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Persistence of extra-medical prescription pain reliever use and alcohol involvement among United States 12-20 year olds

Author Note

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Abstract

The peak risk of first extra-medical use of prescription pain relievers (PPR) is in mid-adolescence, often after underage drinking has begun. This research aims to investigate discrete classes of similar young people based on their newly incident extra-medical use of PPR and alcohol involvement, with empirical evaluation of the underlying structure of identified subgroups and their epidemiological distributions in the United States (US). The US National Surveys on Drug Use and Health, 2002-2013, sampled, recruited, and assessed 24,789 12-20-year-old newly incident extra-medical PPR users, with self-interviews on PPR, alcohol, and covariates. Latent classes of persistence were formed using PPR and alcohol status variables. Then, age and sex were studied as potentially important predictors of class membership. Analysis-weighted estimates and delta method variances were derived. Three classes were distinguished by extra-medical PPR and alcohol use patterns: (1) Non-persistent (79%), (2) Intermittent (15%), and (3) Persistent (6%). There were no differences across classes by age, but being female was associated with greater odds of being in the Intermittent class or Persistent class compared to the Non-persistent class. Presenting clinical features of alcohol and/or opioid use disorder that have become manifest at or near time of first PPR use can be indicators of persisting in extra-medical use of PPR, particularly for young people who have recently started extra-medical PPR use. Persistent adolescent and young adult extra-medical PPR users require tailored public health prevention and intervention strategies based on their vulnerability to continue use over time.

Public Significance: Based on their recent alcohol and opioid involvement, this study suggests that there are distinct subgroups of 12-20-year-olds who have just begun to use prescription pain relievers outside a prescriber's intent. Screening for alcohol and prescription pain relievers

before prescribing opioids in the primary care setting may be an integral step in beginning to address a persistent opioid problem or preventing one from beginning.

Keywords: opioids; adolescents; alcohol; dependence; persistence

Persistence of extra-medical prescription pain reliever use and alcohol involvement among United States 12-20 year olds

Extra-medical use of prescription pain relievers (PPR, mainly opioids) remains a serious public health concern in the United States (US; Compton, Boyle, & Wargo, 2015). Here, the term 'extra-medical' is used to encompass misuse or use that is beyond the boundaries of what a prescriber has intended (e.g., using 'to get high,' in an amount more than was prescribed, etc.; Parker & Anthony, 2015). While estimates claim the use of extra-medical PPR has been stable in recent years, dependence and overdose increases indicate a persistent problem (Rudd, Aleshire, Zibbell, & Gladden, 2016; United States, 2015). Research suggests extra-medical PPR use is declining and heroin is on the rise (Carlson, Nahhas, Martins, & Daniulaityte, 2016; Cerdá, Santaella, Marshall, Kim, & Martins, 2015; Cicero, Ellis, & Harney, 2015). Studies show that extra-medical PPR use is a strong risk factor for using heroin and more severe consequences such as overdose (e.g., Compton, Jones, & Baldwin, 2016).

Not only has the use of extra-medical PPR associated morbidity and mortality persisted, but also underage drinking continues to be a threat for adolescents and young adults alike (i.e., drinking before age 21; Han, B., Compton, W.M., Jones, C.M., & Cai, R., 2015; Reboussin, Preisser, Song, & Wolfson, 2010; United States, 2007). Studies have consistently shown that use of extra-medical PPRs is highly associated with alcohol drinking in adolescents and young adults (Huang et al., 2006; Mccabe, Cranford, & Boyd, 2006). In 2017, the Director of the National Institute on Drug Abuse (NIDA) announced a shift in priorities toward research focused on concurrent use of PPR and alcohol, given the enduring character of the US opioid epidemic and the resurgence of a heroin epidemic (Volkow, 2017).

