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Early Exposure to Stimulant Medications and Substance-Related Problems: The Role of Medical and Nonmedical Contexts

Sean Esteban McCabe[*,†], **Phil Veliz**[*], and **Carol J. Boyd**[*,#,‖]

[*]Institute for Research on Women and Gender, University of Michigan, Ann Arbor, MI, 204 S. State St., Ann Arbor, MI, USA 48109-1290

[†]Substance Abuse Research Center, University of Michigan, Ann Arbor, MI

[#]School of Nursing, University of Michigan, Ann Arbor, MI

[‖]Addiction Research Center, University of Michigan, Ann Arbor, MI

Abstract

Background—The age of onset (early vs. late) and context (medical vs. nonmedical) of exposure to stimulant medications for attention-deficit/hyperactivity disorder (ADHD) have been identified as important factors in the addictive potential of these controlled medications. This study examines the role of medical and nonmedical contexts in the association between early exposure to stimulant medications and substance use and substance-related problems among adolescents.

Methods—A Web-based survey was self-administered by Detroit-area secondary school students (N = 4,755) between the 2009–10 and 2012–13 school years. The sample consisted of 51% females, 62% Whites, 32% African-Americans, and 6% from other racial categories.

Results—During the study period, an estimated 11.7% of respondents were ever diagnosed with ADHD. Approximately 6.7% (n = 322) of respondents indicated lifetime medical use of prescription stimulants while 2.6% (n = 124) indicated lifetime nonmedical use. The odds of substance use and substance-related problems were significantly lower among those who initiated earlier medical use of stimulant medications relative to later medical initiation. In contrast, the odds of substance use and substance-related problems were significantly greater among those who initiated earlier nonmedical use of stimulant medications relative to later nonmedical initiation.

Conclusions—More than one in every ten adolescents in this epidemiologically-derived community-based sample was diagnosed with ADHD. This is the first investigation to demonstrate that context (medical vs. nonmedical) plays a critical role in the relationship between early exposure to stimulant medications and the subsequent risk of substance-related problems during adolescence within the same diverse youth sample.

Telephone: (734) 615-8840, Fax: (734) 615-2931, plius@umich.edu.

Keywords

Attention-deficit/hyperactivity disorder; adolescence; stimulant medication; medical use; nonmedical use; age of onset; substance use; drug problems; substance use disorder

1. INTRODUCTION

Approximately one in every six U.S. high school seniors has had some exposure to prescription stimulants, either in a medical or nonmedical context (McCabe and West, 2013). The diagnosis of attention-deficit/hyperactivity disorder (ADHD), the prescribing of stimulant medications to treat ADHD, and the medical and nonmedical use of stimulant medications have increased significantly among U.S. children and adolescents over the past decade (Castle et al., 2007; Center for Behavioral Health Statistics and Quality, 2015; Garfield et al., 2012; McCabe et al., 2014; Miech et al., 2015; Visser et al., 2014; Zuvekas and Vitiello, 2012). The context (medical vs. nonmedical) and expectation of drug effects are hypothesized to play key roles in the addictive potential of stimulant medications (Compton and Volkow, 2006; Teter et al., 2005). For example, stimulant medication taken with a legitimate prescription to treat ADHD in a medical context may be inherently less reinforcing than the same stimulant medication taken for recreational purposes in a nonmedical context (Compton and Volkow, 2006). For the present study, medical use of stimulant medications (e.g., Ritalin®, Dexedrine®, Adderall®, Concerta®, methylphenidate) refers to the use of these medications prescribed by a doctor within a medical context while nonmedical use of stimulant medications refers to the non-prescribed use of these medications within a nonmedical context (e.g., using someone else's stimulant medication).

While the nonmedical use of stimulant medications has increased significantly over the past decade among U.S. adolescents, the long-term adverse health consequences associated with this behavior have not been determined (Bagot and Kaminer, 2014; Johnston et al., 2015; Kaminer, 2013; Miech et al., 2015; Smith and Farah, 2011; Young et al., 2012). A comprehensive review of relevant research found that the cognitive benefits associated with nonmedical use of stimulant medications among individuals without ADHD were minimal relative to the medical risks (Bagot and Kaminer, 2014). Although there is some evidence for possible benefits of prescription stimulants with specific memory tasks by normal healthy non-ADHD individuals in controlled laboratory settings (Bagot and Kaminer, 2014; Smith and Farah, 2011), there is more compelling evidence from "real world" settings that the nonmedical use of prescription stimulants is associated with lower grade point averages, sleep difficulties, irritability, dizzy/lightheaded, headaches, stomachaches, and depressed mood/sadness (Arria et al., 2008; McCabe et al., 2005; Rabiner et al., 2009; Teter et al., 2010). While the nonmedical use of stimulant medications is associated with increased odds of substance use behaviors and substance-related problems among U.S. college students and adults (Arria et al., 2008; McCabe and Teter, 2007; McCabe et al., 2005, 2007, 2009; Rabiner et al., 2009), there is a need for more research to examine whether early onset of nonmedical use of stimulant medications is associated with subsequent substance-related problems among adolescents. Indeed, two comprehensive reviews concluded that more

research on this topic is needed to examine the health consequences associated with the nonmedical use of stimulant medications among U.S. children and adolescents (Bagot and Kaminer, 2014; Young et al., 2012).

