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Medical and nonmedical use of prescription sedatives and anxiolytics: Adolescents' use and substance use disorder symptoms in adulthood

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Abstract

Objectives—This study assessed the longitudinal associations between medical and nonmedical use of prescription sedatives/anxiolytics (NMPSA) during adolescence (age 18) and substance use disorder (SUD) symptoms during adulthood (age 35).

Methods—Multiple cohorts of nationally representative samples of U.S. high school seniors (n = 8,373) were surveyed via self-administered questionnaires and followed longitudinally from adolescence (age 18, 1976–1996) to adulthood (age 35, 1993–2013).

Results—An estimated 20.1% of adolescents reported lifetime medical or nonmedical use of prescription sedatives/anxiolytics. Among adolescents who reported medical use of prescription sedatives/anxiolytics, 44.9% also reported NMPSA by age 18. Based on multivariate analyses that included age 18 sociodemographic and other substance use controls, medical use of prescription sedatives/anxiolytics without any history of NMPSA during adolescence was not associated with SUD symptoms in adulthood relative to adolescents with no prescription sedative/anxiolytic use. In contrast, adolescents with a history of both medical and nonmedical use of prescription

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Contributors

Drs. McCabe and Schulenberg designed the study, wrote the protocol, conducted literature searches, and provided summaries of previous research studies. Dr. Veliz conducted the statistical analysis and Dr. Boyd helped interpret the data.
Dr. McCabe wrote the first draft of the manuscript, and all authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare that they have no conflicts of interest.

sedatives/anxiolytics and adolescents who reported only NMPSA had between two to three times greater odds of SUD symptoms in adulthood relative to adolescents with no prescription sedative/anxiolytic use and those who reported only medical use of prescription sedatives/anxiolytics.

Conclusions—One in every five U.S. high school seniors report ever using prescription sedatives/anxiolytics either medically or nonmedically. This study provides compelling evidence that the medical use of prescription sedatives/anxiolytics (without any NMPSA) during adolescence is not associated with increased risk of SUD symptoms in adulthood while any NMPSA during adolescence serves as a signal for SUDs in adulthood.

Keywords

Longitudinal; Medical use; Nonmedical use; Sedative; Anxiolytic; Substance Use Disorders

1. Introduction

There has been an increase in the prescribing of sedative/hypnotic and tranquilizer/anxiolytic medications in the United States (U.S.) during the past two decades (Fortuna et al., 2010; Skaer et al., 2000; Witek et al., 2005; Zito et al., 2003). Despite the short-term efficacy of prescription anxiolytics and sedatives for the treatment of anxiety and sleep disorders, there are substantial concerns about the abuse potential of these controlled medications including the high prevalence of diversion and nonmedical use of prescription sedatives and anxiolytics (NMPSA), and the increase in adverse consequences such as U.S. emergency department visits and overdose deaths associated with NMPSA (Compton & Volkow, 2006; Fenton et al., 2010; Johnston et al., 2015; Jones & McAninch, 2015; Kokkevi et al., 2008; McCabe et al., 2007, 2011; Miech et al., 2015; SAMHSA, 2012, 2013, 2014).

Approximately 9% and 13% of U.S. young adults have reported lifetime nonmedical use of prescription sedatives and anxiolytics, respectively (Johnston et al., 2015). While at least four cross-sectional or regional studies have examined the relationships between medical use of prescription sedatives/anxiolytics and NMPSA during adolescence (Boyd et al., 2015; Kokkevi et al., 2008; McCabe et al., 2007, McCabe & West, 2014), a systematic review concluded there is a need for longitudinal research examining temporal patterns of NMPSA associated with substance use disorders (SUDs) in adulthood (Young et al., 2012). At least two cross-sectional studies found that adolescents reporting medical use of prescription anxiolytics without a history of nonmedical use of prescription anxiolytics did not have significantly greater odds of past-year substance use behaviors relative to their peers who have never used prescription anxiolytics (McCabe et al., 2007; McCabe & West, 2014). In contrast, past-year substance use behaviors were more prevalent among adolescents who reported NMPSA compared to those who never used prescription sedatives/anxiolytics (McCabe et al., 2007; McCabe & West, 2014). Adolescents prescribed sedatives/anxiolytics in the past were more likely to use someone else's sedatives/anxiolytics during a three-year period (Boyd et al., 2015). Since more than 25% of young adults in the U.S. meet DSM-5 criteria for a past-year SUD (Grant et al., 2015, 2016), an important question is whether adolescents' medical and/or nonmedical exposure to sedatives/anxiolytics increases the risk for developing SUDs in adulthood.