To address the opioid epidemic, this study aims to identify subgroups of individuals with

newly incident extra-medical use by focusing on the array of extra-medical PPR use and the complex relationship between alcohol and extra-medical PPR involvement. Drug involvement can be conceptualized across a spectrum of experiences that range from first trying the drug to persisting to more serious addictive states or overdose (Parker, Lopez-Quintero, & Anthony, 2018). Although there are harmful consequences associated with the co-occurrence of alcohol use and use of extra-medical PPR (Centers for Disease Control and Prevention, 2014), in young people there has been little research on the relationship between the two (McCabe, Cranford, Morales, & Young, 2006).

It is important to address the idea that alcohol involvement leads to extra-medical PPR use and more serious involvement among adolescents and young adults (Parker & Anthony, 2018). It could be that facets of alcohol and extra-medical PPR use are influenced by the same sets of underlying genetic influences that predispose one to alcohol dependence or extra-medical PPR use/opioid dependence (Reyes-Gibby, Yuan, Wang, Yeung, & Shete, 2015). Work on recently active use of alcohol as a predictor and correlate among 12-17 year olds who have initiated extra-medical PPR use is implicative of a causal relationship (Schepis & Krishnan-Sarin, 2008; Sung, Richter, Vaughan, Johnson, & Thom, 2005).

This work illustrates the empirically based multivariate Latent Class Analysis (LCA) approach in the study of an important contemporary problem of drug dependence research – namely, initiation and persistence of extra-medical PPR use. The ‘steppingstone’ or gateway concept supports the idea that alcohol involvement and the interplay between its use and extra-medical PPR are precursors to extra-medical PPR related problems (Anthony, 2012; Kandel, Yamaguchi, & Chen, 1992). Alcohol use has been shown to precede some drug use (Yamaguchi & Kandel, 1984b, 1984a). With this in mind, alcohol use could lead to extra-medical PPR use,

and eventual opioid dependence. Another theory, 'opportunity to try,' postulates that drug initiation cannot occur without an exposure opportunity. For those who eventually go on to use a drug, most transition from the first opportunity to use within one year (Van Etten & Anthony, 1999). Here we study those individuals who have recently experienced an opportunity to try PPR.

As mid-adolescence is the estimated peak risk of first extra-medical PPR use (between 16-19 years of age), the focus was on 12-20 year olds (Meier, Troost, & Anthony, 2012; Parker & Anthony, 2015). This peak often occurs after beginning underage alcohol use (Fiellin, Tetrault, Becker, Fiellin, & Desai, 2013). Many newly incident extra-medical PPR users transition to opioid dependence in the first year after onset of such use. Among young people, approximately 5-6% manifest the syndrome of opioid dependence within the first year of use, which varies by age (Parker & Anthony, 2015).

For sex, contradictory findings have been common in the literature, some with a female excess, and vice versa (McCabe, Boyd, & Teter, 2005; McCabe, Boyd, & Young, 2007). Investigation of sex differences have disclosed that females are more likely than males to start using extra-medical PPR (Seedall & Anthony, 2013; Sung et al., 2005; United States, 2014). However, males have been found to use more frequent lifetime use (Havens, J.R., Young, A.M., & Havens, C.E., 2011; Palamar, Shearston, Dawson, Mateu-Gelabert, & Ompad, 2015; Vaughn, Nelson, Salas-Wright, Qian, & Schootman, 2016).

The purpose of this research was to estimate distinct subgroups of persistence among young people based on their extra-medical PPR and alcohol involvement. To determine individual characteristics that were associated with these latent classes and examine patterns of drug use, covariates for age and sex were included in a regression model of the grouped data. If

dependence criteria and/or underage recency of drinking can classify groups of adolescents who persist in their extra-medical PPR use, public health intervention and prevention strategies can be catered for this vulnerable population.