Although ADHD is associated with heightened risk for substance use disorders (SUDs; Biederman et al., 1995; Charach et al., 2011; Molina et al., 2007; Wilens et al., 1997, 2011), evidence from clinical samples indicates that childhood stimulant medication therapy for ADHD does not increase the subsequent risk for SUDs during adolescence and young adulthood (Barkley et al., 2003; Biederman et al, 1999; Katusic et al., 2005; Manuzza et al., 2008; Wilens et al., 2003). However, many clinical studies focus largely on young white males, youth from high socioeconomic levels, and those with a disproportionate rate of conduct disorder (Barkley et al., 2003; Katusic et al., 2005; Manuzza et al., 2008; Biederman et al., 2006). As a result, more community-based research is needed to examine whether findings from previous homogeneous small clinical studies can be replicated regarding the relationships between early exposure to stimulant medication therapy for ADHD and substance-related problems in larger heterogeneous epidemiologically-derived samples of children and adolescents.

The main objective of the study was to enhance our understanding of the associations among medical use of stimulant medications, nonmedical use of stimulant medications, substance use, and substance-related problems among adolescents in a large diverse community-based sample. More specifically, we examined how ages of onset of medical and nonmedical use of stimulant medications were associated with substance use and substance-related problems. Based on previous clinical literature, we hypothesized that early onset of stimulant medications in a medical context would not increase the risk for substance-related problems relative to later medical initiation while early exposure to stimulant medications in a nonmedical context would significantly increase the risk for substance-related problems.

2. METHODS

2.1 Study design

The sample includes adolescents from five public middle and high schools in southeastern Michigan. Data came from the cross-sectional web-based Secondary Student Life Survey (SSLS) conducted during the winter semester on an annual basis across a four-year period (2009–10 through 2012–13 school years) among 7^{th} - 12^{th} graders. Active parental consent and adolescent assent were obtained and the appropriate Institutional Review Board approved the study. Classes were assigned to a computer lab during the school day, and the entire class when to the computer labs to take the web-based survey on hooded computers; research assistants monitored these survey sessions. If students opted out of the SSLS, they were routed to a learning module during their time in the computer lab. The SSLS takes approximately 45 minutes to complete. The response rate for this study was 68% based on guideline #2 (RR2) of the American Association for Public Opinion Research (AAPOR). The final response rate falls within the range of response rates from a 2013 national school-based study of secondary school students using comparable data collection procedures (Brener et al., 2013).

2.2 Sample

The study sample included 5,217 unique adolescent respondents across the four waves of the study. We excluded 462 adolescents across the four waves due to incomplete data, leaving a final sample of 4,755 respondents. The sample consisted of 51.1% females and 48.9% males. The racial distribution was 62.4% White, 32.1% African American, and 5.7% from other racial categories. Nonresponse was associated with gender, race, and grade level. Excluded adolescents were more likely to be male ($p < 0.05$) and African American ($p < 0.001$).

2.3 Measures

The SSLS web-based survey includes several items adapted from national studies of alcohol and other drug use among secondary school students (Brener et al., 2013; Miech et al., 2015). Standard measures of past-year substance use behaviors were included such as cigarette smoking, binge drinking, marijuana use, cocaine use, nonmedical use of prescription medications (anxiolytics, opioid analgesics, and sleeping medications), and other drug use (i.e., LSD, other psychedelics, crystal methamphetamine, heroin, inhalants, ecstasy, GHB, and Rohypnol).

2.3.1 Medical use of stimulant medications—was measured using the following question “The following questions are about the use of prescribed medicines. We are not interested in your use of over-the-counter medicines that can be bought in drug or grocery stores without a prescription, such as aspirin, Sominex®, Benadryl®, Tylenol PM®, cough medicine, etc. On how many occasions (in your lifetime/in the past 12 months) has a doctor, dentist, or nurse prescribed the following types of medicine for you?” A separate question was asked for six different classes of prescription medications, including “Prescribed stimulant medication (e.g., Ritalin®, Dexedrine®, Adderall®, Concerta®, methylphenidate).” The response scale ranged from (1) 0 occasions to (7) 40 or more occasions.

2.3.2 Age of onset of medical use of prescription stimulants—was assessed by asking respondents at what age they began using prescribed stimulant medication (e.g., Ritalin®, Dexedrine®, Adderall®, Concerta®, methylphenidate) in number of years of age. The mean age of medical onset of prescription stimulants was 10.9 years of age (SD = 3.5). Consistent with prior work (Manuzza et al., 2008), a categorical variable was constructed with the following sub-categories based on the mean age of medical onset: (1) Never used, (2) First used at age 11 or younger, and (3) First used between ages 12 and 18.

2.3.3 Nonmedical use of prescription stimulants—was assessed with the following question “Sometimes people use prescription medicines that were meant for other people, even when their own health professional (e.g., doctor, dentist, nurse) has not prescribed it for them. On how many occasions (in your lifetime/in the past 12 months) have you used the following types of medicines, not prescribed to you?” A separate question was asked for six different classes of prescription medications, including “Stimulant medication (e.g., Ritalin®, Dexedrine®, Adderall®, Concerta®, methylphenidate).” The response scale was identical to that for medical use of prescription stimulants.

2.3.4 Age of onset of nonmedical use of prescription stimulants—was assessed by asking respondents at what age they began using stimulant medication (e.g., Ritalin®, Dexedrine®, Adderall®, Concerta®, methylphenidate) not prescribed to you in number of years of age. The mean age of nonmedical onset of prescription stimulants was 14.1 years of age (SD = 3.0). A categorical variable was constructed with the following sub-categories based on the mean age of nonmedical onset: (1) Never used, (2) First used at age 14 or younger, and (3) First used between the ages of 15 and 18.