The majority of adolescents who report NMPSA engage in concurrent or simultaneous polysubstance use (McCabe et al., 2006, 2007; Schepis et al., 2016), creating major challenges to isolating drug-specific-related problems resulting from NMPSA. For instance, nearly 73% of adolescent past-year nonmedical users of prescription anxiolytics simultaneously co-ingested these medications with at least one other substance, primarily cannabis and alcohol (Schepis et al., 2016). As a result, attempts to examine substance-related problems associated with NMPSA must control for a wide range of substances for assessing the risk of developing SUDs. Other common risk factors for NMPSA and SUD include age (i.e., 18–34 years), sex, race/ethnicity, parental education, geographical regional location, urbanicity, truancy and other problem behaviors, family history of SUD, substance-related consequences, and anxiety and mood disorders (Blanco et al., 2007; Grant et al., 2015, 2016; Havens et al., 2011; Johnston et al., 2015).

We hypothesize that the medical use of prescription sedatives/anxiolytics (when necessary) without NMPSA offers adolescent patients an appropriate opportunity to manage their anxiety and sleep disorders/symptoms and thus reduces the likelihood of later adult SUD symptoms. We further hypothesize individuals who initiate any NMPSA during adolescence (with or without medical use) are at substantially greater risk for later adult SUD symptoms based on the abuse potential of these medications and related problem behaviors, including polysubstance use.

2. Material and methods

2.1. Study design

This prospective study used national panel data from the Monitoring the Future (MTF) study (Bachman et al., 2015; Johnston et al., 2015). Based on a three-stage sampling procedure, MTF surveys nationally representative samples of approximately 17,000 U.S. high school seniors each year using questionnaires administered in classrooms during the regular school day. Stage 1 is the selection of geographic areas; stage 2 is the selection of schools; and stage 3 is the selection of students within each school. Approximately 2,400 high school seniors are randomly selected for biennial follow-ups each year and surveyed biennially using mailed questionnaires through age 30; they are also followed up at age 35 by mail.

The study period for respondents at age 35 was between 1993 and 2013 (12th grade cohorts 1976–1996). The response rates at baseline ranged from 77% to 86% during the study period; most all non-response was due to the given student being absent from school (less than 1% refuse to participate). The MTF panel oversamples drug users from the 12th grade sample to secure a population of drug users to follow into adulthood. The overall weighted response rate for the longitudinal sample from baseline (12th grade) to age 35 was 54%. Given potential non-response bias, this study incorporates nonresponse adjustments (i.e., attrition weights) to the panel weights (i.e., unequal probabilities of selection into the panel sample) that explicitly account for key factors in the MTF that have been shown to be associated with nonresponse at future follow-ups (e.g., Johnston et al., 2015; McCabe et al., 2014; Schulenberg et al., 2016). The project design and sampling methods are described in greater detail elsewhere (Bachman et al., 2015; Johnston et al., 2015; Schulenberg et al., 2016).

2.2. Sample

As illustrated in Table 1, the weighted longitudinal sample included 8,373 individuals (52.9% female and 47.1% male). The racial/ethnic distribution was 73.5% White, 11.9% Black, 6.4% Hispanic, and 8.1% multiracial or from other racial/ethnic categories.

