non-stimulant medication therapy. To date, the associations between medication therapy for ADHD, substance use, and SUDs have yet to be examined in large probability-based samples of U.S. children and adolescents.[19]

Few national studies have examined the relationships of age of onset, duration, and type of medication therapy for ADHD with subsequent substance use. A recent Danish study found that older age of onset of stimulant treatment for ADHD increased the risk of later substance use in a clinical sample, while early initiation decreased risk.[20] While the risk of SUDs in adulthood increased by a factor of 1.46 for every year older at onset of stimulant treatment, the duration of stimulant treatment in childhood did not predict later SUD.[20] Given the relatively limited U.S. studies, it is important to understand the associations between age of onset of medication therapy for ADHD and risk for substance use among U.S. youth. A naturalistic clinical prospective study of males found that individuals who initiated methylphenidate treatment for ADHD at age 8 or later had greater rates of lifetime non-alcohol SUDs in young adulthood than the subgroup with earlier onset of methylphenidate (before age 8) for ADHD (44% versus 27%, respectively).[21] Notably, the rates of lifetime SUD did not differ between the early methylphenidate therapy group and the comparison participants without ADHD (27% versus 29%, respectively).[21]

Most studies examining the association between medication therapy for ADHD and substance use have not featured large national samples of U.S. youth. For example, the sample sizes of children receiving stimulant medication therapy for ADHD ranged from 53 to 182 in a meta-analytic review conducted over a decade ago,[18] while more recent studies on this topic have included anywhere from 46 to 487 youth.[9,15-17,20-24] Therefore, the main objective of this study was to examine the relationships among age of onset, duration, and type of medication therapy for ADHD and substance use during late adolescence in a large national multi-cohort sample of U.S. adolescents.

Method

Study Design

The Monitoring the Future (MTF) study surveys a cross-sectional, nationally representative sample of high school seniors annually in approximately 127 public and private schools in the coterminous U.S., using self-administered paper-and-pencil questionnaires in classrooms. The samples analyzed in this study consisted of high school seniors from ten independent cohorts (senior years 2005 to 2014), and the MTF study used a multi-stage sampling procedure in each year. In stage 1, geographic areas (or primary sampling units) are selected; in stage 2, schools within primary sampling units are selected (with probability proportionate to school size); and in stage 3, students within schools are selected. Corrective weighting was used in the analyses presented in this study to account for the unequal probabilities of selection that occurred at any stage of sampling.

The mean student response rate for high school seniors was 82% from 2005 to 2014. Because so many questions are included in the MTF study, much of the questionnaire content is divided into six different questionnaire forms, which are randomly distributed. This approach results in six virtually identical subsamples. The measures most relevant for this study were asked on Form 1, so this study focuses on the cross-sectional subsamples receiving Form 1 within each year cohort. Additional details about the MTF design and methods are available elsewhere.[25] Institutional review board approval was granted for this study by the University of Michigan Institutional Review Board.

Sample

The sample for this study included 40,358 individuals who completed questionnaires during the spring of their senior year from 2005 to 2014 (10 independent sample cohorts), including 3,539 individuals ever prescribed stimulant medication therapy for ADHD and 1,332 individuals prescribed only non-stimulant medication therapy for ADHD. After applying the MTF sampling weights provided for each cohort, this combined sample represented a population that was 52% female, 62% White, 10% African-American, 14% Hispanic, and 14% other/not disclosed during this time period. The modal age in the combined sample was 18. The 10 cohorts varied slightly in terms of gender (with earlier cohorts having more females), race/ethnicity (with earlier cohorts having more White individuals), and geography (with earlier cohorts having more respondents from the Northeast and North Central regions). Given this slight variability in the MTF sample composition over time (introducing

the possibility of cohort effects), we explicitly control for all of these sociodemographic factors in our multivariate analyses.

Measures

The MTF study assesses a wide range of attitudes, behaviors, and values. For this study, we selected specific measures for analysis, including demographic characteristics and standard measures of substance use such as binge drinking, cigarette smoking, marijuana, cocaine, and other drug use.