2.3.5 The Drug Abuse Screening Test, Short Form (DAST-10)—was used to assess drug use related problems and potential drug use disorders (Skinner, 1982). Respondents who used drugs other than alcohol during the past year were asked whether they had experienced any of 10 drug use related problems in the past 12 months (e.g., “Have family members ever complained about your involvement with drugs?” or “Have you experienced withdrawal symptoms (felt sick) when you stopped taking drugs?”). The DAST-10 has been shown to have good reliability and temporal stability and identifies individuals who need more intensive assessment for substance use disorders (Cocco and Carey, 1998). Based on past research, if a respondent positively endorsed two or more DAST items, this was considered a positive screen that signified a possible risk for a drug use disorder and were assigned a value of 1 (those who only endorsed one item or less were assigned a value of 0) (Cocco and Carey, 1998; French et al., 2001; Skinner, 1982). The average Cronbach’s alpha across the four waves of the sample for the DAST-10 was good ($\alpha = 0.8$).

2.3.6 The CRAFFT—was also used to screen for possible substance use disorders involving alcohol and other drugs (Knight et al., 1999). The “CRAFFT” represents an acronym based on six yes/no questions that measure different aspects of substance use disorders (i.e, **C**ar, **R**elax, **A**lone, **F**orget, **F**riends, **T**rouble). It has good internal consistency ($\alpha = 0.8$) and is highly correlated ($r = 0.8$) with the Personal Involvement with Chemicals Scale (PICS), the criterion standard for alcohol and other drug screening (Knight et al., 1999). A score of 2 or higher on the CRAFFT has been used to detect potential substance use disorders among adolescents (Knight et al., 2002). Thus, if a respondent positively endorsed two or more items on the CRAFFT this was considered a positive screen to detect a possible substance use disorder and was assigned a value of 1 (those who only endorsed one item or less were assigned a value of 0). The average Cronbach’s alpha across the four waves of the sample for the CRAFFT was good ($\alpha = 0.8$).

Sex, race, and socioeconomic status (SES) could be important factors in terms of the risk for initiating substance use and experiencing substance-related problems associated with medical and nonmedical onset of prescription stimulants (Katusic et al., 2005). Although the prevalence rates of ADHD and SUD are greater among males, Whites, and those aged 18–29 years (Bernardi et al., 2012; Compton et al., 2007; Grant et al., 2004), a Danish-based study found an increased risk of SUDs in females with ADHD compared to males with ADHD (Dalsgaard et al., 2014). In order to control for these potentially confounding factors, we include measures that assess respondents sex, race/ethnicity, grade-level and SES (i.e., at least one parent has a college degree or higher). Moreover, in order to assess the influence of

the age of onset of medical and nonmedical stimulant use, we control for whether the respondent was ever diagnosed with ADHD, whether the respondent used stimulants in a medical context during the past year, and whether the respondent nonmedically used stimulants during the past year. Finally, the Youth Self-Report (YSR; Achenbach and Rescorla, 2001) is designed for ages 11–18 and includes 105 items that assess emotional, behavioral, and social problems. Categorical variables based off t-scores calculated by the Youth Self-Report (YSR/11–18) were used to account for whether the student reported normal (t-score between 50 and 64), borderline (t-score between 65 and 68), or clinically significant levels (t-score between 69 and 100) for both ADHD and conduct disorder symptom severity (Achenbach and Rescorla, 2001).

2.4 Data analysis

The data analysis strategy is divided into two major sections. First, we computed descriptive statistics for the key independent variables and dependent variables to examine characteristics of the sample. Second, we fitted logistic regression models using the generalized estimating equations (GEE) methodology with an independent correlation structure, to assess how ages of onset of both medical and nonmedical use of prescription stimulants were associated with substance use and substance-related problems across the four waves of the study (Hanley et al., 2003; Zeger et al., 1988). Based on the estimated logistic regression models, we computed adjusted odds ratios (AORs) and 95% confidence intervals (95% CIs) describing the relationships of the predictors with the odds of substance use and substance-related problems. We note that all models included respondents' sex, race/ethnicity, grade-level, past-year stimulant use (medical or nonmedical), parents' highest level of education, and respondents' ADHD severity and conduct disorder severity that were derived from the YSR/11–18, number of waves respondent participated in the SSLS, and the survey year as covariates. Moreover, all variables used in the GEE analyses were treated as time-varying given that some respondents could have participated in the SSLS multiple times. All the statistical analyses were performed using commercially available software (STATA/SE v.13; STATA Corp., College Station, TX). .

3. RESULTS

3.1 Prevalence of ADHD diagnosis, medical and nonmedical use of prescription stimulants

Tables 1 through 3 show descriptive statistics for the key dependent and independent variables used in the analyses. An estimated 11.7% of the respondents were ever diagnosed with ADHD. During the study period, approximately 6.7% (n = 322) of respondents indicated lifetime medical stimulant use while 2.6% (n = 124) of respondents indicated lifetime nonmedical use of prescription stimulants. The mean age of onset of medical stimulant use was 10.9 years of age (SD = 3.51) while the mean age of nonmedical stimulant use was 14.1 years of age (SD = 3.02). Moreover, an estimated 3.1% of respondents began using prescription stimulants medically at age 11 or younger, while 3.6% of respondents began using prescription stimulants medically between the ages of 12 and 18. Approximately 1.0% of respondents began using prescription stimulants nonmedically at

age 14 or younger, while 1.6% of respondents began using prescription stimulants nonmedically between the ages of 15 and 18.

