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Prescription Drug Misuse Sources of Controlled Medications in Adolescents RH = Adolescent Prescription Misuse Sources

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Abstract

Objective: Adolescent controlled prescription drug misuse (PDM) co-occurs with significant consequences, including lower educational achievement, substance use disorder (SUD) symptoms, and psychopathology. Nonetheless, adolescent PDM sources and the prevalence of other substance use, SUD and mental health outcomes associated with sources remain poorly understood.

Method: Data were from the 2009–2014 National Survey on Drug Use and Health, including 103,920 adolescents (12–17 years). Six mutually exclusive sources were used: physician source only, theft/fake prescription only, friend/relative for free only, purchases only, other source only, or multiple sources. Analyses occurred separately for prescription opioids, stimulants and tranquilizer/sedatives. PDM source prevalence across adolescents and by sex and school

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Conflicts of Interest/Disclosure

Drs. Schepis and McCabe note no conflicts of interest and have no financial/personal disclosures to report.

In the past two years, Dr. Timothy Wilens is or has been a consultant for Alcobra, Neurovance/Otsuka, and Ironshore. He also has a published book: *Straight Talk About Psychiatric Medications for Kids (Guilford Press);* and co-edited books *ADHD in Adults and Children (Cambridge University Press), Massachusetts General Hospital Comprehensive Clinical Psychiatry (Elsevier) and Massachusetts General Hospital Psychopharmacology and Neurotherapeutics (Elsevier).* Dr. Wilens is co-owner of a copyrighted diagnostic questionnaire (Before School Functioning Questionnaire) and has a licensing agreement with Ironshore for this questionnaire. Finally, he serves as a clinical consultant to the US National Football League (ERM Associates), U.S. Minor/Major League Baseball; Phoenix/Gavin House and Bay Cove Human Services.

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enrollment/engagement were estimated. Adjusted odds of past-year *DSM-IV* substance-specific SUD, marijuana use, any SUD, major depression (MDD), anxiety diagnosis and mental health treatment and past-month binge drinking were estimated by source.

Results: Friends/relatives for free was the most common source (29.0%−33.2%), followed by physician sources for opioids (23.9%) and purchases for stimulants (23.5%) and tranquilizer/sedatives (22.7%). Few school enrollment/engagement differences existed, but females were more likely to use multiple sources. Over 70% of adolescents using multiple sources had a past-year SUD. Multiple sources, purchases, and theft/fake prescription were more strongly associated with other substance use than physician source use, and multiple source use was linked with MDD.

Conclusion: Adolescents using multiple sources, purchases and theft/fake prescriptions have elevated rates of other substance use, SUD and MDD and particularly warrant intervention. Also, adolescents with other SUD and MDD should be screened for PDM and misuse sources.

Keywords

opioid; stimulant; tranquilizer; source; adolescent

INTRODUCTION

In 2016, over 1.3 million US adolescents (5.3%) engaged in prescription drug misuse (PDM) of a controlled medication.[1] PDM is medication use in ways not intended by the prescriber or use without a prescription. Data from 2013 indicate that US prescription opioid misuse resulted in $78.5 billion in costs,[2] a notable increase over previous estimates.[3, 4] The true societal costs of PDM are certainly higher, as these estimates do not include stimulant or tranquilizer/sedative medication misuse. Significant cross-sectional evidence links PDM and psychopathology in adults[5, 6] and adolescents,[7] with prospective evidence associating adult PDM with incidence and recurrence of major depression (MDD), generalized anxiety and panic disorder at a three-year follow-up.[8] Adolescent PDM also co-occurs with substance use disorder (SUD) development in adulthood,[9] poorer adult educational outcomes[10] and other poor psychosocial outcomes (e.g., aggressive behavior).[11]

The most commonly misused medication class was opioids (3.5%), with roughly half as many adolescents (1.7% each) engaged in prescription stimulant or tranquilizer (a term capturing primarily benzodiazepine medication) misuse.[1] Of adolescents engaged in past-year PDM, between 48.0% (opioids) and 57.1% (stimulants) initiated PDM in the past year, and adolescents appear to initiate PDM at rates only trailing those of alcohol use initiation.[1] Past-year PDM prevalence peaks in late adolescence,[12] and adolescents engaged in PDM already suffer significant consequences, including psychopathology and other substance use.[13] Longitudinal evidence links PDM initiation during adolescence with greater risk of PDM-related SUD symptoms and lower educational attainment in adulthood.[9, 10, 14] Given the consequences of adolescent PDM, limiting it is a worthy public health goal.

Previous research on PDM sources in adolescents suggests that specific sources correlate with engagement in other substance use and prevalence of MDD;[15] thus, identifying adolescent PDM sources can help with understanding that adolescent's clinical profile. In

terms of prevalence, a review by Hulme and colleagues[16] found that, across ages, obtaining medications for PDM was most commonly done from friends/family for free, with purchases and healthcare sources also frequently used. This review also called for more research on specific PDM sources and the associated characteristics of those using different sources. To our knowledge, only three studies have examined PDM sources in adolescents only, with the limited prevalence data on adolescent sources consistent with Hulme et al.[15–17]

The evidence also suggests important sex differences in adolescent PDM sources and that, as noted above, sources correlate with differential involvement in other substance use and mental health outcomes. Schepis and Krishnan-Sarin[15] used data on adolescent sources at the last PDM episode from the 2005 and 2006 National Survey on Drug Use and Health (NSDUH). In these analyses males were more likely to use physician sources or purchases, and females were more likely to use friends/family (for free) or theft. Other substance use and MDD prevalence varied by source, as adolescents using physician sources were less likely to use other substances than those using theft, purchases or friends/family for free, but physician source use was associated with elevated major depression odds.[15] McCabe and collaborators[18] used nationally representative data from the 2007 to 2010 Monitoring the Future studies to examine opioid sources in US high school seniors. This work indicated that whereas females were more likely to misuse their own leftover opioid medication or misuse both their medication and opioids from other sources, males were more likely to solely misuse opioids diverted from others.[18]