Methods

Study Design

This was a nationally representative cross-sectional survey of non-institutionalized civilian community residents in the United States (US), with Institutional Review Board-approved protocols for National Surveys on Drug Use and Health (NSDUH), completed each year between 2002 and 2013 (United States, 2002). The Substance Abuse and Mental Health Data Archive (SAMHDA) makes NSDUH public use datasets available, consisting of a large sub-sample of each year's independently drawn nationally representative samples (n~55,000 yearly). Participation levels were approximately 70%-75% of eligible participants, once appropriate consent/assent processes are complete. This study was deemed exempt by the Michigan State University Institutional Review Board as data was not obtained through interaction or intervention or private identifiable information. Publications and online reports provide detailed descriptions of the NSDUH methods (e.g., https://www.samhsa.gov/data/all-reports: last accessed November 2018).

Sample

In aggregate, summed across years, the samples included 304,361 participants age 12-20 years old. From those, a total of 24,789 newly incident extra-medical PPR users were identified by their time since last extra-medical use. These individuals had started using extra-medical PPR within 24 months prior to the date of assessment. Other 12-20-year-olds began use more than two years before their interview (n=15,601); the majority never used extra-medical PPR

(n=263,971). This amounted to an overall weighted incidence estimate of 8.3% between 2002-2013.

Measures

Most participants completed the NSDUH assessment via an audio computer self-interview (ACASI) method after instructions from a field staff member. Each assessment includes multiple standardized multi-item modules used to assess topics of drug use and health, including the number of days of extra-medical PPR use in the 12 months prior to the assessment date, alcohol dependence, opioid dependence, and alcohol recency.

For the number of days of extra-medical PPR use, it was important to differentiate between individuals whose onset of use began in the past 12 months and those who began 13-24 months ago. Among newly incident extra-medical PPR users with onset during the 12 months prior to survey assessment, the first day of use was subtracted from total days of use in order to form the latent class of persistence (i.e., continuing to use or 'days of use' minus 1). For newly incident extra-medical PPR users with onset during months 13-24 prior to assessment, the trial use had occurred before the most recent 12 months and for this reason, the response variable was the actual number of days of extra-medical PPR use during the 12 months prior to assessment (i.e., 'days of use').

Alcohol and opioid dependence were measured using a standardized NSDUH multi-item module based on the *Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition* (DSM-IV) clinical feature criteria of the American Psychiatric Association (American Psychiatric Association, 1994). Alcohol recency was classified as (i) Drank within the past month, (ii) Drank more than 30 days ago, but within the past year, (iii) Drank more than a year ago (iv) Never used alcohol.

The primary expectation for this application of LCA was that subgroup membership would depend upon concurrent extra-medical PPR and alcohol involvement. Measures of extra-medical PPR involvement included both opioid dependence (yes/no) and number of days used extra-medical PPR in the past year (range: 0-365). Measures of alcohol involvement included both alcohol dependence (yes/no) and recency of alcohol use in the past year.

Statistical Analysis

Since it was posited that alcohol and extra-medical PPR involvement may precipitate future persistence of extra-medical PPR use, LCA measurement models used four observed variables, 1) number of days of extra-medical PPR use in the 12 months prior to the assessment date, 2) alcohol dependence, 3) opioid dependence, and 4) alcohol recency to identify unobserved subgroups or " latent classes" of persistence. The analysis designated the number of days of extra-medical PPR use in the 12 months was as a zero-inflated count variable due to an abundance of observed zeroes. In the past year, 41.1% of the sample had used extra-medical PPR zero days after their first trial use.