2.3. Measures

The MTF study assesses a wide range of behaviors, attitudes, and values. Based on previous research, we selected specific measures for these analyses from the age 18 surveys to include as controls (Blanco et al., 2007; Colliver et al., 2006; Havens et al., 2011; Johnston et al., 2015; McCabe et al., 2014; Miech et al., 2015; Schulenberg et al., 2016; Young et al., 2012), including baseline cohort year, sex (i.e., Male and Female), race/ethnicity (i.e., White, Black, Hispanic, and other race), parental education (i.e., at least one parent has a college degree or higher or neither parent has a college degree), U.S. Census geographic location (i.e., Northeast, Midwest, South and West), truancy (number of whole days of school skipped in past-month), urbanicity based on metropolitan statistical area (MSA) (i.e., large MSA, other MSA, and non-MSA), annual alcohol, cannabis, and other drug use (i.e., cocaine, heroin, LSD, other hallucinogens, inhalants, nonmedical use of prescription opioids, and nonmedical use of prescription stimulants), and substance-related consequences (i.e., received a ticket or was in accident while under the influence of alcohol, cannabis, or other drugs).

Medical and nonmedical use of prescription sedatives/anxiolytics at baseline (age 18) used four separate questions measuring lifetime medical use by asking respondents if they had ever taken prescription sedatives or anxiolytics because a doctor had told them to use them and lifetime nonmedical use by asking respondents if they had taken sedatives or anxiolytics on their own—that is, without a doctor telling them to take them. Respondents were prompted that these medications are prescribed by doctors to help people relax or get to sleep and cannot be sold without a prescription. Respondents were also provided a list of several examples of prescription sedatives and anxiolytics such as Valium® and Librium®. Based on these questions, a variable with four mutually exclusive categories was constructed to include the following for lifetime use of prescription sedatives and anxiolytics at baseline: (1) no medical and nonmedical use, (2) medical use only, (3) medical and nonmedical use, and (4) nonmedical use only.

Substance use disorder (SUD) symptoms at age 35 were measured with questions based on the DSM criteria for alcohol use disorder (AUD), cannabis use disorder (SUD), and other drug use disorders (ODUD). Although these measures of SUD symptoms do not yield a clinical diagnosis, the items are consistent with SUD as measured in other large scale surveys (Harford & Muthén, 2001; Muthén, 1996; Nelson et al., 1998) and have been used in the past to reflect DSM-IV and DSM-5 alcohol and cannabis use disorders (Merline et al., 2008; Patrick et al., 2011; Schulenberg et al., 2016). Respondents were asked to report SUD symptoms during the past five years related to AUD, CUD and ODUD (which included illicit drug classes such as cocaine, LSD, other hallucinogens, heroin, inhalants as well as nonmedical use of prescription anxiolytics, opioids, sedatives, and stimulants). Fifteen items were used to develop eight of the eleven DSM-5 criteria that were consistent with AUD,

CUD, and ODUD: substance use resulting in a failure to fulfill major role obligations (e.g., “caused you financial difficulties”), continued substance use when physically hazardous (e.g., “caused you to drive unsafely”), continued substance use despite persistent or recurrent interpersonal or social problems, tolerance (e.g., “you found that over time you need more of the drug to get the same effect”), withdrawal (e.g., “stopping or reducing your use of the drug made you physically ill or sick”), persistent desire or unsuccessful efforts to cut down substance use (e.g., “you wanted to try to stop or cut down, but you found that you could not”), health related issue due to substance use (e.g., “caused your physical health to be bad”), and craving (e.g., “you felt such a strong desire to use the drug that you could not resist or think of anything else”). For each item, the responses were recoded to none vs. a little/some/a lot. For each criterion, respondents were coded as meeting it, if they responded other than “none” within the past 5 years. For criterion with multiple items, the respondent was coded as endorsing the criterion if he/she indicated other than “none” for any of the items. The eight criteria were summed to obtain an overall number of criterion endorsed. We followed recommended practice that any use disorder (including mild, moderate, or severe) is indicated by meeting two or more of the criteria (American Psychiatric Association, 2013; Goldstein et al., 2015; Grant et al., 2015, 2016).