Gaps remain, however, in our knowledge. Evidence in young adults[19] and older adults[20] suggests that multiple sources for PDM are associated with higher rates of substance-specific (e.g., opioid SUD in those using multiple opioid sources) and any SUD, but this has not been evaluated in adolescents. Furthermore, evidence links adolescent school dropout with elevated PDM rates,[7, 21] and educational status/attainment is associated with unique patterns of PDM sources in young adults.[19] Evaluating whether school enrollment/engagement was associated with specific PDM sources could help direct school- and community-based interventions to limit PDM. Finally, much of the evidence on adolescent PDM sources[15, 17] uses data from the mid- 2000s, prior to the full development of the opioid epidemic. Updating these previous findings will also allow for better intervention efforts, and including analyses of sex differences can further improve these efforts, given evidence of sex differences in substance use generally[22] and PDM specifically[23]. We intended to fill these gaps with a series of analyses on adolescent PDM sources, using data from the 2009 to 2014 NSDUH surveys.

Aims and Hypotheses

Our aims were as follows. First, we estimated the adolescent-wide prevalence of mutually exclusive PDM sources (e.g., purchases only). Following this, we estimated PDM sources by sex and by school enrollment/engagement. Third, we evaluated differences in substance-specific DSM-IV SUD prevalence by PDM sources. Finally, using adolescents who obtained their medication for PDM from physician sources only as the reference, we evaluated likelihood of substance use outcomes and past-year mental health outcomes by PDM source. Analyses occurred separately by medication class (i.e., opioids, stimulants, tranquilizer/

sedatives), with tranquilizer/sedative medication pooled due to low sedative PDM prevalence[1] and in line with previous work.[24, 25]

First, we hypothesized that source use across adolescents would be consistent with past work,[15, 16] with friends/family for free most commonly used. Second, we expected males to make greater use of physician sources and females to utilize friends/family for free more often,[15] and, third, we expected those not in school and at-risk for dropout to be more likely to use multiple sources, purchases and theft, as these are associated with greater other substance use.[19] Fourth, we expected that multiple source use would be most clearly associated with other substance use, substance-specific SUD, any SUD, and mental health outcomes and that physician source use only would be associated with lower prevalence levels of other substance use but not mental health outcomes, per past work.[15, 19, 20]

METHOD

The NSDUH is an annual US survey of substance use, mental health and associated behaviors across the population aged 12 and older. Sampling uses an independent, multistage area probability design including all states and Washington, DC; this design allows for creation of population-based weights to inform nationally representative estimates. To maximize honest reporting and participant confidentiality, the NSUDH assesses all sensitive variables (e.g., PDM sources) using audio computer-assisted self-interviewing (ACASI). The 2009–14 NSDUH included skip-outs and consistency checks to encourage full responding and data consistency. Weighted screening response rates varied from 88.4% (2009/2010) to 81.9% (2014), and full interview response rates varied from 75.6% (2009) to 71.2% (2014). More information on the NSDUH, including psychometrics, is available elsewhere.[26, 27]

Participants

Participants were those 12 to 17 years of age, inclusive, in the 2009–14 NSDUH public use files; 103,920 (unweighted) adolescents provided data. Within adolescents, 48.9% of the weighted sample was female, and the three most common weighted racial or ethnic groups were white/Caucasian (56.0%), African-American (14.3%) and Hispanic/Latino (21.4%). For age, 15.5% were 12 years of age, 16.4% were 13, 16.8% were 14, 17.1% were 15, 17.2% were 16, and 17.1% were 17. Of adolescents, 1,987 provided data on opioid misuse sources, 370 provided data on stimulant misuse sources and 540 provided data on tranquilizer/sedative misuse sources. These adolescents are the sample of focus in this study.

Measures

To aid recall, the NSDUH used trade and generic drug names and pictures of all commonly misused medications. Examples include: codeine, hydrocodone, oxycodone and methadone for opioids; methylphenidate and amphetamine formulations for stimulants; alprazolam, lorazepam, clonazepam and zolpidem for tranquilizer/sedatives. For a more detailed list of medications included, please see the NSDUH codebook.[27] In those endorsing past-month PDM, medication source is assessed: "...during the past 30 days, you used prescription [medication class] that were not prescribed for you or that you took only for the experience

or feeling they caused. How did you get these prescription [medication class]? Please enter all of the ways that you got the prescription [medication class] you used in the past 30 days." Ten choices are offered, with sources aggregated into six mutually exclusive categories: (1) physician only ("got from one doctor" or "got from more than one doctor"), (2) stole/fake prescription only ("took from friend or relative without asking," "wrote fake prescription," or "stole from doctor's office, clinic, hospital, or pharmacy"), (3) free from friend or relative only ("got from friend or relative for free"), (4) purchased only ("bought from friend or relative," "bought from drug dealer or other stranger," or "bought on the internet"), (5) other only ("got some other way"), and (6) multiple sources (use of two or more sources).

Included sociodemographic variables were: *sex, race/ethnicity, age, household income, parental involvement,* and *school enrollment/engagement*. Parental involvement captured the frequency with which respondents' parents checked homework, helped with homework and restricted time out on weeknights; for those not in school, homework checking and help were coded as "never". School enrollment/engagement was classified as: (1) in school, low risk for dropout; (2) in school, at-risk for dropout; (3) not in school. *Risk for school dropout* was based 28 on previous research on school dropout risk factors[28] and was positive with at least one of: (a) D or worse grades in the last grading period; (b) history of being retained in grade; and/or (c) stating that the respondent "hated going to school".