3.2 Substance use and substance-related problems as a function of onset of medical and nonmedical use of stimulant medication (overall sample)

Table 4 shows the logistic regression results of early and late onset of medical and nonmedical use of prescription stimulants when compared to their peers who did not use prescription stimulants within these contexts. The results indicate that late onset of medical prescription stimulant use was associated with greater odds of past-year cigarette use, past-year marijuana use, past-year 'other drug' use, past-year drug-related problems (based on the DAST-10 screen), and lifetime substance-related problems (based on the CRAFFT) when compared to their peers who did not use stimulants in a medical context. With the exception of past-year cocaine use, no statistically significant differences were found between respondents who indicated early onset of medical stimulant use and those who did not use prescription stimulants in a medical context for the outcomes assessing substance use and substance-related problems. In contrast, we found that both early and late onset of nonmedical stimulant use was significantly associated with greater odds of all substance use and substance-related problems when compared to their peers who did not use stimulants in a nonmedical context.

3.3 Substance use and substance-related problems as a function of onset of medical and nonmedical use of stimulant medication (medical and nonmedical users only)

Table 5 shows how the age of onset of medical use of stimulants was associated with substance use and substance-related problems over the study period and indicates that as age of onset of medical use increases, the odds of engaging in past-year cigarette use (AOR = 1.11, 95% C.I. [1.02, 1.20]), past-year binge drinking (AOR = 1.10, 95% C.I. [1.00, 1.22]), past-year marijuana use (AOR = 1.14, 95% C.I. [1.05, 1.23]), past-year 'other drug' use (AOR = 1.16, 95% C.I. [1.01, 1.33]), and past-year drug-related problems based on the DAST-10 (AOR = 1.10, 95% C.I. [1.01, 1.19]) or lifetime substance-related problems based on the CRAFFT (AOR = 1.21, 95% C.I. [1.11, 1.32]) also ***increases***. Unlike the categorical age of onset finding, there was no statistically significant association found between the age of onset of medical use of stimulants and the odds of past-year cocaine use. In contrast, as age of onset on nonmedical use of stimulants increases, the odds of engaging in past-year cocaine use (AOR = .566, 95% C.I. [.408, .785]), past-year nonmedical prescription drug use (AOR = .755, 95% C.I. [.598, .952]) and past-year drug-related problems based on the DAST-10 (AOR = .745, 95% C.I. [.567, .978]) ***decreases***.

4. DISCUSSION

This study is the first investigation to examine the impact of early exposure of prescription stimulant medication on substance use and substance-related problems in both medical and nonmedical contexts within the same diverse youth sample. Given some of the limitations in previous studies, it was critical to understand if and how early exposure of stimulant medication therapy for ADHD in medical vs. nonmedical contexts impacts the risk of substance use and related problems in a large diverse epidemiologically-derived community-

based sample. The findings of the present study indicate the odds of substance use and substance-related problems were significantly lower among those who initiated earlier medical onset of stimulant medications relative to later medical onset.

There is growing evidence that initiation of ADHD stimulant medication therapy in middle school or high school may represent a risky developmental period that deserves greater clinical and research attention (Dalsgaard et al., 2014; Kaloyanides et al., 2007; Mannuzza et al., 2008; McCabe et al., 2006). For example, the effect of age of medical onset on drug use related problems found in the present study are consistent with two clinical studies indicating that late onset of stimulant medication therapy increased the risk of developing SUDs relative to early onset of stimulant medication therapy (Dalsgaard et al., 2014; Mannuzza et al., 2008). In addition, 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 substance-related problems compared to non-users, while those who initiated stimulant medication therapy for ADHD during middle school or later had an increased risk for substance use and substance-related problems (Kaloyanides et al., 2007; Mannuzza et al., 2008; McCabe et al., 2006).

While the present study found increased odds of past-year cocaine use associated with early exposure to stimulant medications relative to those who never used stimulant medications, the significant relationship associated with early exposure was no longer present when age of onset measure was examined for medical users of prescription stimulants only. Additionally, early exposure to stimulant medications was not associated with other substance use or substance-related problems in the present study while later onset of stimulant medications in secondary school (middle or high school) was consistently associated with increased odds of substance use and substance-related problems for the overall sample as well as medical users only. While the causality of substance use in proximity to initiating stimulant treatment during adolescence remains unclear, these data suggest that older adolescents in secondary school with new onset stimulant medication treatment need to be carefully monitored for substance use and substance-related problems. Based on the growing evidence in clinical and epidemiologically-derived samples, the increased risk of substance-related problems associated with new onset stimulant treatment in secondary school deserves more research attention because this may signify a differential expression of ADHD, comorbid mental health disorders, self-medication as a result of untreated ADHD, and/or peer influences.

To date, most clinical studies have not examined the association between nonmedical use of prescription stimulant medications and substance-related problems because they tend to focus on smaller and less diverse clinical samples than larger epidemiologically-derived samples. The results of the present study provide strong support that the nonmedical context represents a critical factor to consider because early exposure to stimulant medications in a nonmedical context was associated with increased odds of substance use and substance-related problems consistent with at least one previous epidemiological study (McCabe et al., 2007). These findings are notable because the nonmedical use of prescription stimulants and

related health consequences have increased significantly among U.S. adolescents over the past two decades (Center for Behavioral Health Statistics and Quality, 2015; Miech et al., 2015; SAMHSA, 2013).