Building the latent class model started with a parsimonious one-class model based on the two PPR and two alcohol status variables. ('all newly incident extra-medical PPR users the same'). Successive models were fit with increasing numbers of classes. The optimal number of classes was identified based on (a) Alkaike's Information Criterion (AIC)/Bayesian information criterion (BIC); (b) Entropy; (c) Subject matter; and (d) the Lo-Mendell-Rubin Likelihood Ratio Test (Collins & Lanza, 2013; Jung & Wickrama, 2008; Nylund, Asparouhov, & Muthén, 2007). In subsequent analysis steps, covariate terms for sex and age were included in a logistic regression model for empirical evaluation of the underlying structure of identified subgroups. A term for age-squared was also included in the model to evaluate whether the relationship of

persistence with age was non-linear as seen in prior work (Parker & Anthony, 2018). Later, stratified analysis was performed for the time elapsed from onset of extra-medical PPR use to interview to see if LCA estimates differed between groups (i.e., 0-12 months versus 13-24 months). In sensitivity analyses, to account for residual covariances, the three class model was amended by allowing local dependency between the four indicators assessed conditional independence. A final model removed the alcohol recency indicator as the residuals between this variable and alcohol dependence were the highest.

Analysis and estimation steps in the statistical analysis plan were based on Mplus version 7. The software addressed the complex NSDUH sample design, interdependence of survey observations, and analysis weights, including use of a 'subpopulation' command focused on the subset of 12-20-year-old newly incident extra-medical PPR users. Analysis-weighted estimates and delta method variances were derived. In these analyses, precision of the informative study estimates is stressed with 95% confidence intervals (CI).

Results

Sample Characteristics & Latent Classes

On average, the study sample of newly incident extra-medical PPR users was 16.7 years old, 48.8% was male, and most were non-Hispanic White (Table 1; n=24,789). About 64% had started to use extra-medical PPR in the past 12 months and 36% began 13-24 months ago. Three classes were identified by extra-medical PPR and alcohol use patterns: Non-persistent (Class 1), Intermittent (Class 2), and Persistent (Class 3). The majority, 79.2%, of newly incident extra-medical PPR users belonged to Class 1 (n = 19,603), 15.1% fit into Class 2 (n = 3,765), and the last 5.7% were designated to Class 3 (n = 1,421).

While the Lo-Mendell-Rubin Likelihood Ratio Test p-values were <0.001 when comparing models with up to seven classes, the entropy for this three-class model was 0.945 (Supplemental Table 1), suggesting good model fit (Jung & Wickrama, 2008). The AIC/BIC was slightly lower by adding another class (and entropy slightly higher; 0.952). However, the fourth class simply divided all members of the smallest class from the three-class model (Class 3), creating two smaller similar classes. This indicated a fourth class may be an artifact, and, therefore, the three-class model was preferred. In sensitivity analyses, two items were found to have high residual correlation, alcohol dependence and alcohol recency, suggesting the three class model may be improved by allowing a local dependency between the items. However, classes did not noticeably change. In a model that removed alcohol recency as an indicator, the classes remained similar to the original analyses as alcohol recency did not vary substantially across subgroups.

Latent Class Membership

Item response probabilities for opioid dependence, alcohol dependence, alcohol recency, and number of days used extra-medical PPR show that those in Class 1 (Non-persistent) had a paucity of opioid dependence (1.5%) and 10.1% reported alcohol dependence (Table 2). The other two classes, Intermittent and Persistent (Classes 2 and 3), included the majority of 12-20-year-old newly incident users with opioid dependence (10.8% and 27.2%, respectively). However, 15.4% of those in Class 2 and 20.2% of newly incident users in Class 3 were alcohol dependent. Probabilities of alcohol recency were similar across classes (Figure 1). The mean number of extra-medical PPR use days in the past year varied between classes with the lowest estimate of five days for Class 1 and the highest for Class 3 (169 days). Within Class 3, the average PPR use days were similar for those dependent on alcohol compared to those not

dependent on alcohol (169 vs. 171; p-value>0.05). However, for opioid dependence, the average extra-medical PPR use days was 192 for those dependent on opioids and 161 for those not dependent on opioids (p-value<0.001). Inflating the number of extra-medical PPR use days was only necessary for Latent class 1 because the majority of users with zero number of days used extra-medical PPR in the past year were classified as Non-persistent.