Other substance use correlates were: *past-year substance-specific SUD* (e.g., opioid SUD in those using multiple opioid sources), *past-month binge drinking, past-year marijuana use,* and *past-year any SUD* (SUD from one of 11 substances: alcohol, cannabis, cocaine, heroin, hallucinogens, inhalants, methamphetamine, or prescription opioids, tranquilizers, sedatives or stimulants). Mental health correlates were: *past-year MDD, past-year anxiety diagnosis,* and *past-year mental health treatment*. Past-month binge drinking was defined as one past-month occasion of consuming 5/4 (men/women) or more alcoholic drinks. MDD, substance-specific SUD and any SUD were all from DSM-IV criteria,[29] with good psychometrics.[26, 30] Past-year anxiety diagnosis was a single self-report item assessing whether the respondent was told by a "doctor or other mental health professional that you had". Data were imputed by the NSDUH for the substance use correlates and past-year MDD.

Analyses

Analyses utilized STATA 15.1 (College Station, TX). Data were weighted, clustered on primary sampling units, and stratified; due to the aggregation of multiple NSDUH datasets, adjusted person-level weights (weight/6) created unbiased population-based estimates. The Taylor series approximation was used, with adjusted degrees of freedom, to create robust variance estimates. Initial analyses employed weighted cross-tabulations to estimate prevalence and 95% confidence intervals (95% CI) of PDM sources across the adolescent sample, by sex and by school enrollment/engagement. Design-based logistic models evaluated post hoc sex- based and school enrollment/engagement-based differences in PDM sources; models adjusted for age, income, parental involvement and race/ethnicity (for sex-based differences) or age, sex, income, parental involvement and race/ethnicity (for school enrollment/engagement-based differences) and *p*-values were Bonferroni-corrected to 0.0167 or lower for school enrollment/engagement-based differences due to three

comparisons. These analyses were repeated using the ten non-mutually exclusive source groups, with similar methodology.

Further analyses used weighted cross-tabulations and design-based logistic regression to examine the relationships between PDM source and prevalence of substance-specific SUD and the other substance use and mental health outcomes outlined above, with analyses adjusted for age, sex, income, parental involvement and race/ethnicity. Also, analyses of other substance use and mental health correlates set the physician only group as the reference, given evidence of lower prevalence than in other source groups.[15] Participants with missing PDM source data were subject to listwise deletion for the analyses involving that missing source data.

RESULTS

PDM Source Prevalence across Adolescents and by Sex

Among all adolescents, 2.2% (95% CI = 2.−2.4) engaged in past-month opioid misuse. For past-month stimulant and tranquilizer/sedative misuse, the proportions were lower, at 0.5% (95% CI = 0.4–0.5%) and 0.6% (95% CI = 0.6–0.7%), respectively. Of those with past-month PDM, 19.5% of adolescents with opioid PDM, 24.4% with stimulant PDM and 19.2% with tranquilizer/sedative PDM were missing data on source of the medication. Analyses found no difference in sex, school enrollment/engagement or household income level by missing data status. In contrast, younger age and non-white race/ethnicity were associated with missing data.

Across medication classes, the most common PDM source was free from friend/family only, varying between 29.0% for stimulants and 33.2% for tranquilizer/sedatives (Table 1). For stimulants and tranquilizer/sedatives, purchases only were the second most common source (23.5% and 22.7%, respectively), while use of physician sources only was second most common for opioid PDM (23.9%). Physician sources were also common for stimulant (18.6%) and tranquilizer/sedative (14.6%) sources, and the physician source group was driven by use of one physician (see Table S1, available online). While prevalence of theft/fake prescription only and other sources only were almost always below 10%, use of multiple sources varied between 20.9% (opioids) and 12.6% (tranquilizer/sedatives). Adolescents only rarely used the internet as a PDM source, with prevalence below 1% across medication classes (see Table S1, available online).

Sex-based differences were common for opioid and stimulant PDM sources (Table 1). Males were more likely to report use of physician sources only for opioids and other sources for stimulants, while females were more likely to report use of friends/family for free only for both opioid and stimulant medication. Females were more also likely than males to take opioids or stimulants from friends/family without asking (see Table S1, available online). Finally, across medication classes, females were more likely to endorse multiple PDM source use.

PDM Source Prevalence by School Enrollment/Engagement

Fewer significant differences were found by school enrollment/engagement (Table 2 and Table S2, available online). Regardless of dropout risk, adolescents in school were more likely to use theft/fake prescription only as an opioid source (both 8.2%) than those not in school (1.8%). Also for opioids, those not in school (23.0%) and those at-risk for dropout (13.3%) were more likely to use purchases only than those at low risk for dropout (6.1%). Finally, those at low risk for dropout (33.9%) were more likely to only obtain stimulants from friends/family for free than were those at-risk for dropout (13.8%).

Other Substance Use Correlates of Adolescent PDM Sources

For opioid sources, use of theft/fake prescription only, purchases only and multiple sources were each associated with an elevated adjusted odds ratio (AOR) of the examined other substance use outcomes (i.e., past-month binge drinking, past-year marijuana use, and any past- year SUD) versus use of physician sources only (Table 3; past-year alcohol, marijuana and substance-specific use disorder prevalence rates by source are captured in Table S3, available online). The prevalence rates varied between 45.8–55.6% for binge drinking, 67.4–79.3% for marijuana use, 24.2–30.7% for MDD and 60.1–69.5% for any SUD. The highest AORs were for purchases only for binge drinking (AOR = 3.06, 95% confidence interval [CI] = 1.71–5.46) and marijuana use (AOR = 7.01, 95% CI = 3.55–13.83), and multiple sources for any SUD (AOR = 5.12, 95% CI = 3.29–7.96). Obtaining opioids from friends/family for free only was associated with elevated AORs of binge drinking (34.5%) and marijuana use (55.4%), as compared to physician sources only; nonetheless, AORs were lower than for purchases only, theft/fake prescription only or multiple sources.