Prescription stimulant medication therapy for ADHD was measured by asking respondents if they had ever taken a prescription stimulant medication under a doctor's supervision for ADHD such as Ritalin (methylphenidate), Adderall (dextroamphetamine and amphetamine), Concerta (methylphenidate), Dexedrine (dextroamphetamine), and/or other methylphenidate formulations.

Age of onset of stimulant medication therapy for ADHD was measured by asking respondents how old they were when they first started using one of these prescription stimulant medications for ADHD under a doctor's supervision. Age of onset responses were coded as follows: 1) 9 years of age or less, 2) 10-14 years of age, and 3) 15 years or older.

Duration of exposure of stimulant medication for ADHD was measured by asking respondents how many years they used stimulant medications for ADHD under a doctor's supervision. Duration responses were coded as follows: 1) 2 years or less, 2) 3-5 years, and 3) 6 or more years.

Non-stimulant medication therapy for ADHD was measured by asking respondents if they had ever taken a non-stimulant prescription medication under a doctor's supervision for ADHD such as Strattera (atomoxetine), Intuniv (guanfacine), Wellbutrin (bupropion), and/or Provigil (modafinil).

Binge drinking was measured with a single item focused on the frequency of having five or more drinks in a row during the past 2 weeks. The response scale ranged from 1) none to 6) 10 or more times.

Cigarette use was measured by asking respondents how frequently they smoked cigarettes during the past 30 days. The response scale ranged from 1) not at all to 7) two or more packs per day.

Marijuana and other drug use included LSD, other psychedelics, cocaine (crack or any other form), heroin, nonmedical use of prescription opioids, sedatives, stimulants, and tranquilizers. These drug use behaviors were each measured by asking respondents on how many occasions they used [specified drug] during the past 12 months. The response scale for each of these items ranged from 1) no occasions to 7) 40 or more occasions.

Statistical Analysis

We considered the following 10 mutually exclusive groups in the analyses:

1. Stimulant medication therapy onset for ADHD during preschool/early elementary school (aged 9 or younger):

    2a) 6 or more years duration,

    2b) 3-5 years duration, or

    2c) 2 years or less duration;

2. Stimulant medication therapy onset for ADHD during late elementary/middle school (10-14 years):

    3a) 6 or more years duration,

    3b) 3-5 years duration, or

    3c) 2 years or less duration;

3. Stimulant medication therapy onset for ADHD during high school (15+ years):

    4a) 3 or more years duration, or

    4b) 2 years or less duration;

4. Non-stimulant medication therapy for ADHD only;

5. Population controls consisting primarily of non-ADHD youth and some ADHD youth who have not received medication therapy for ADHD in their lifetime estimated to be 3% of the population controls based on national estimates.[4]

We first estimated the percentages of the target MTF population falling into each of these 10 subgroups from 2005-2014, using the MTF sampling weights. We then used Rao-Scott Chi-square tests of homogeneity[26] and design-based logistic regression analyses, or logistic regression analyses incorporating the complex sample design features of the MTF (including the sampling weights) and the effects of these features on variance estimates,[27,28] to determine whether history of medication therapy for ADHD (as measured by a categorical variable with the 10 levels described above) was significantly associated with substance use (e.g., cigarette use, binge drinking, marijuana use, cocaine use, any drug use).

Because differences in substance use behaviors among these 10 subgroups may be a result of differences among the subgroups in terms of confounding factors that could influence substance use (e.g., race/ethnicity), we included several covariates in the logistic regression models to adjust for these potential confounding factors when evaluating the subgroup differences.[5,17,20] These covariates included sex (male/female), race/ethnicity (black, white, Hispanic, not reported), cohort year (2005 to 2014), the school's U.S. geographical region (Northeast, North Central, West, South), parental education (at least one parent has some college education vs. otherwise), and truancy (number of days of school skipped in that year).