This study has several notable strengths that build upon previous clinical research examining the impact of early exposure to stimulant medications for ADHD and substance-related problems among adolescents. First, the wide range of measures and self-administration for sensitive behaviors represent strengths of this study. Second, the diverse nature and overall size of the epidemiologically-derived sample represent additional strengths. There were also some limitations that should be noted when considering the implications of the study. First, the present study was cross-sectional, naturalistic and stimulant medications for ADHD could not be randomized at baseline; this is similar to past clinical and epidemiological studies. As a result, attempts to disentangle protective or harmful effects of ADHD stimulant therapy from the severity of the underlying condition(s) are potentially confounded (Faraone et al., 1992; Volkow and Insel, 2003). Second, we acknowledge that the regional sample and reliance on self-report may limit generalizability of the findings. Indeed, Michigan has the highest rate of medication treatment among children ages 4 to 17 with ADHD in the U.S. according to parent report (American Academy of Pediatrics, 2011). Third, the lack of details regarding dosage and route of administration, and co-ingestion with other drugs represents a limitation because these are all additional factors that influence the abuse potential of stimulant medications (Compton and Volkow, 2006). Finally, adolescents excluded from the sample were more likely to be males, African Americans, lower grade levels, and living in lower socio-economic school districts. However, less than 5% of the sample was excluded and the overall impact of these excluded cases is likely to be minimal.

In conclusion, the findings of the present epidemiologically-derived sample provide a valuable complement to the available clinical literature. The present study extended previous research because we examined the effects of both age of onset (early vs. late) and context (medical vs. nonmedical) of stimulant medication therapy for ADHD in a racially diverse sample that was comprised of young adolescent males and females from a wide range of socio-economic backgrounds. The findings of the present study support the hypothesis that context plays an important role in the association between early exposure to stimulant medication and subsequent substance abuse (Compton and Volkow, 2006; Volkow and Swanson, 2008; Wilens et al., 2003). The present study reinforces clinical findings that early medical onset of stimulant medications taken with a legitimate prescription within a medical context is associated with less risk for substance use and substance-related problems than later medical onset while the inverse relationship was true for the early nonmedical onset of stimulant medications taken without a prescription in a nonmedical context.

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Highlights

- -Examine role of medical vs. nonmedical context in early stimulant exposure.
- -Early medical prescription stimulant onset did not predict substance abuse.
- -Early nonmedical prescription stimulant onset predicted substance abuse.
- -Medical and nonmedical context play critical role in early stimulant onset.
- -Nonmedical use should be assessed when prescribing stimulants for ADHD.

Table 1

Percentage distributions of sample characteristics (total across the 4 waves of the SSLS; n = 4755)

	%
Gender	
Male (ref.)	48.9%
Female	51.1%
Race	
White (ref.)	62.4%
African-American	32.1%
Other Race	5.7%
Grade level	
7th or 8th grade (ref.)	34.6%
9th or 10th grade	32.1%
11th or 12th grade	33.4%
Parental education	
Parents have less than a college degree (ref.)	25.0%
At least one parent has a college degree or higher	75.0%
YSR conduct disorder severity	
YSR conduct disorder severity t-score between 50 and 64 (normal) (ref.)	88.5%
YSR conduct disorder severity t-score between 65 and 68 (borderline)	5.1%
YSR conduct disorder severity t-score between 69 and 100 (clinically significant)	6.4%
ADHD diagnosis	
Not diagnosed with ADHD (ref.)	88.3%
Diagnosed with ADHD	11.7%
YSR ADHD severity	
YSR ADHD severity t-score between 50 and 64 (normal) (ref.)	89.6%
YSR ADHD severity t-score between 65 and 68 (borderline)	6.9%
YSR ADHD severity t-score between 69 and 100 (clinically significant)	3.5%
Past-year medical use of prescription stimulants	
Did not medically use prescription stimulants during the past year (ref.)	94.9%
Medically used prescription stimulants during the past year	5.1%
Past-year nonmedical use of prescription stimulants	
Did not nonmedically use prescription stimulants during the past year (ref.)	98.1%
Nonmedically used prescription stimulants during the past year	1.9%
Age of onset of medical use of prescription stimulants	
Never used prescription stimulant medication (ref.)	93.2%
First used stimulant medication medically at age 11 or younger (Early Onset)	3.1%
First used stimulant medication medically between the ages of 12 and 18 (Late Onset)	3.6%
Age of onset of nonmedical use of prescription stimulants	
Never used stimulant medication nonmedically (ref.)	97.4%
First used stimulant medication nonmedically at age 14 or younger (Early Onset)	1.0%
First used stimulant medication nonmedically between the ages of 15 and 18 (Late Onset)	1.6%

	%
Cigarette smoking during the past 12 months	11.7%
Binge drinking during the past 12 months	10.7%
Marijuana use during the past 12 months	19.2%
Cocaine use during the past 12 months	1.1%
Other drug use during the past 12 months	4.1%
Nonmedical use of prescription drugs during the past 12 months	11.1%
Positive DAST-10 screen during the past 12 months	12.8%
Positive CRAFFT screen	18.9%

(ref.) indicates that this category was used as the reference group in the GEE analyses.