The AOR patterns were less consistent for stimulant and tranquilizer/sedative sources. Purchases only and other source use only were associated with elevated AORs of both past-month binge drinking (prevalence range = 62.9–74.2%) and past-year marijuana use (prevalence range = 81.7–89.3%). Theft/fake prescription use was also associated with elevated binge drinking prevalence (54.9%). AORs of any SUD did not differ by stimulant or tranquilizer/sedative PDM source, with the exception of theft/fake prescription use for stimulants. The *lowest* prevalence rates of past-year SUD were 53.0% for stimulants (friends/family for free only) and 61.7% for tranquilizer/sedatives (physician only). Strikingly, over 75% of those using purchases only, theft/fake prescription only or multiple sources of stimulants or tranquilizer/sedatives had a past-year SUD.

Mental Health Correlates of Adolescent PDM Sources

All non-physician only sources of tranquilizer/sedatives were associated with elevated MDD prevalence rates and AORs (prevalence range: 25.5–45.8%; AORs range: 3.46–6.86), with the exception of other source use only (Table 4). Otherwise, the pattern of significant mental health correlates of adolescent PDM sources was inconsistent. Multiple opioid source use was associated with elevated MDD prevalence (30.7%, AOR = 1.91), and theft/fake prescription use to obtain stimulants was linked with elevated MDD prevalence (34.9%, AOR = 4.23). Theft/fake prescriptions and use of friends/family to obtain stimulants and other source use for tranquilizer/sedative medication were each associated with lower adjusted odds of past-year anxiety diagnosis (AORs ≤ 0.15). Finally, past-year mental health

treatment was more prevalent in those using theft/fake prescriptions to obtain opioids (52.6%, AOR = 1.78), though mental health treatment was less likely in those obtaining stimulants from other sources (25.1%, AOR = 0.20).

Adolescent PDM Sources and Substance-Specific SUD Prevalence

Across medication classes, adolescents reporting multiple sources were more likely to have a DSM-IV substance-specific SUD diagnosis (e.g., opioid SUD in those using a specific opioid source) than those using single sources only (Table 5). Among adolescents with multiple PDM sources, substance-specific SUD prevalence ranged from 43.6% for opioids to 34.7% for tranquilizer/sedatives. In contrast, between 22.9% (stimulants) and 13.7% (opioids) of adolescents not using multiple sources had substance-specific SUD.

Those who obtained either opioids or tranquilizer/sedatives only from friends/family for free had a significantly lower prevalence of substance-specific SUD (11.1% and 13.3%, respectively) than those who did not use friends/family for free to obtain opioids or tranquilizer/sedatives (23.7% and 23.8%, respectively). Otherwise, lower substance-specific SUD prevalence was found for stimulant purchases only (13.5% versus 29.6%) and other opioid sources only (8.9% versus 21.1%).

DISCUSSION

Data from the 2016 NSDUH indicate that over 1.3 million adolescents engaged in past-year PDM, with nearly 900,000 engaged in past-year opioid PDM.[1] Further clarifying PDM processes, this research indicates that adolescent use of multiple sources for opioid, stimulant and tranquilizer/sedative medication was associated with the highest rates of substance-specific DSM-IV SUD diagnoses. Use only of friends/family for free was the most common adolescent PDM source, with physician sources only the second most common for opioids and use of purchases only the second most common for stimulant or tranquilizer/sedative medication. Very high rates of substance use, SUD, and MDD were observed with PDM, with some specificity related to source. Female adolescents were more likely to use multiple sources across medication classes and were more likely to only use friend/family sources (for free) for opioids and stimulants; males were more likely to use physician sources only or other sources for opioid or stimulant medication, respectively. Finally, remarkably few differences were found by school enrollment/engagement.

This study found rates of roughly 35% or higher of substance-specific SUD (i.e., opioid SUD in those using multiple opioid sources) in those using multiple sources. This work also found high rates of any SUD in those using multiple sources (≥ 69.5%), purchases only (≥ 62.8%) or theft/fake prescriptions only (≥ 60.1%). The association of multiple sources with substance-specific SUD across medications and, for opioids, other the substance use outcomes is consistent with work in young adults[19] and older adults.[20] Together, these three studies signal strongly that those using multiple sources are a high-risk group in need of intervention, including specialty SUD treatment. Medication therapies for SUD have preliminary evidence of effectiveness in adolescents,[31] including methadone for opioid use disorder.[32] Psychosocial treatments that are adapted for adolescent SUD, including

cognitive-behavioral therapy (CBT), motivational-based interventions, contingency management (CM) and family-based group treatments, all have evidence of efficacy.[33]

As in previous work,[15] adolescents who purchase medication or use theft/fake prescriptions are more likely to also engage in other substance use than those using physician sources. In particular, the very high odds ratios for past-year marijuana use in adolescents who purchased opioid or stimulant medication were notable. This association may signal elevated deviance and risk-taking, given that purchases of both the medications and marijuana necessitated use of illicit markets to obtain the substances. Work in young adults[19] also found that use of purchases was associated with greater other substance use, but those findings for theft/fake prescriptions were more equivocal. Developmental changes in medication management, with young adults assuming increased responsibility, could influence these age-based differences. Ultimately, these findings reinforce the importance of assessing adolescent and young adult PDM separately, with clinicians attending to different outcomes by age group.