Estimated (linearized) variances of all weighted estimates were multiplied by an average MTF design effect factor prior to the construction of confidence intervals,[28] and weighted Pearson chi-square statistics were divided by this same design effect factor[26] per the

recommendation of Johnston et al.[25] The goodness-of-fit of all logistic regression models was tested using the design-based methods developed by Archer and Lemeshow,[29] and all models were found to have acceptable fit. All statistical analyses were performed using commands for the analysis of complex sample survey data in the Stata software (Version 14.1; StataCorp, College Station, TX).

Results

Prevalence of Medication Therapy for ADHD

Approximately 12.2% of U.S. high school seniors had used stimulant or non-stimulant medication therapy for ADHD in their lifetime. An estimated 3.1% initiated stimulant medication therapy onset during preschool/early elementary school (aged 9 years or less), 2.9% initiated during late elementary/middle school (aged 10-14 years), 3.0% initiated during high school (aged 15 years or older), and approximately 3.2% of the population received non-stimulant medication therapy only (see Table 1). There were notable sex differences in the prevalence of stimulant medication therapy for ADHD; males were more likely than females to initiate stimulant medication therapy for ADHD, especially during preschool and early elementary school (4.2% of males vs. 2.1% of females, $p < .001$). Interestingly, there were no significant sex differences in the prevalence of non-stimulant medication therapy for ADHD without any history of stimulant medication therapy for ADHD (3.5% of males vs. 3.1% of females).

Age of Onset, Duration, and Type of Medication Therapy for ADHD and Substance Use

Initial bivariate Rao-Scott Chi-square tests revealed significant associations between each of the four individual substance use behaviors, an indicator of any drug use in the past year, and history of medication therapy for ADHD ($p < .001$; see Table 2). In general, the prevalence of substance use was highest among individuals who reported the latest onset and shortest duration of prescription stimulant medication therapy for ADHD. For example, the majority of individuals who initiated prescription stimulant medication therapy for ADHD in high school also reported marijuana use in the past year.

Logistic regression analyses adjusting for the aforementioned confounding factors reinforced the bivariate findings; the odds of reporting substance use were considerably higher among individuals who reported later onset and shorter duration of prescription stimulant medication therapy for ADHD after adjusting for sex, race/ethnicity, cohort year, school geographical region, parental education, and past-year truancy (see Table 3). In contrast, individuals who reported early onset (aged 9 or younger) and long duration (6 or more years) of prescription stimulant medication therapy for ADHD had similar odds of substance use compared to population controls (consisting of youth without ADHD and some unmedicated youth with ADHD). Notably, individuals who only used non-stimulant medication therapy for ADHD had significantly higher odds of several substance use compared to individuals who reported early onset and long duration of prescription stimulant medication therapy for ADHD. Finally, logistic regression analyses were conducted separately for females and males and results were similar to the overall sample (results not shown).

Discussion

This is the first study to provide detailed national-level estimates of the relationships among type of medication therapy for ADHD (stimulant vs. non-stimulant), age of onset of stimulant medication therapy for ADHD, duration of stimulant medication therapy for ADHD, and substance use behaviors during adolescence in the U.S. The present study found that 12.2% of high school seniors in the U.S. had used stimulant or non-stimulant medication therapy for ADHD in their lifetime. The findings indicate that there are no significant differences in the risk for most substance use behaviors during late adolescence between individuals who initiated stimulant medication therapy for ADHD while in preschool or early elementary school (aged 9 or younger) for a longer duration (6 or more years) and the overall U.S. secondary school population controls. Moreover, those who initiated treatment earlier (aged 9 or younger) had lower risk for substance use compared to those who initiated treatment in adolescence. The findings of the present study support the conclusion that early initiation of stimulant treatment for ADHD reduces the risk of substance use relative to later onset of treatment, and that the resulting risk is similar to that in the general population.