Latent Class Comparisons

Adjusted odds ratios (OR) depict Class 1 as having significantly less opioid and alcohol dependence than the other two classes (p-values < 0.05; see Supplemental Table 2). In addition, there were significantly less individuals in Class 2 with opioid and alcohol dependence than Class 3 (ORs<1 for both opioid and alcohol dependence). Interestingly, compared to Class 2, Class 1 had more current drinkers (Drank within the past month; OR=1.16; 95% CI=1.05, 1.27). There was no statistically significant difference between Class 1 and Class 3 for recency of alcohol use (Supplemental Table 2).

Analysis of LCA-defined Groups

In logistic regression analysis, results depict being in the Persistent class compared to the Non-persistent class associated with greater odds of being female (OR=1.25; 95% CI=1.07, 1.46; results not shown in a table). Being female was also associated with being in the Persistent class compared to the Intermittent class (OR=1.24; 95% CI=1.05, 1.46). No statistically significant differences were found for age between latent classes. In comparing estimates between those who started extra-medical PPR use within the past 12 months and those who started within the past 13-24 months, all 95% CI overlapped.

Discussion

This study found evidence of three distinct subgroups designated by extra-medical PPR and alcohol use patterns: (1) Non-persistent, (2) Intermittent, and (3) Persistent. Latent classes were ordered by involvement with extra-medical PPR and alcohol. Findings were largely driven by days of extra-medical PPR use, opioid dependence, and alcohol dependence. Young people with recent onset extra-medical PPR use had elevated levels of alcohol dependence regardless of their level of PPR involvement (10%-20%). In comparison, about 5% of adolescents meet criteria for alcohol dependence (Swendsen et al., 2012).

Most 12-20-year-olds fell into the first of the three classes (~79%). This Non-persistent subgroup was the least likely to be opioid or alcohol dependent. After trying extra-medical PPR for the first time, there was an average of five days of use in the past year. These young people could have previously used opioids with a prescription and the novelty of the drug effects may have led to extra-medical PPR use (Miech, Johnston, O'Malley, Keyes, & Heard, 2015). It is worth noting that drinking within the past month differentiated this class from the Intermittent (Class 2). Class 1 members were more likely to have drank alcohol in the past month than those in Class 2. Otherwise, recency of alcohol use did not vary much when comparing the three groups.

The second class (~15%), the Intermittent subgroup, fell in between the other two classes for both dependence measures. The mean number of extra-medical PPR use days was nearly 42, which may indicate possible weekend use over the past year. The third class, the Persistent subgroup was the smallest (~6%), but was most likely to have both opioid and alcohol dependent members. They also used extra-medical PPR 169 days in the past year, which is use about once every two days. While there was some variation in the number of use days by opioid dependence

status, it is surprising that for some dependence criteria was not met for this amount of extra-medical PPR. Frequent users of extra-medical PPR (≥100 days have been found to be more likely to use heroin when compared to non-frequent users (<30 days; Jones, 2013). A next step might be to examine the source of extra-medical PPR and whether it differs by frequency of use (Jones, Paulozzi, & Mack, 2014) and dependence characteristics.

Given that this age group of 12-20-year-olds had the highest rates of newly incident extra-medical PPR use (United States, 2016), it is worth noting that estimates did not differ based on time elapsed since beginning extra-medical PPR use. Classes were not significantly different whether newly incident users began 0-12 months or 13-24 months ago.

Being female was associated with greater odds of being in the Intermittent class or Persistent class compared to the Non-persistent class, which is consistent with prior findings (Seedall & Anthony, 2013; Wu, Woody, Yang, & Blazer, 2010). However, after including a squared term for age, there was no age variation between the three designated subgroups. This contrasts with other findings of adults, but may be due to the relative homogeneity of this younger age group (Carlson et al., 2014; Hedden et al., 2010).