The elevated MDD rates found in adolescents using theft/fake prescriptions, purchases and multiple sources for tranquilizer/sedative medication are also notable and suggest that assessing depressive symptoms in those with such PDM is warranted. In contrast to this work, Schepis and Krishnan-Sarin[15] found that adolescents using physician sources were most likely to report past-year MDD. Ultimately, this discrepancy is likely to result from methodological differences; while the previous work only assessed last source used, this work included all past-month sources. The link between specific PDM sources and MDD in this study is consistent with the clustering of PDM, across medication classes, and MDD in adolescents [7, 34–37] and highlights the need for comprehensive mental health evaluations of and intervention in at-risk youth. Links between past-year anxiety diagnosis or mental health treatment and PDM were much more inconsistent, suggesting a general lack of an association. Nonetheless, past-year mental health treatment rates were high in those engaged in PDM, indicating that PDM may generally signal increased psychiatric symptom levels.

While the adolescent-wide pattern of PDM sources was expected, the finding of minimal differences by school enrollment/engagement status was unexpected. McCabe et al.[19] found a greater number of educational-based differences in young adult sources, though neither that nor this study uncovered a strong and consistent pattern. Evidence suggests elevated PDM prevalence in adolescents not in school,[7, 21] but it may be that while PDM engagement differs, the pattern of sources used by adolescents in different school enrollment/engagement situations is more invariant. Finally, the finding that males are more likely to use physician sources and that females are more likely to use multiple sources is consistent with work in both adolescents[15] and young adults.[18] Unlike with many substances of abuse,[38] females may be as likely to engage in PDM as males.[5, 36] The more frequent use of multiple sources in females is concerning, and it may signal a greater vulnerability to PDM-related consequences. On the other hand, greater use of multiple sources in females may signal inadequate treatment of conditions, with increased medication seeking as a coping tool. Regardless, screening for multiple source use in females with PDM, and underlying motivations, is recommended.

First, because the data are cross-sectional, no inferences about causality can be made. Further research that examines how PDM sources and development of MDD, substance-specific SUD, other SUD, and other substance use interact dynamically would have significant value in identifying causal pathways and treatment targets. Second, the self-report nature of the data means that self-report bias was possible. With that said, self-report substance use data appear reliable and valid, though some underreporting of use and participant misclassification (e.g., into PDM source category) is likely;[39, 40] self-report bias should be limited by the use of ACASI methods, medication pictures, and numerous trade and generic medication names in the NSUDH. [41] Third, self-selection bias was likely, as some individuals refused to participate in either the screening or interview phases.

Between 19 and 25 percent of adolescents engaged in past-month PDM had missing data on sources and were excluded from analyses for that medication class. Those with missing data were younger and more likely to be non-white, and these results should be interpreted in light of that missing data and the corresponding sociodemographic profiles. Cell sizes for analyses of stimulant PDM sources (especially other and theft/ fake prescription sources) were somewhat limited by small cell sizes, and the analyses involving those not in school were also limited by small samples. The psychopathology variables and variables related to school dropout were limited by the available measures in the NSDUH, and the single-item past-year anxiety diagnosis measure was likely to misclassify a greater proportion of participants than a diagnostic interview. Finally, owing to the nature of the PDM assessment in the 2009–2014 NSUDH surveys, it is not possible to disentangle PDM due to use of another's medication (i.e., nonmedical use) from misuse of one's own medication (i.e., medical misuse). Future studies that evaluated links between PDM type and PDM sources are needed.

The findings from our analyses on PDM in adolescents have important clinical ramifications. Adolescents with PDM have elevated rates of SUD, and those with tranquilizer/sedative PDM who use non-physician sources have elevated rates of MDD. Our data show also that the source(s) of misused prescriptions medications is important in judging likelihood of SUD and other substance use. For instance, adolescents using multiple sources to obtain controlled medications for PDM have higher rates of substance-specific SUD - necessitating more robust clinical interventions to mitigate more severe consequences (e.g., school dropout, health consequences, overdose). Over seven in ten adolescents using multiple sources had a past-year SUD, further highlighting the urgent need for effective interventions in this group. In addition to those using multiple sources, adolescents who purchase or commit theft or use fake prescriptions to obtain controlled medications are also more likely to have deleterious outcomes in multiple domains.

Our data signals that adolescents prescribed controlled substances should be counseled about the medical, legal, and ethical risks of PDM, and parents or guardians should be enlisted to help monitor appropriate medication storage, use and disposal. All adolescents who report PDM or who have signs of PDM (e.g., early refill requests) should be carefully assessed for problematic substance use, SUD symptoms and MDD specifically and psychopathology more generally. Similarly, adolescents with MDD or other substance use disorders should be screened for PDM and, if present, for the PDM source.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Prescription Drug Misuse (PDM) Sources Across Adolescents (12–17 years) and by Sex