Type of medication therapy for ADHD

The present study revealed several new findings regarding non-stimulant medication therapy for ADHD among U.S. secondary school students. First, we found no sex differences in the prevalence of only non-stimulant medication therapy for ADHD, while males were significantly more likely than females to report stimulant medication therapy for ADHD, which is consistent with previous research.[1,3,4] Second, youth who reported only non-stimulant medication therapy for ADHD had significantly higher odds of most substance use compared to individuals who reported early onset (aged 9 or younger) and long duration (6 or more years) of stimulant medication therapy for ADHD. Although these findings provide a new contribution to the clinical literature regarding the association between non-stimulant medication therapy for ADHD and substance use, more research is needed that examines youth treated with non-stimulant medication for ADHD, including the age of onset and duration of non-stimulant medication therapy.

Age of onset of stimulant medication therapy for ADHD

The present study found that the odds of substance use behaviors during late adolescence were significantly greater among those who initiated stimulant medication therapy for ADHD in late elementary or middle school (10-14 years of age) and high school (15 years and older), especially among those with the shortest exposure to the medication. Indeed, the majority of those who initiated stimulant medication therapy for ADHD while in high school also reported past-year marijuana use their senior year. The available measures and the cross-sectional nature of the study do not allow us to determine whether marijuana use served as a signal for greater ADHD severity and/or need for treatment, or whether the late onset stimulant medication therapy for ADHD resulted in marijuana use. Nevertheless, the age of onset of stimulant medication therapy for ADHD findings in the present study are consistent with two previous college studies and a clinical study that found those who initiated stimulant medication therapy for ADHD in early elementary school did not have an

increased risk of substance use and abuse compared to non-users, while those who initiated stimulant medication therapy for ADHD during secondary school or later had an increased risk for all substance use and SUD.[21,23,24] While the causality of substance use in proximity to initiating treatment for ADHD remains unclear, these data suggest that older adolescents with new onset stimulant treatment for ADHD need to be carefully monitored for substance-related behaviors.

Duration of stimulant medication therapy for ADHD

The present study offered further evidence against the possibility that longer duration of stimulant medication therapy for ADHD is associated with higher odds of cocaine and other substance use in late adolescence.[18] Conversely, we found that longer duration of stimulant medication therapy for ADHD was associated with lower rates of substance use during late adolescence as compared to shorter duration of stimulant medication therapy for ADHD at all developmental periods, especially among those who initiated stimulant medication therapy for ADHD in preschool, elementary, and middle school. However, the length of duration of stimulant medication therapy for ADHD on substance use appeared to play a less pronounced role among those who initiated stimulant medication therapy for ADHD in high school.

The proposed study has several strengths that build upon previous literature examining medication therapy for ADHD and substance use. The MTF study measures a large national sample and includes detailed questions regarding medication therapy for ADHD (e.g., age of onset, duration, and medication type) and substance use. The heterogeneous MTF sample also allowed for subgroups to be defined based on age of onset, duration, and type of medication therapy for ADHD. Finally, the assessment of non-stimulant medication therapy for ADHD in the MTF study permitted the youth treated with stimulant medication for ADHD to be compared to a treated group of ADHD youth without any history of using prescription stimulants. Based on the increased odds of substance use found among youth who reported only non-stimulant medication therapy for ADHD, more research is needed to fully understand the context and adequacy of treatment, age of onset, duration, and associations with specific substance use behaviors. Youth who are perceived by a physician to be more likely to misuse substances may be more likely to receive a prescription for non-stimulants, and future research in this area is needed to explore these potential explanations.