Note: The mean age of onset of medical stimulant use was 10.9 years of age (SD=3.51) and the mean age of nonmedical stimulant use was 14.1 years of age (SD=3.02).

Table 2

Sample characteristics based on age of onset of medical use of prescription stimulants (total across the 4 waves of the SSLS; n = 4755)

	Age of onset of medical use of prescription stimulants								
	Contrast 1			Contrast 2			Contrast 3		
	Never Used (n = 4433) %	Early Onset (n = 150) %	p[(a)]	Never Used (n = 4433) %	Late Onset (n = 172) %	p[(a)]	Early Onset (n = 150) %	Late Onset (n = 172) %	p[(a)]
Gender									
Male	48.3%	66.0%	***	48.3%	49.4%		66.0%	49.4%	**
Female	51.7%	34.0%		51.7%	50.6%		34.0%	50.6%	
Race									
White	61.0%	80.7%	***	61.0%	83.1%	***	80.7%	83.1%	
Black	33.1%	16.0%		33.1%	13.4%		16.0%	13.4%	
Other Race	5.9%	3.3%		5.9%	3.5%		3.3%	3.5%	
Grade level									
7th or 8th grade	35.1%	34.7%		35.1%	20.3%	***	34.7%	20.3%	**
9th or 10th grade	31.9%	25.3%		31.9%	41.9%		25.3%	41.9%	
11th or 12th grade	33.0%	40.0%		33.0%	37.8%		40.0%	37.8%	
Parental education									
Parents have less than a college degree	25.3%	22.0%		25.3%	19.2%		22.0%	19.2%	
At least one parent has a college degree or higher	74.7%	78.0%		74.7%	80.8%		78.0%	80.8%	
YSR conduct disorder severity									
Conduct disorder severity (normal)	89.3%	79.3%	***	89.3%	76.2%	***	79.3%	76.2%	
Conduct disorder severity (borderline)	4.7%	10.0%		4.7%	11.0%		10.0%	11.0%	
Conduct disorder severity (clinically significant)	6.0%	10.7%		6.0%	12.8%		10.7%	12.8%	
ADHD diagnosis									
Never diagnosed with ADHD	92.8%	19.3%	***	92.8%	30.8%	***	19.3%	30.8%	*
Diagnosed with ADHD	7.2%	80.7%		7.2%	69.2%		80.7%	69.2%	
YSR ADHD severity									
ADHD severity (normal)	91.2%	66.0%	***	91.2%	68.0%	***	66.0%	68.0%	
ADHD severity (borderline)	6.0%	18.0%		6.0%	21.5%		18.0%	21.5%	
ADHD severity (clinically significant)	2.8%	16.0%		2.8%	10.5%		16.0%	10.5%	

	Age of onset of medical use of prescription stimulants								
	Contrast 1			Contrast 2			Contrast 3		
	Never Used (n = 4433) %	Early Onset (n = 150) %	p[(a)]	Never Used (n = 4433) %	Late Onset (n = 172) %	p[(a)]	Early Onset (n = 150) %	Late Onset (n = 172) %	p[(a)]
Past-year medical use of prescription stimulants									
Did not medically use prescription stimulants	100.0%	23.3%	***	100.0%	26.7%	***	23.3%	26.7%	
Medically used prescription stimulants	0.0%	76.7%		0.0%	73.3%		76.7%	73.3%	
Past-year nonmedical use of prescription stimulants									
Did not nonmedically use prescription stimulants	98.5%	92.0%	***	98.5%	92.4%	***	92.0%	92.4%	
Nonmedically used prescribed stimulants	1.5%	8.0%		1.5%	7.6%		8.0%	7.6%	
Onset of nonmedical use of prescription stimulants									
Never used stimulant medication nonmedically	98.0%	90.7%	***	98.0%	87.2%	***	90.7%	87.2%	
Early onset of nonmedical use	0.6%	7.3%		0.6%	5.8%		7.3%	5.8%	
Late onset of nonmedical use	1.4%	2.0%		1.4%	7.0%		2.0%	7.0%	
Past-year cigarette smoking	10.4%	24.0%	***	10.4%	33.7%	***	24.0%	33.7%	
Past-year binge drinking	9.9%	16.7%	**	9.9%	26.7%	***	16.7%	26.7%	*
Past-year marijuana use	18.0%	28.0%	**	18.0%	41.3%	***	28.0%	41.3%	*
Past-year cocaine use	.83%	6.0%	***	.83%	4.1%	***	6.0%	4.1%	
Past-year other illicit drug use	3.4%	13.3%	***	3.4%	14.0%	***	13.3%	14.0%	
Past-year other nonmedical prescription drug use	10.6%	17.3%	**	10.6%	20.3%	***	17.3%	20.3%	
Positive DAST-10 screen	11.6%	26.0%	***	11.6%	33.7%	***	26.0%	33.7%	
Positive CRAFFT screen	17.6%	26.7%	**	17.6%	44.2%	***	26.7%	44.2%	***

*p<.05,

**p<.01,

***p<.001

[(a)]Significance tests were based on Chi-square tests of independence (2×2 and 2×3). Results for 2×2 analyses were truncated, refer to table 1 for truncated groups.