PDM Sources[a]	**All Adolescents**	**Males**	**Females**	**Sex Difference p- value**[b]
	% (95% CI)	**% (95% CI)**	**% (95% CI)**	
Prescription Opioids (n = 1,987)		(n = 823)	(n = 1164)	
Physician only (n = 447)	23.9 (21.7–26.3)	28.3 (24.1–32.9)	20.6 (18.2–23.3)	**0.0001**
Theft/fake prescription only (n = 147)	7.9 (6.5–9.7)	7.6 (5.3–10.9)	8.2 (6.5–10.3)	0.75
Free from friend/relative only (n = 582)	29.8 (27.0–32.8)	26.4 (22.7–30.5)	32.3 (28.3–36.6)	0.038
Purchased only (n = 152)	8.2 (6.7–10.0)	10.1 (7.7–13.1)	6.7 (5.0–9.1)	0.12
Other source only (n = 218)	9.3 (7.8–11.1)	10.9 (8.6–13.7)	8.1 (6.4–10.3)	0.12
Multiple sources (n = 441)	20.9 (18.4–23.6)	16.7 (13.3–20.8)	24.0 (21.0–27.3)	**0.0003**
Prescription Stimulants (n = 370)		(n = 169)	(n = 201)	
Physician only (n = 69)	18.6 (13.5–25.0)	24.9 (16.3–36.1)	13.4 (8.4–20.8)	0.06
Theft/fake prescription only (n = 29)	6.7 (4.3–10.2)	7.6 (3.9–14.2)	5.9 (3.4–10.1)	0.75
Free from friend/relative only (n = 109)	29.0 (22.8–36.0)	20.9 (14.2–29.7)	35.6 (26.7–45.6)	0.035
Purchased only (n = 76)	23.5 (18.9–28.9)	27.0 (18.7–37.4)	20.7 (14.3–29.0)	0.38
Other source only (n = 17)	4.2 (2.4–7.3)	7.3 (3.8–13.5)	1.6 (0.6–4.1)	**0.007**
Multiple sources (n = 70)	18.1 (13.6–23.6)	12.3 (7.6–19.2)	22.8 (16.4–30.7)	**0.046**
Prescription Sedatives/Tranquilizers (N = 540)		(n = 223)	(n = 317)	
Physician only (n = 76)	14.6 (10.6–19.7)	15.7 (9.9–24.0)	13.8 (8.1–22.4)	0.83
Theft/fake prescription only (n = 54)	10.2 (7.3–14.0)	9.0 (5.0–15.9)	11.0 (7.3–16.4)	0.75
Free from friend/relative only (n = 187)	33.2 (28.2–38.7)	30.8 (22.3–40.9)	35.0 (28.5–42.0)	0.39
Purchased only (n = 119)	22.7 (18.4–27.7)	27.7 (21.5–35.0)	19.0 (13.6–25.9)	0.075
Other source only (n = 35)	6.7 (4.1–10.6)	9.6 (5.4–16.3)	4.5 (2.3–8.7)	0.057
Multiple sources (n = 69)	12.6 (9.2–17.1)	7.2 (3.8–13.3)	16.9 (11.8–23.0)	**0.034**

Note: Source: National Survey on Drug Use and Health, 2009–2014 cohorts. PDM = Prescription drug misuse.

[a] PDM sources are mutually exclusive from one another.

[b] p-values were based on logistic models adjusted for age, race/ethnicity, household income and parental involvement.

* $p < .05$,
** $p < .01$.

Table 2:

Adolescent Prescription Drug Misuse (PDM) Sources by School Enrollment and Engagement

PDM Sources[a]	**In School, Low Drop-Out Risk (A)**	**In School, HighRisk for Drop-Out (B)**	**Not in School (C)**	**Pairwise Comparisons**[b]
	% (95% CI)	**% (95% CI)**	**% (95% CI)**	
Prescription Opioids (n = 1,987)	(n = 1436)	(n = 464)	(n = 87)	
Physician only (n = 447)	22.9 (20.1–25.9)	22.9 (17.9–28.9)	8.8 (3.4–21.2)	---[c]
Theft/fake prescription only (n = 147)	8.2 (6.2–10.7)	8.2 (5.6–12.1)	1.8 (0.5–6.1)	A, B > C
Free from friend/relative only (n = 582)	31.2 (28.1–34.6)	28.4 (23.0–34.6)	28.6 (17.6–42.9)	---
Purchased only (n = 152)	6.1 (4.6–8.1)	13.3 (9.3–18.5)	23.0 (11.3–41.1)	B, C > A
Other source only (n = 218)	9.7 (8.0–11.8)	7.5 (5.0–11.2)	11.4 (4.6–25.8)	---
Multiple sources (n = 441)	21.9 (19.1–25.0)	19.6 (15.3–24.8)	26.3 (16.3–39.7)	---
Prescription Stimulants (n = 370)	(n = 254)	(n = 96)	(n = 20)	
Physician only (n = 69)	17.1 (11.3–25.0)	21.2 (12.5–33.6)	6.5 (1.4–24.9)	---
Theft/fake prescription only (n = 29)	6.2 (3.5–10.6)	9.4 (3.1–25.1)	no cases	---
Free from friend/relative only (n = 109)	33.9 (25.7–43.2)	13.8 (7.3–24.7)	49.0 (21.7–77.0)	A > B
Purchased only (n = 76)	24.3 (18.3–31.4)	25.5 (16.8–36.8)	22.3 (6.9–52.8)	---
Other source only (n = 17)	3.4 (1.7–6.4)	6.9 (2.4–18.0)	no cases	---
Multiple sources (n = 70)	15.2 (10.3–21.9)	23.2 (13.8–36.3)	22.2 (7.2–51.3)	---
Prescription Sedatives/T ranquilizers (N = 540)	(n = 346)	(n = 163)	(n = 31)	
Physician only (n = 76)	14.4 (9.3–21.5)	14.3 (7.9–24.6)	no cases	---
Theft/fake prescription only (n = 54)	7.0 (4.1–11.5)	15.3 (9.1–24.6)	12.6 (4.1–32.6)	---
Free from friend/relative only (n = 187)	37.2 (29.2–45.8)	25.1 (16.5–36.3)	52.9 (32.5–72.4)	---
Purchased only (n = 119)	24.0 (18.4–30.7)	22.5 (15.2–32.0)	19.5 (7.9–40.7)	---
Other source only (n = 35)	5.5 (2.8–10.3)	7.3 (3.0–16.8)	10.5 (2.5–34.8)	---
Multiple sources (n = 69)	12.0 (7.8–18.2)	15.5 (9.7–23.8)	4.5 (1.0–18.5)	---

Note: Source: NSDUH, 2009–2014 cohorts. PDM = Prescription drug misuse.

[a] PDM sources are mutually exclusive from one another.