2.4. Statistical Analysis

All analyses were conducted using STATA 13.1 (Stata Corp, College Station, Texas) and were weighted to adjust for the unequal probabilities of selection. Descriptive statistics and logistic regression were used to examine SUD symptoms at age 35 as a function of medical use and NMPSA. Prevalence of two or more SUD symptoms were based on eight DSM-5 criteria for AUD, CUD, and ODUD. Logistic regression analyses provided adjusted odds ratios (AOR) and 95% confidence intervals for two or more SUD symptoms at age 35 as a function of lifetime medical use or NMPSA at age 18. Multivariable logistic regression analyses controlled for socio-demographics, other substance use behaviors, truancy, and substance-related consequences at age 18 (see Measures section for more details regarding covariates). Prescription sedatives and anxiolytics were combined in the present study to be consistent with the DSM-5 and other recent national studies examining DSM-5 SUDs (Grant et al., 2016). In addition, we repeated all of the analyses separately for prescription sedatives and anxiolytics, analyses were similar to the combined results (results not shown).

3. Results

As shown in Table 1, the estimated prevalence of lifetime medical or nonmedical use of prescription sedatives or anxiolytics was 20.1% at age 18: approximately 7.6% of individuals indicated only medical use, while 6.2% reported both medical use and NMPSA, and 6.3% reported only NMPSA. Among respondents who reported past-year NMPSA at age 18, approximately 92.9% reported polysubstance use, primarily involving alcohol and cannabis. Among respondents who reported any medical use of prescription sedatives/anxiolytics at age 18, approximately 44.9% reported a history of NMPSA at age 18. As shown in Table 1, lifetime prevalence estimates of NMPSA fell between lifetime nonmedical use of prescription opioids and stimulants. No statistically significant differences were found between males (12.2%) and females (12.8%) with respect to NMPSA at age 18. Whites

(14.6%) and respondents from 'other races' (11.1%) had the highest lifetime prevalence of NMPSA at age 18 when compared to Blacks (4.5%) and Hispanics (6.7%) ($\chi 2 = 92.85$, df = 3, $p<.001$). Finally, at age 35, approximately 4.7% indicated past-year NMPSA, 3.4% indicated past-year nonmedical use of prescription opioids, and 1.5% indicated past-year nonmedical use of prescription stimulants.

Tables 2 and 3 show the bivariate prevalence estimates and multivariable adjusted odds ratios of two or more SUD symptoms during adulthood (age 35) as a function of medical use and NMPSA during adolescence (age 18). There were no differences in the adjusted odds ratios (AORs) of two or more AUD, CUD, or ODUD symptoms at age 35 between respondents who indicated only medical use of prescription sedatives or anxiolytics at age 18 and respondents who had no medical use or NMPSA at age 18.

As illustrated in Table 3, the referent group for the following analyses was respondents with no history of medical use or NMPSA at age 18. Compared to the referent group, respondents who indicated only NMPSA at age 18 had significantly higher adjusted odds of AUD, CUD, and ODUD symptoms at age 35. Similarly, respondents who reported both medical use and NMPSA at age 18 had the higher adjusted odds of AUD, CUD, and ODUD symptoms at age 35.

We conducted additional logistic regression analysis to compare medical use only (referent group) to the other two groups. We found significantly higher adjusted odds of two or more AUD, CUD, and ODUD symptoms at age 35 among respondents who engaged in NMPSA at age 18 (with and without a history of medical use), relative to respondents who reported only medical use of prescription sedatives/anxiolytics at age 18 (results not shown). We also conducted additional logistic regression analyses using a higher cut-point threshold of three or more SUD symptoms and found similar findings (results not shown). Finally, we repeated all of the above-mentioned analyses separately for adolescent females and males and found similar results to the overall sample (results not shown).