Table 3

Sample characteristics based on age of onset of nonmedical use of prescription stimulants (total across the 4 waves of the SSLS; n = 4755)

	Age of Onset of Nonmedical Use of Prescription Stimulants								
	Contrast 1			Contrast 2			Contrast 3		
	Never Used (n = 4631) %	Early Onset (n = 46) %	p[(a)]	Never Used (n = 4631) %	Late Onset (n = 78) %	p[(a)]	Early Onset (n = 46) %	Late Onset (n = 78) %	p[(a)]
Gender									
Male	49.1%	45.7%		49.1%	37.2%	*	45.7%	37.2%	
Female	50.9%	54.3%		50.9%	62.8%		54.3%	62.8%	
Race									
White	61.8%	78.3%	*	61.8%	89.7%	***	78.3%	89.7%	
Black	32.5%	15.2%		32.5%	3.8%		15.2%	3.8%	
Other Race	5.7%	6.5%		5.7%	6.4%		6.5%	6.4%	
Grade level									
7th or 8th grade	35.2%	26.1%		35.2%	5.1%	***	26.1%	5.1%	***
9th or 10th grade	31.8%	45.7%		31.8%	38.5%		45.7%	38.5%	
11th or 12th grade	33.0%	28.3%		33.0%	56.4%		28.3%	56.4%	
Parental education									
Parents have less than a college degree	25.1%	28.3%		25.1%	16.7%		28.3%	16.7%	
At least one parent has a college degree or higher	74.9%	71.7%		74.9%	83.3%		71.7%	83.3%	
YSR conduct disorder severity									
Conduct disorder severity (normal)	89.6%	30.4%	***	89.6%	56.4%	***	30.4%	56.4%	*
Conduct disorder severity (borderline)	4.9%	17.4%		4.9%	12.8%		17.4%	12.8%	
Conduct disorder severity (clinically significant)	5.5%	52.2%		5.5%	30.8%		52.2%	30.8%	
ADHD diagnosis									
Never diagnosed with ADHD	88.7%	54.3%	***	88.7%	83.3%		54.3%	83.3%	***
Diagnosed with ADHD	11.3%	45.7%		11.3%	16.7%		45.7%	16.7%	
YSR ADHD severity									
ADHD severity (normal)	90.3%	52.2%	***	90.3%	71.8%	***	52.2%	71.8%	
ADHD severity (borderline)	6.5%	28.3%		6.5%	17.9%		28.3%	17.9%	
ADHD severity (clinically significant)	3.2%	19.6%		3.2%	10.3%		19.6%	10.3%	

	Age of Onset of Nonmedical Use of Prescription Stimulants								
	Contrast 1			Contrast 2			Contrast 3		
	Never Used (n = 4631) %	Early Onset (n = 46) %	p[(a)]	Never Used (n = 4631) %	Late Onset (n = 78) %	p[(a)]	Early Onset (n = 46) %	Late Onset (n = 78) %	p[(a)]
Past-year medical use of prescription stimulants									
Did not medically use prescription stimulants	95.3%	65.2%	***	95.3%	91.0%		65.2%	91.0%	***
Medically used prescription stimulants	4.7%	34.8%		4.7%	9.0%		34.8%	9.0%	
Past-year nonmedical use of prescription stimulants									
Did not nonmedically use prescription stimulants	100.0%	39.1%	***	100.0%	17.9%	***	39.1%	17.9%	**
Nonmedically used prescribed stimulants	0.0%	60.9%		0.0%	82.1%		60.9%	82.1%	
Onset of medical use of prescription stimulants									
Never used prescribed stimulants medically	93.8%	54.3%	***	93.8%	80.8%	***	54.3%	80.8%	***
Early onset of medical use	2.9%	23.9%		2.9%	3.8%		23.9%	3.8%	
Late onset of medical use	3.2%	21.7%		3.2%	15.4%		21.7%	15.4%	
Past-year cigarette smoking	10.0%	67.4%	***	10.0%	76.9%	***	67.4%	76.9%	
Past-year binge drinking	9.1%	60.9%	***	9.1%	78.2%	***	60.9%	78.2%	*
Past-year marijuana use	17.4%	78.3%	***	17.4%	91.0%	***	78.3%	91.0%	*
Past-year cocaine use	0.5%	41.3%	***	0.5%	12.8%	***	41.3%	12.8%	**
Past-year other illicit drug use	2.7%	67.4%	***	2.7%	48.7%	***	67.4%	48.7%	*
Past-year other nonmedical prescription drug use	9.8%	76.1%	***	9.8%	52.6%	***	76.1%	52.6%	**
Positive DAST-10 screen	11.0%	78.3%	***	11.0%	82.1%	***	78.3%	82.1%	
Positive CRAFFT screen	17.0%	80.4%	***	17.0%	93.6%	***	80.4%	93.6%	*

*p<.05,

**p<.01,

***p<.001

(a)Significance tests were based on Chi-square tests of independence (2×2 and 2×3). Results for 2×2 analyses were truncated, refer to table 1 for truncated groups

Table 4

Substance use and substance-related problems as a function of onset of medical use and nonmedical use of stimulant medication (overall sample, n = 4755)