[b] Pairwise comparisons were Bonferroni-corrected for multiple comparisons, with comparisons only noted when they differ at a p-level of 0.05 or less (ie, A, B > C indicates that adolescents in school, at low drop-out risk [A] and adolescents in school, at high-risk for drop-out [B] had significantly higher prevalence rates than those not in school [C]). The post hoc comparisons were based on logistic models adjusted for age, race/ethnicity, sex, household income and parental involvement.

[c] --- indicates no significant post hoc differences between groups.

* $p < .05$

** $p < .01$.

Table 3:

Prevalence of Other Substance Use Outcomes by Adolescent Prescription Drug Misuse (PDM) Source

	30-day Binge Alcohol Use		Past-Year Marijuana Use		Past-Year Any SUD[a]	
	%	AOR (95% CI)[b]	%	AOR (95% CI)[b]	%	AOR (95% CI)[b]
Prescription Opioids[c] (n = 1,987)						
Physician only (n = 447)	20.7	---Reference—	28.7	---Reference—	26.7	---Reference—
Theft/fake prescription only (n = 147)	45.8	2.40 (1.24–4.66) **	68.7	4.70 (2.58–8.59) **	60.1	3.10 (1.67–5.74) **
Free from friend/relative only (n = 582)	34.5	1.47 (0.95–2.27)	55.4	2.56 (1.62–4.04) **	37.2	1.31 (0.82–2.06)
Purchased only (n = 152)	55.6	3.06 (1.71–5.46) **	79.3	7.01 (3.55–13.83) **	62.8	3.35 (1.84–6.08) **
Other source only (n = 218)	28.6	1.35 (0.82–2.22)	46.7	2.29 (1.37–3.83) **	35.8	1.34 (0.78–2.30)
Multiple sources (n = 441)	52.0	2.92 (1.92–4.45) **	67.4	4.17 (2.72–6.40) **	69.5	5.12 (3.29–7.96) **
Prescription Stimulants[3] (n = 370)						
Physician only (n = 69)	30.7	---Reference—	59.6	---Reference—	62.1	---Reference—
Theft/fake prescription only (n = 29)	54.9	3.75 (1.07–13.12) *	66.1	2.14 (0.49–9.30)	85.2	5.66 (1.26–25.41) *
Free from friend/relative only (n =109)	47.8	1.77 (0.76–4.10)	71.2	1.63 (0.55–4.80)	53.0	0.85 (0.32–2.24)
Purchased only (n = 76)	62.9	3.05 (1.11–8.36) *	89.3	4.89 (1.32–18.15) *	75.1	2.40 (0.77–7.53)
Other source only (n = 17)	74.2	9.34 (2.01–43.42) **	81.7	6.99 (1.07–45.81) *	75.0	2.53 (0.52–12.38)
Multiple sources (n = 70)	50.2	1.71 (0.67–4.34)	77.7	2.71 (0.64–11.40)	74.6	2.35 (0.88–6.27)
Prescription Sedatives/ Tranquilizers[c] (n = 540)						
Physician Only (n = 76)	38.8	---Reference—	58.7	---Reference—	61.7	---Reference—
Theft/fake prescription only (n = 54)	52.0	1.08 (0.36–3.30)	84.1	3.53 (1.15–10.87) *	76.0	1.19 (0.43–3.33)
Free from friend/relative only (n =187)	52.9	0.91 (0.36–2.31)	82.0	1.89 (0.74–4.81)	62.0	0.52 (0.18–1.48)
Purchased only (n = 119)	70.2	1.85 (0.71–4.85)	86.2	2.39 (0.77–7.44)	78.2	1.24 (0.44–3.51)
Other source only (n = 35)	55.1	1.62 (0.35–7.49)	70.3	1.97 (0.32–11.99)	66.6	1.21 (0.31–4.65)
Multiple sources (n = 69)	61.5	1.87 (0.64–5.44)	74.5	1.45 (0.57–3.72)	82.9	2.07 (0.59–7.18)

Note: Source: National Survey on Drug Use and Health, 2009–2014 cohorts. AOR = Adjusted odds ratio; PDM = Prescription drug misuse; SUD = Substance Use Disorder.

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[a]Any SUD denotes SUD from one of 11 substances (ie, alcohol, cannabis, cocaine, heroin, hallucinogens, inhalants, methamphetamine, or prescription opioids, tranquilizers, sedatives or stimulants)

[b]AORs controlled for age, race/ethnicity, sex, household income and parental involvement.

[c]PDM sources are mutually exclusive from one another.

* $p < .05$

** $p < .01$.

Table 4:

Prevalence of Mental Health Outcomes by Adolescent Prescription Drug Misuse (PDM) Source