4. Discussion

The significant increase in medical use of sedatives and anxiolytics among U.S. adolescents and young adults during the past two decades is likely the result of public awareness of anxiety and insomnia symptoms, widespread availability of new medications, and pervasive direct-to-consumer marketing (Fortuna et al., 2010; Olfson et al., 2015; Skaer et al., 2000). The present study found that about one in every five U.S. high school seniors had lifetime medical or nonmedical exposure to prescription sedatives or anxiolytics.

To our knowledge, this is the first national study to show that SUD symptoms at age 35 were more prevalent among those with a history of both medical use and NMPSA during adolescence and among those who reported only NMPSA, relative to those who only reported medical use of prescription sedatives/anxiolytics during adolescence. While the findings from this study should offer prescribers some reassurance that appropriate use of prescription sedatives and anxiolytics is not associated with increased risk of SUD symptoms in adulthood relative to population controls suggesting the importance of early

detection and proper treatment, there is some cause for concern. Nearly 45% of adolescents who reported medical use of prescription sedatives/anxiolytics at age 18 had also engaged in NMPSA. A similar study conducted in Europe found that among adolescents aged 16 who were prescribed sedatives/anxiolytics, approximately 28% reported NMPSA (Kokkevi et al., 2008).

The high prevalence of NMPSA among medical users of sedatives/anxiolytics during adolescence is likely related to many factors. First, many individuals become responsible for their own medication during late adolescence which increases NMPSA and diversion. For instance, a prospective study found that adolescents prescribed sedatives/anxiolytics medications were twelve times more likely to use someone else's sedative/anxiolytic medication relative to adolescents never prescribed sedatives/anxiolytics (Boyd et al., 2015). At least two cross-sectional studies found that between 30% and 44% of adolescents and 54% of adults prescribed prescription sedatives/anxiolytics reported misusing their own medications, primarily by exceeding the recommended dosage followed by deliberately co-ingesting the medication with alcohol or other drugs (McCabe et al., 2011; McLarnon et al., 2011). Second, several studies have shown friends and peers are the leading diversion sources for NMPSA among adolescents and young adults (McCabe & Boyd, 2005; Miech et al., 2015). Indeed, more than 70% of those who reported NMPSA indicated peer sources in one college study (McCabe & Boyd, 2005). Second, past research indicates that the majority of adolescents with a history of medical and nonmedical use of prescription anxiolytics initiated nonmedical use of prescription anxiolytics before medical use (McCabe & West, 2014). Third, more than one in every eight adolescents report using their own leftover prescription anxiolytic medications for subsequent NMPSA (Miech et al., 2015).

The findings from this study provide evidence that any NMPSA during adolescence serves as a signal for later AUD, CUD and ODUD symptoms in early mid-life, after adjusting for potential confounding variables (e.g., baseline alcohol, cannabis, other drug use, etc.). These longitudinal results are consistent with findings regarding the association between nonmedical use of prescription opioids during adolescence and subsequent SUD symptoms (McCabe et al., 2013). The findings from the present study also found no sex differences and address an important gap regarding the temporal patterns of sedative and anxiolytic use and subsequent SUDs during the transition to adulthood (Young et al., 2012).

This study found that more than nine in every ten adolescents who reported NMPSA engaged in polysubstance use during the past-year which is similar to prior studies examining nonmedical use of prescription opioids, sedatives, stimulants and anxiolytics (McCabe et al., 2006; Catalano et al., 2011; Schepis et al., 2016). In fact, recent work has shown that the majority of past-year nonmedical users of prescription opioids, anxiolytics and sedatives engage in simultaneous co-ingestion with at least one other substance placing such individuals at increased risk of consequences such as overdose (McCabe et al., 2006; McCabe and Boyd, 2005; SAMHSA, 2012, 2013; Schepis et al., 2016).

The present study offers a new contribution by showing that adolescents who reported NMPSA were much more likely to report AUD symptoms than other SUD symptoms at age 35. More specifically, we found that approximately 45% of adolescents who reported

NMPSA at age 18 reported two or more AUD symptoms at age 35 while 13% reported two or more CUD symptoms, and 11% reported two or more ODUD symptoms at age 35 which included sedative/anxiolytic use disorder symptoms. Therefore, these findings reinforce the importance of screening for a wide range of substances when assessing the risk for SUDs associated with NMPSA.