Despite these strengths, the present study also had some limitations that need to be taken into account when considering the implications of the findings. First, the study had all of the limitations of large-scale survey research using self-administered surveys and retrospective assessment, including non-response bias, under-reporting of sensitive information, and different methods for assessing psychiatric disorders than clinical settings. While the MTF study could not establish formal *DSM-V* diagnoses and relied on self-report medication therapy questions to identify participants with ADHD given the study methods, the prevalence of stimulant medication therapy for ADHD in the present study closely resembles other national estimates.[3,5] Nevertheless, the stimulant medication measures (i.e., age of onset, duration, and type) in the present study require further psychometric testing. While not all children or adolescents with ADHD require or are treated with medications,

over 70% of U.S. children and adolescents with ADHD receive pharmacotherapy for their ADHD.[3] As a result, a small percentage of unmedicated youth with ADHD (estimated at 3%) were included in our population controls based on national estimates.[3,5]

Second, there are some important segments of the U.S. youth population missing from the MTF data collected each year, such as youth absent from class at the time of data collection and youth who have dropped out of school. Third, although self-report data in the MTF study generally have been found to be reliable and valid, studies on youth suggest that misclassification and under-reporting of substance use does occur.[30-32] The MTF study attempted to minimize the bias associated with self-report surveys by utilizing certain conditions that past research has shown improves the validity and reliability of substance use data collected via self-report surveys, such as explaining the relevance of the study and informing potential respondents that participation is voluntary and data will remain anonymous.[31] In the MTF study, no adjustments are made to correct for any under-reporting; thus, results from the present study may be conservative and underreport the actual prevalence of sensitive behaviors.

Fourth, the MTF study does not assess some factors associated with substance use and help seeking behaviors (e.g., conduct disorder, family SUD history, family environment, childhood trauma, early-onset anxiety, health insurance, low self-esteem, and willingness to seek treatment).[33-35] The lack of an ADHD severity measure represents an important limitation because ADHD severity is likely related to the age of onset, duration, and type of ADHD medication (stimulant or non-stimulant). Therefore, ADHD severity could be confounding the relationship seen between age of onset and risk of substance use. The MTF study also did not separate amphetamine from methylphenidate treatments, which is important because they may differ in their abuse liability. Furthermore, the MTF study did not contain information regarding age of onset of ADHD, and without this information it was not possible to control for person-time in the evaluation of the association between stimulant treatment and risk of substance use.

Finally, the cross-sectional nature of the study limited our ability to establish a causal link between medication therapy for ADHD and substance use, and indicates the need for more longitudinal research. For instance, substance use could have contributed to the onset of symptoms that are clinically recognized as ADHD and partially accounted for the observed association between later onset of ADHD stimulant medications and substance use.

Despite these limitations, the findings of the present study showed that the combination of early onset and longer duration of ADHD stimulant medication therapy was associated with lower rates of subsequent substance use behaviors. A recent Swedish register-based study of nearly 40,000 individuals also found no increased risk of substance abuse among individuals prescribed ADHD stimulant medication.[36] Indeed, earlier onset and longer duration of ADHD stimulant medication was associated with significant reductions in substance abuse, consistent with our findings.[36] More specifically, for each year an individual was taking ADHD stimulant medication before follow-up, there was a 13% reduction in the rate substance abuse.[36] There were several notable differences between the MTF study and some clinical studies such as the Multimodal Treatment of ADHD (MTA) study, which found no

association between cumulative stimulant treatment and adolescent substance use. For instance, the MTF sample (N = 40,358) included 4,871 individuals prescribed ADHD stimulant or non-stimulant medication, while the MTA clinical sample had inclusion and exclusion criteria and consisted of 579 children diagnosed with *DSM-IV* ADHD-combined subtype at baseline.[37] There is evidence that the ADHD-combined subtype is more strongly associated with SUDs compared to other ADHD subtypes.[38] Next, the MTF study assessed adolescents between 2005 and 2014 while the MTA study recruited children aged 7-9 in 1994.[37] The prescribing patterns of ADHD stimulant medications have changed greatly between the time the MTA and MTF studies were conducted.