	Past-Year MDD		Past-Year Anxiety Diagnosis		Past-Year Mental Health Treatment	
	%	AOR (95% CI)[1]	%	AOR (95% CI)[1]	%	AOR (95% CI)[1]
Prescription Opioids (n = 1,987)						
Physician only (n = 447)	13.6	---Reference—	6.4	—Reference---	35.6	---Reference—
Theft/fake prescription only (n = 147)	27.9	1.77 (0.98–3.21)	14.3	1.96 (0.78–4.92)	52.6	1.78 (1.02–3.11) *
Free from friend/relative only (n = 582)	24.3	1.51 (0.93–2.45)	6.2	0.79 (0.37–1.69)	33.6	0.87 (0.57–1.35)
Purchased only (n = 152)	24.2	1.71 (0.89–3.26)	11.1	1.48 (0.58–3.79)	35.7	0.94 (0.50–1.75)
Other source only (n = 218)	16.8	1.21 (0.64–2.29)	7.8	1.21 (0.48–3.01)	35.2	0.93 (0.55–1.59)
Multiple sources (n = 441)	30.7	1.91 (1.21–3.01) **	14.7	1.85 (0.90–3.77)	48.2	1.54 (0.95–2.51)
Prescription Stimulants (n = 370)						
Physician only (n = 69)	17.2	---Reference—	30.9	—Reference---	59.3	---Reference—
Theft/fake prescription only (n = 29)	34.9	4.23 (1.42–12.58) **	5.9	0.11 (0.15–0.83) *	65.3	1.04 (0.31–3.48)
Free from friend/relative only (n = 109)	37.5	1.87 (0.68–5.12)	10.3	0.15 (0.07–0.35) *	49.5	0.43 (0.18–1.04)
Purchased only (n = 76)	30.7	2.15 (0.73–6.31)	20.7	0.40 0.14–1.15)	52.7	0.54 (0.23–1.25)
Other source only (n = 17)	17.6	2.10 (0.47–9.44)	17.4	0.59 (0.11–3.18)	25.1	0.20 (0.05–0.80) *
Multiple sources (n = 70)	34.5	1.67 (0.48–5.84)	35.3	0.83 (0.25–2.81)	68.4	0.95 (0.35–2.61)
Prescription Sedatives/Tranquilizers (n = 540)						
Physician only (n = 76)	10.5	---Reference—	24.9	—Reference---	41.9	---Reference—
Theft/fake prescription only (n = 54)	43.0	5.73 (1.83–17.91) **	12.3	0.29 (0.06–1.21)	56.2	1.76 (0.62–4.97)
Free from friend/relative only (n = 187)	32.0	3.27 (1.34–7.93) **	17.6	0.45 (0.14–1.44)	51.4	1.47 (0.63–3.40)
Purchased only (n = 119)	25.5	3.00 (1.03–8.76) *	19.1	0.56 (0.17–1.85)	39.9	0.99 (0.36–2.69)
Other source only (n = 35)	9.0	1.05 (0.20–5.47)	1.9	0.05 (0.01–0.38) **	26.9	0.63 (0.19–2.10)
Multiple sources (n = 69)	45.8	5.46 (1.90–15.69) **	28.0	0.93 (0.26–3.36)	62.1	2.58 (0.93–7.17)

Note: Source: National Survey on Drug Use and Health, 2009–2014 cohorts. AOR = Adjusted odds ratio; MDD = Major Depressive Disorder Episode; PDM = Prescription drug misuse,.

[1]AORs controlled for age, race/ethnicity, sex, household income and parental involvement.

[2]PDM sources are mutually exclusive from one another.

* $p < .05$

** $p < .01$.

Table 5:

Adolescent Prescription Drug Misuse (PDM) Sources and Medication Class-Specific SUD

	Medication Class- Specific[a] SUD in Those Not Using the Source	Medication Class- Specific[a] SUD Prevalence in Those Using the Source	Pairwise Comparison p-valuesb
	% (95% CI)	% (95% CI)	
Prescription Opioids[c] (n = 1,987)	19.9 (17.7–22.5) across sources		
Physician only (n = 447)	22.1 (19.4–25.2)	12.9 (9.5–17.4)	0.054
Theft/fake prescription only (n = 147)	19.3 (16.9–22.0)	27.0 (18.9–36.9)	0.44
Free from friend/relative only (n = 582)	23.7 (20.8–26.8)	11.1 (8.2–14.9)	< **0.0001**
Purchased only (n = 152)	20.1 (17.8–22.6)	18.1 (11.7–26.9)	0.41
Other source only (n = 218)	21.1 (18.5–23.9)	8.9 (5.4–14.5)	**0.001**
Multiple sources (n = 441)	13.7 (11.7–16.0)	43.6 (37.0–50.4)	< **0.0001**
Prescription Stimulants[c] (n = 370)	25.8 (20.7–31.7) across sources		
Physician only (n = 69)	24.5 (18.8–31.1)	31.5 (18.9–47.6)	0.50
Theft/fake prescription only (n = 29)	25.0 (19.4–31.6)	36.3 (22.2–53.2)	0.19
Free from friend/relative only (n = 109)	27.8 (22.2–34.2)	20.9 (11.3–35.3)	0.25
Purchased only (n = 76)	29.6 (23.4–36.6)	13.5 (8.3–21.2)	**0.015**
Other source only (n = 17)	25.6 (20.4–31.5)	31.0 (10.1–64.1)	0.57
Multiple sources (n = 70)	22.9 (17.3–29.7)	38.7 (26.3–52.7)	**0.049**
Prescription Sedatives/Tranquilizers[c] (N = 540)	20.3 (16.3–25.0) across sources		
Physician only (n = 76)	20.7 (16.3–25.9)	18.2 (10.7–29.2)	0.92
Theft/fake prescription only (n = 54)	20.5 (16.2–25.7)	18.3 (9.8–31.8)	0.26
Free from friend/relative only (n = 187)	23.8 (18.5–29.9)	13.3 (8.3–20.7)	**0.018**
Purchased only (n = 119)	19.4 (15.4–24.1)	23.5 (13.9–36.8)	0.36
Other source only (n =35)	20.0 (15.7–25.1)	24.6 (11.3–45.7)	0.45
Multiple sources (n = 69)	18.2 (14.0–23.3)	34.7 (21.8–50.3)	**0.019**

Note: Source: MDD = Major Depressive Disorder Episode, 2009–2014 cohorts. PDM = Prescription drug misuse, SUD = Substance use disorder.

[a] Medication Class-Specific SUD denotes presence of a DSM-IV substance use disorder from the medication class in question (ie, opioid SUD prevalence in those using multiple opioid sources).

[b] Pairwise comparisons were based on logistic models adjusted for age, race/ethnicity, sex, household income and parental involvement.

[c] PDM sources are mutually exclusive from one another.