The MTF study has the strengths and limitations of large-scale longitudinal survey research using self-administered surveys. While the MTF study could not establish formal DSM-based diagnoses, the prevalence of SUD symptoms for non-users in the MTF study closely resembles other national estimates (Compton et al., 2007; Grant et al., 2015, 2016; Hasin et al., 2007). Nonetheless, the present study did not include three of 11 DSM-5 SUD criteria, SUD symptoms related to prescription sedatives or anxiolytics were not assessed, and "other drug" symptoms could have represented different drugs. As a result, future research is needed to examine the sensitivity and specificity of the SUD symptoms. Second, the MTF study did not include some variables related to substance use at baseline nor SUD symptoms at follow-up (e.g., early-onset anxiety and family history of SUD). Third, while self-report data in the MTF study are reliable and valid, studies on youth suggest that misclassification and under-reporting of drug use occurs (Johnston & O'Malley, 1985; Morral et al., 2003; O'Malley et al. 1983). Fourth, there are two important segments missing from the MTF database and this could provide under-estimates: students absent from class at the time of data collection and students who dropped out of school (Johnston et al., 2014). As is common in the case of longitudinal studies regarding substance use, attrition is differential with respect to drug use, indicating that drug users are less likely to remain in longitudinal samples; nonetheless, the use of attrition weights helped correct biases associated with differential attrition. Finally, the definition of nonmedical use in the present study was broad to account for all subtypes of NMPSA and future research is needed to disentangle the different subtypes of NMPSA and subsequent consequences.

To our knowledge this study is the first to identify longitudinal associations between NMPSA during adolescence and SUD symptoms into adulthood. The findings indicate prescribers can play an important role in identifying patients who are at risk for NMPSA and SUD. Based on the strong association between NMPSA and SUD symptoms, clinicians should educate adolescent patients and their parents regarding the abuse liability of prescription sedatives and anxiolytics. The findings suggest the need for comprehensive screening before prescribing sedatives/anxiolytics and careful monitoring for NMPSA. The results also indicate the need for safe storage and proper disposal during and following medication therapy. Adolescents who report NMPSA before or during medication therapy should be considered for alternative treatments where appropriate and vigilant monitoring. These recommended clinical practices require further evaluation to determine whether they have an impact on reducing NMPSA and development of SUDs during the transition from adolescence to adulthood.

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Table 1

Sociodemographic characteristics for the longitudinal sample at age 18

Baseline Characteristics at Age 18	Weighted Study Sample (n = 8,373)
Sex	%
Male	47.1
Female	52.9
Race/Ethnicity	
White	73.5
Black	11.9
Hispanic	6.4
Other race	8.1
Parental Education	
At least one parent has a college degree or higher	40.0
Neither parent has a college degree	60.0
Region	
Northeast	21.3
Midwest	27.3
South	33.9
West	17.5
Truancy (Past-Month)	
Did not cut/skip at least one whole day	69.1
Cut/skipped at one whole day	30.9
Substance-Related Consequences (Past-Year)	
Did not receive a ticket or was not in an accident while intoxicated	94.8
Received a ticket or was in an accident while intoxicated	5.2
Urbanicity	
Large metropolitan statistical area	23.4
Other metropolitan statistical area	46.4
Non-metropolitan statistical area	30.2
12th Grade Cohort Year	
1976–1980	23.0
1981–1985	24.2
1986–1990	25.0
1991–1996	27.8
Lifetime Nonmedical Use of Prescription Drugs	
Lifetime nonmedical use of prescription opioids	8.8
Lifetime nonmedical use of prescription sedatives/anxiolytics	12.6
Lifetime nonmedical use of prescription stimulants	16.6
Lifetime Medical and Nonmedical Use of Prescription Sedatives/Anxiolytics	
No lifetime medical or nonmedical use	79.9

Baseline Characteristics at Age 18	Weighted Study Sample (n = 8,373)
Lifetime medical use only	7.6
Lifetime medical and nonmedical use	6.2
Lifetime nonmedical use only	6.3

Note: Weighted samples and estimates with attrition weights are provided.