The findings of the present study add to the growing evidence that initiation of ADHD stimulant medication therapy in high school may represent a risky developmental period that deserves greater clinical and research attention. Based on the findings of the present study, prospective studies with large samples of ADHD and non-ADHD youth are necessary in order to more carefully evaluate the potential consequences of stimulant exposure at high-risk developmental periods such as adolescence.[39] The findings of the present study reinforce the importance of early and persistent treatment of ADHD in reducing substance-related outcomes (to the level of the general population). Indeed, some have asserted that early detection and appropriate medication management (when necessary) may decrease core ADHD symptoms, such as impulsivity, and promote adaptive behaviors that could reduce SUDs later in life.[14] Health professionals are encouraged to consult the most recent practice parameters for the assessment and treatment of children and adolescents with ADHD and the use of psychotropic medication in children and adolescents.[40-42] For the insights that the findings of this study provide for guiding future clinical practice, prescribing practices, and research, see Clinical Guidance, below.

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Clinical Guidance

- We found that nearly one in every eight high school seniors in the U.S. had ever used stimulant or non-stimulant medication therapy for ADHD.
- The results indicated that the combination of early onset and longer duration of ADHD stimulant medication therapy was associated with fewer substance use behaviors in late adolescence (similar to the level of the general population).
- Given that higher substance use behaviors were associated with later initiation of stimulant medications for ADHD during adolescence, we recommend monitoring this later initiation subgroup carefully for pre-existing risk factors and/or the onset of substance use behaviors.

Table 1

Age of Onset and Duration of Stimulant Medication Therapy for Attention-Deficit/ Hyperactivity Disorder (ADHD), Non-Stimulant Medication Therapy for ADHD, and Population Controls

	Overall sample (N=40,358)
	n (%)
Stimulant medication therapy onset for ADHD during preschool / early elementary (aged 9 or younger)	
6 years or more duration	596 (1.5)
3-5 years duration	237 (0.6)
2 years or less duration	409 (1.0)
Stimulant medication therapy onset for ADHD during late elementary / middle school (aged 10-14 years)	
6 years or more duration	268 (0.7)
3-5 years duration	390 (1.0)
2 years or less duration	482 (1.2)
Stimulant medication therapy onset for ADHD during high school (aged 15 or older)	
3 years or more duration	263 (0.7)
2 years or less duration	934 (2.3)
Non-stimulant medication therapy for ADHD only	1,332 (3.2)
Population controls (non-ADHD and unmedicated ADHD)	35,447 (87.8)
Overall sample	40,358 (100)

Note: Source: The Monitoring the Future study 2005-2014, modal age = 18 years. All estimates are weighted.

Table 2

Prevalence Estimates of Substance Use Behaviors as a Function of Age of Onset and Duration of Stimulant Medication Therapy for Attention-Deficit/Hyperactivity Disorder (ADHD), Non-Stimulant Medication Therapy for ADHD Only, and Population Controls

	Past two-week binge drinking	Past-month cigarette smoking	Past-year marijuana use	Past-year cocaine use	Past-year any substance use
	%	%	%	%	%
Stimulant medication therapy onset for ADHD during preschool / early elementary (aged 9 or younger)					
6 years or more duration (n = 596)	22.1	21.4	35.3	5.2	68.5
3-5 years duration (n = 237)	32.2	25.0	41.5	6.4	72.6
2 years or less duration (n = 409)	39.2	32.8	44.0	9.9	71.6
Stimulant medication therapy onset for ADHD during late elementary / middle school (aged 10-14 years)					
6 years or more duration (n = 268)	28.5	25.8	45.1	8.6	74.8
3-5 years duration (n = 390)	38.1	39.1	58.0	10.6	78.0
2 years or less duration (n = 482)	38.3	38.1	59.0	12.2	80.7
Stimulant medication therapy onset for ADHD during high school (aged 15 or older)					
3 years or more duration (n = 263)	41.1	34.9	51.1	14.8	74.7
2 years or less duration (n = 934)	41.2	36.3	59.1	10.2	85.6
Non-stimulant medication therapy for ADHD only (n = 1,332)	30.8	29.7	42.0	7.8	74.8
Population controls (non-ADHD and unmedicated ADHD) (n = 35,447)	22.4	16.4	31.5	3.0	65.0
Design-Adjusted Rao-Scott Test	P < .0001	P < .0001	P < .0001	P < .0001	P < .0001

Note: Source: The Monitoring the Future study, 2005-2014, N=40,358. Past-year any substance use consisted of any past-year use of alcohol, marijuana, cocaine, LSD, other hallucinogens, heroin, nonmedical use of prescription stimulants, nonmedical use of prescription opioids, nonmedical use of prescription sedatives, nonmedical use of prescription tranquilizers, and/or cigarette smoking (past-month).