Before detailed discussion of the results, several strengths and limitations should be noted. One strength is using large nationally representative survey data. In addition, LCA enabled identification of classes based on clustering of drug use behaviors as well as estimation of the degree to which the classes differed by sex and age. These results are generalizable to the US population of young people who recently have begun extra-medical PPR use. An important study limitation is the cross-sectional nature of the data, which makes it so that causal interpretations cannot be made. However, in comparing onset ages, extra-medical PPR use predated onset of drinking in 96% of adolescents with newly incident extra-medical PPR use.

Although the analysis is person-centered rather than variable-centered, the sample is not person-centered and, therefore, does not follow one individual over time. For this reason, the findings provide a population-averaged snapshot that may be helpful at the public health level.

This LCA model also did not satisfy the assumption of conditional dependence a priori. In sensitivity analyses, allowing for local dependence among items with high residual correlations did not produce noticeably different classes or change the interpretation of the results (Storr, Reboussin, & Anthony, 2005; Timberlake, 2008). Furthermore, although important transitions are captured by studying 12-20-year-olds, this age group does not include 21-year-olds and might miss what happens when drinking becomes legal. There could may be some censoring for the youngest adolescents for the 'opportunity to try' PPRs extra-medically. Some newly incident users in the population were not observed in the sample such as those with a rapid onset of opioid dependence (e.g., due to non-response). Similarly, the most severe cases alcohol dependence might not be captured in a community sampling design. Lastly, stratifying by time since first use may not have thoroughly addressed the exposure and opportunity to develop alcohol or opioid dependence, especially for those 12-20 year olds who began their PPR use within the past month. Future research should explore the progression of extra-medical PPR use soon after initiation in this vulnerable population.

Most adolescents and young adults who try extra-medical PPR do not persist in their use and develop opioid dependence. However, extra-medical PPR use is pervasive in this young population especially for those who also drink alcohol. Three distinct subgroups of newly incident extra-medical PPR users were identified based on their past year involvement with PPR and alcohol. Although the smallest subgroup was the most persistent in their extra-medical PPR and alcohol involvement, they may represent an unmet treatment need in the US and require

tailored intervention strategies based on their vulnerability to continue use and progress over time. One opportunity for intervention in this vulnerable group of adolescents might be in the emergency department after an alcohol-related event or an opioid overdose (e.g., Spirito et al., 2004). Considering the morbidity and mortality for persistent extra-medical PPR users, findings may help reduce the risk of future transition to heroin use or unintentional overdose (Kanouse & Compton, 2015).

For the second class, in the medical setting it might be possible to use presenting alcohol and/or opioid use disorder criteria that have become manifest at or near time of first PPR use onset as indicators of persisting in extra-medical PPR use. This could be particularly important for young females who have recently began extra-medical PPR use. Knowledge about this co-occurrence of extra-medical PPR and alcohol involvement can help inform pediatricians, family doctors, dentists, oral surgeons, and others who now write pain relief prescriptions for young people. Nondrug pain management plans should be considered, including special surveillance with analgesic drugs prescriptions (Parker & Anthony, 2018). The study's evidence also might be used as a guide to the refinement of treatment service programs and their extra-medical PPR prevention or opioid dependence management strategies.

For the largest class, extra-medical PPR and alcohol involvement characteristics could be used at the public health level to target middle schools, high schools, and colleges/universities in prevention initiatives so that use does not progress to persistence. Dissemination of this crucial information should not only be aimed at adolescents who engage in extra-medical PPR use but also family members and friends. After one's own prescription, relatives are a common source of PPR that may be used extra-medically (Jones et al., 2014; McCabe, Teter, Boyd, Wilens, & Schepis, 2018). Therefore, school-level interventions aimed at educating students about the

dangers of extra-medical PPR use and sharing prescriptions may help. Educating parents about keeping prescriptions safeguarded, adhering to medical use in the home as indicated by a prescribing physician, and discussing the risks of 'problem behaviors' is advisable.