	Model 1 Cigarette Smoking	**Model 2 Binge Drinking**	**Model 3 Marijuana Use**	**Model 4 Cocaine Use**	**Model 5 Other Drug Use**	**Model 6 Nonmedical Rx Drug Use**	**Model 7 Positive DAST-10**	**Model 8 Positive CRAFFT**
History of Medical Use for Overall Sample (n = 4755)	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**
No history of medical use of stimulant medication	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**
Early onset of medical use of stimulant medication	.851 [.518, 1.39]	.957 [.540, 1.69]	.839 [.547, 1.28]	**3.49** * [1.08, 11.21]	1.61 [.796, 3.28]	1.00 [.570, 1.78]	1.29 [.802, 2.08]	.792 [.494, 1.26]
Late onset of medical use of stimulant medication	**1.69** * **[1.10, 2.58]**	1.24 [.754, 2.03]	**1.72** ** **[1.19 , 2.48]**	2.29 [.656, 8.02]	**2.94** *** **[1.59, 5.45]**	1.16 [.687, 1.95]	**1.92** ** **[1.26, 2.93]**	**2.23** *** **[1.52, 3.26]**
	Model 9 Cigarette Smoking	**Model 10** Binge Drinking	**Model 11** Marijuana Use	**Model 12** Cocaine Use	**Model 13** Other Drug Use	**Model 14** Nonmedical Rx Drug Use	**Model 15** Positive DAST-10	**Model 16** Positive CRAFFT
History of Nonmedical Use for Overall Sample (n = 4755)	AOR 95% CI	AOR 95% CI	AOR 95% CI	AOR 95% CI	AOR 95% CI	AOR 95% CI	AOR 95% CI	AOR 95% CI
No history of nonmedical use of stimulant medication	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**	**Reference**
Early onset of nonmedical use of stimulant medication	**15.01** *** **[8.07, 27.9]**	**19.19** *** **[10.3, 35.8]**	**21.30** *** **[10.7, 42.6]**	**135.21** *** **[61.7, 296.3]**	**49.57** *** **[27.0, 90.7]**	**30.99** *** **[17.1, 55.9]**	**33.61** *** **[17.2, 65.3]**	**21.77** *** **[10.9, 43.2]**
Late onset of nonmedical use of stimulant medication	**20.47** *** **[12.2, 34.2]**	**18.96** *** **[11.5, 31.3]**	**47.12** *** **[22.3, 99.2]**	**27.17** *** **[10.6, 69.2]**	**41.23** *** **[24.8, 68.4]**	**13.80** *** **[8.67, 21.9]**	**31.51** *** **[18.0, 54.8]**	**45.83** *** **[21.6, 96.9]**

* p<.05,

** p<.01,

*** p<.001;

AOR=adjusted odds ratio; 95% CI=95% confidence interval.

Notes: Models 1 through 8 control for gender, race, grade level of respondent, highest level of parental education, lifetime ADHD diagnosis, ADHD symptom severity, conduct disorder symptom severity, past-year nonmedical use of stimulant medication, number of waves respondent participated in the SSLS, and wave respondent participated in the SSLS. Models 9 through 16 control for gender, race, grade level of respondent, highest level of parental education, lifetime ADHD diagnosis, ADHD symptom severity, past-year medical use of stimulants, number of waves respondent participated in the SSLS, and wave respondent participated in the SSLS. All variables used in the analyses were time-varying.

Table 5

Substance use and substance-related problems as a function of onset of medical use and nonmedical use of stimulant medication (medical and nonmedical users only)

	Model 17 Cigarette Smoking	**Model 18 Binge Drinking**	**Model 19 Marijuana Use**	**Model 20 Cocaine Use**	**Model 21 Other Drug Use**	**Model 22 Nonmedical Rx Drug Use**	**Model 23 Positive DAST-10**	**Model 24 Positive CRAFFT**
Lifetime Medical Users Only (n = 322)	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**	**AOR 95% CI**
Age of medical onset of prescription stimulants (continuous measure)	**1.11** ** **[1.02, 1.20]**	**1.10** * **[1.00, 1.22]**	**1.14** *** **[1.05, 1.23]**	.912 [.670, 1.24]	**1.16** * **[1.01, 1.33]**	1.05 [.934, 1.19]	**1.10** * **[1.01, 1.19]**	**1.21** *** **[1.11, 1.32]**
	Model 25 Cigarette Smoking	**Model 26** Binge Drinking	**Model 27** Marijuana Use	**Model 28** Cocaine Use	**Model 29** Other Drug Use	**Model 30** Nonmedical Rx Drug Use	**Model 31** Positive DAST-10	**Model 32** Positive CRAFFT
Lifetime Nonmedical Users Only (n = 124)	AOR 95% CI	AOR 95% CI	AOR 95% CI	AOR 95% CI	AOR 95% CI	AOR 95% CI	AOR 95% CI	AOR 95% CI
Age of nonmedical onset of prescription stimulants (continuous measure)	.912 [.733 , 1.13]	.818 [.656 , 1.01]	.950 [.726 , 1.24]	**.566** *** **[.408 , .785]**	.845 [.686, 1.04]	**.755** * **[.598, .952]**	**.745** * **[.567 , .978]**	.851 [.629 , 1.15]

* p<.05,

** p<.01,

*** p<.001;

AOR=adjusted odds ratio; 95% CI=95% confidence interval. Note: : Models 17 through 24 control for gender, race, grade level of respondent, highest level of parental education, ADHD symptom severity, past year nonmedical use of stimulants, conduct disorder symptom severity, number of waves respondent participated in the SSLS, and wave respondent participated in the SSLS. Models 25 through 32 control for gender, race, grade level of respondent, highest level of parental education, lifetime ADHD diagnosis, ADHD symptom severity, past year medical use of stimulants, number of waves respondent participated in the SSLS, and wave respondent participated in the SSLS. All variables used in the analyses were time-varying.