Table 3

Substance Use Behaviors as a Function of Age of Onset and Duration of Stimulant Medication Therapy for Attention-Deficit/Hyperactivity Disorder (ADHD), Non-Stimulant Medication Therapy for ADHD Only, and Population Controls Based on Logistic Regression Analyses

	Past two-week binge drinking	Past-month cigarette smoking	Past-year marijuana use	Past-year cocaine use	Past-year any substance use
	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
Stimulant medication therapy onset for ADHD during pre-school / early elementary (aged 9 or younger)					
6 years or more duration	Reference	Reference	Reference	Reference	Reference
3-5 years duration	1.7 (1.1-2.7) *	1.2 (0.8-1.9)	1.3 (0.9-1.9)	1.1 (0.6-2.2)	1.2 (0.8-1.8)
2 years or less duration	2.3 (1.6-3.3) ***	1.7 (1.2-2.3) **	1.3 (0.9-1.7)	1.6 (0.9-2.8)	1.0 (0.8-1.5)
Stimulant medication therapy onset for ADHD during late elementary / middle school (aged 10-14 years)					
6 years or more duration	1.4 (1.0-2.1)	1.3 (0.9-2.0)	1.5 (1.1-2.1) *	1.7 (0.9-3.5)	1.4 (0.9-2.1)
3-5 years duration	2.1 (1.5-2.9) ***	2.3 (1.6-3.2) ***	2.3 (1.7-3.2) ***	1.8 (1.0-3.1)	1.5 (1.0-2.0) *
2 years or less duration	2.1 (1.5-2.8) ***	2.2 (1.6-3.0) ***	2.5 (1.9-3.4) ***	2.1 (1.2-3.6) **	1.8 (1.3-2.6) **
Stimulant medication therapy onset for ADHD during high school (aged 15 or older)					
3 years or more duration	2.3 (1.6-3.4) ***	1.9 (1.3-2.7) **	1.6 (1.2-2.3) **	2.7 (1.5-5.1) **	1.2 (0.8-1.8)
2 years or less duration	2.3 (1.7-3.0) ***	1.9 (1.4-2.5) ***	2.4 (1.8-3.1) ***	1.6 (1.0-2.6)	2.4 (1.8-3.2) ***
Non-stimulant medication therapy for ADHD only	1.6 (1.2-2.1) **	1.5 (1.2-2.0) **	1.3 (1.0-1.6)	1.4 (0.8-2.2) *	1.3 (1.0-1.7) *
Population controls (non-ADHD and unmedicated ADHD)	1.2 (0.9-1.5)	0.8 (0.6-1.0)	0.9 (0.7-1.0)	0.6 (0.4-0.9) **	0.9 (0.7-1.1)

Notes: Source: The Monitoring the Future study, 2005-2014, modal age=18 years. The sample sizes for the models ranged from 38,315 (for past two-week binge drinking) to 40,358 (for past year any drug use) due to missing data on individual covariates. Past-year any substance use consisted of any past-year use of alcohol, marijuana, cocaine, LSD, other hallucinogens, heroin, nonmedical use of prescription stimulants, nonmedical use of prescription opioids, nonmedical use of prescription sedatives, nonmedical use of prescription tranquilizers, and/or cigarette smoking (past-month). Adjusted odds ratios (AORs) were adjusted for sex, race/ethnicity, cohort year, school geographical region, parental education, and past-year truancy.

* $p < .05$,

** $p < .01$,

*** $p < .001$.