Conclusion

In clinical practice, prescribing non-opioids for this population when appropriate especially for drug-naïve individuals is paramount. Underage drinking is often the first step of drug involvement (Barry et al., 2016). Screening for alcohol and extra-medical PPR before prescribing opioids in the primary care setting may be an integral step in beginning to address a persistent extra-medical PPR problem or preventing one from beginning (Chung et al., 2012; Han et al., 2017). The National Institute on Alcohol Abuse and Alcoholism suggest the two-question Alcohol Screening and Brief Intervention for Youth (https://www.niaaa.nih.gov/YouthGuide), which can be followed up with other adolescent specific tools (Knight, Sherritt, Harris, Gates, & Chang, 2003; Knight, Sherritt, Shrier, Harris, & Chang, 2002). Future studies will explore other drug use or psychiatric conditions as characteristics that further persistence in this population.

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Table 1. Selected characteristics of newly incident extra-medical prescription pain reliever using young people (n=24,789). Data from the National Surveys on Drug Use and Health, United States 2002-2013.

Sample characteristics	Unweighted n	%[a]
Sex		
Male	12,090	48.8
Female	12,699	51.2
Age (at interview)[b]	16.7	2.1
Time elapsed (from onset of EMPPR use to interview)		
0-12 months	15,970	64.4
13-24 months	8,819	35.6
Race/ethnicity		
Non-Hispanic white	16,617	67.0
Non-Hispanic black	2,389	9.6
Hispanic	3,744	15.1
Other	2,039	8.2
Number of days used EMPPR in the past year[b]	18.8	45.6
Opioid dependence	2,867	4.7
Alcohol dependence	1,165	11.6
Recency of alcohol use		
Drank within the past month	14,315	57.7
Drank more than 30 days ago, but within the past year	5,494	22.2
Drank more than a year ago	1,797	7.3
Never used alcohol	3,183	12.8

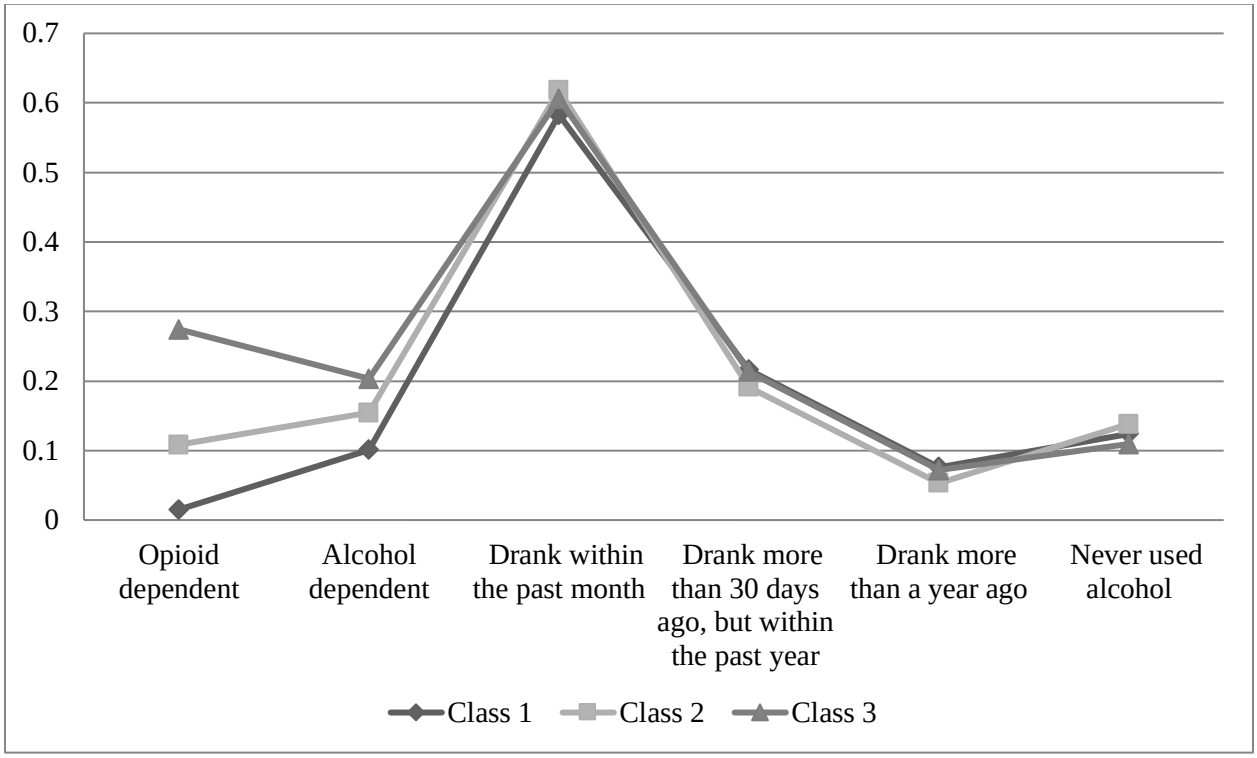
[a]Due to rounding, some percentages may not add to 100%.
[b]Mean with standard deviation.