Table 2

Prevalence of substance use disorder symptoms at age 35 as a function of medical and nonmedical use of prescription sedatives/anxiolytics at age 18

	Alcohol Use Disorder (AUD) Symptoms at Age 35 2 or More Symptoms %	Cannabis Use Disorder (CUD) Symptoms at Age 35 2 or More Symptoms %	Other Drug Use Disorder (ODUD) Symptoms at Age 35 2 or More Symptoms %
Prescription Sedative/Anxiolytic Use at Age 18			
No medical or nonmedical use (n = 6189)	24.2%	5.0%	2.8%
Medical use only (n = 589)	29.5%	5.7%	4.5%
Medical and nonmedical use (n = 482)	35.2%	10.0%	10.2
Nonmedical use only (n = 489)	44.8%	13.3%	10.7%
	[1] n = 7533	[1] n = 7664	[1] n = 7264

[1] Sample sizes vary due to missing data on the dependent measures (i.e., AUD, CUD, and ODUD symptoms at age 35).

Table 3

Adjusted odds of substance use disorder symptoms at age 35 as a function of medical and nonmedical use of prescription sedatives/anxiolytics at age 18

	Alcohol Use Disorder (AUD) Symptoms (Age 35) 2 or More Symptoms [1] AOR (95% CI)	Cannabis Use Disorder (CUD) Symptoms (Age 35) 2 or More Symptoms [1] AOR (95% CI)	Other Drug Use Disorder (ODUD) Symptoms (Age 35) 2 or More Symptoms [1] AOR (95% CI)
Prescription Sedative/Anxiolytic Use (Age 18)			
No medical or nonmedical use (n = 6189)	Reference	Reference	Reference
Medical use only (n = 589)	1.25 (.957, 1.63)	1.06 (.656, 1.71)	1.41 (.786, 2.54)
Medical and nonmedical use (n = 482)	1.48 (1.14, 1.93)**	1.73 (1.18, 2.54)**	2.97 (1.88, 4.69)***
Nonmedical use only (n = 489)	2.11 (1.58, 2.81)***	2.41 (1.64, 3.54)***	3.01 (1.92, 4.71)***
	[2] n = 7533	[2] n = 7664	[2] n = 7264

Reference = Reference group for each model was respondents who did not report medical or nonmedical use of prescription sedatives or anxiolytics.

** p < 0.01,

*** p < 0.001

[1] Adjusted odds ratios (AOR's) were adjusted for race (i.e., White, Black, Hispanic, Other race), sex (i.e., Male and Female), parental education at baseline (age 18), geographic region (i.e., northeast, northcentral, south and west), metropolitan statistical area (i.e., large MSA, other MSA, and non-MSA), cohort year at baseline (age 18), annual alcohol use at baseline (age 18), annual cannabis use at baseline (age 18), and annual other drug use (i.e., cocaine, heroin, LSD, other hallucinogens, inhalants, nonmedical use of prescription opioids, and nonmedical use of prescription stimulants) at baseline (age 18), truancy (i.e., number of whole days of school skipped in past-month) at baseline (age 18), and substance-related consequences (i.e., received a ticket or was in an accident while driving under the influence of alcohol, cannabis, or other drugs) at baseline (age 18). The AOR's and 95% CI's for these variables are not shown in Table 3. For the AUD model, the significant (p < 0.01) baseline covariates were truancy, DUI, alcohol, cannabis and other drug use. For the CUD model, the significant (p < 0.01) baseline covariates were truancy, alcohol, cannabis and other drug use. For the ODUD model, the significant (p < 0.01) baseline covariates were truancy, DUI, alcohol, cannabis and other drug use.

[2] Sample sizes vary due to missing data on the dependent measures (i.e., AUD, CUD, ODUD symptoms at age 35).