Table 2. Item response probabilities for latent class membership for newly incident extra-medical prescription pain reliever using young people. Data from the National Surveys on Drug Use and Health, United States 2002-2013.

	Latent Classes		
Item	Class 1	Class 2	Class 3
Opioid dependent	0.015	0.108	0.272
Alcohol dependent	0.101	0.154	0.202
Recency of alcohol use			
Drank within the past month	0.583	0.618	0.610
Drank more than 30 days ago, but within the past year	0.216	0.191	0.211
Drank more than a year ago	0.076	0.053	0.071
Never used alcohol	0.124	0.138	0.107
Number of days used EMPPR in the past year[a]	5.0	41.6	169.0

[a] = Means

Figure 1. Estimated proportion of individual categorical indicators for persistence, by latent class of newly incident extra-medical prescription pain reliever using young people. Data from the National Surveys on Drug Use and Health, United States, 2002-2013.



Supplemental Table 1. Indicators of fit for models with one through seven latent classes. Data from the National Surveys on Drug Use and Health, United States 2002-2013.

Number of Classes	Entropy	AIC	BIC
1	-	1067367	1067456
2	0.949	391472	391602
3	0.945	271570	271774
4	0.952	243985	244269
5	0.929	225295	225652
6	0.934	219780	220210
7	0.881	216593	217096

Supplemental Table 2. Latent class adjusted odds ratios for newly incident extra-medical prescription pain reliever using young people.[a,b] Data from the National Surveys on Drug Use and Health, United States 2002-2013.

	Latent Class Comparisons Adjusted Odds Ratio (95% Confidence Interval)		
Item	Class 1 vs. Class 2	Class 1 vs. Class 3	Class 2 vs. Class 3
Opioid dependent	**0.13 (0.10, 0.16)**	**0.04 (0.03, 0.05)**	**0.32 (0.26, 0.40)**
Alcohol dependent	**0.62 (0.53, 0.72)**	**0.44 (0.37, 0.53)**	**0.72 (0.58, 0.89)**
Recency of alcohol use			
Drank within the past month	**1.16 (1.05, 1.27)**	1.12 (0.96, 1.28)	0.97 (0.80, 1.17)
Drank more than 30 days ago, but within the past year	1.06 (0.92, 1.22)	1.15 (0.93, 1.42)	1.09 (0.85, 1.39)
Drank more than a year ago	0.88 (0.74, 1.06)	1.18 (0.91, 1.53)	1.34 (1.00, 1.79)
Never used alcohol	1.00	1.00	1.00

[a] Adjusted for age, age-squared, and sex.

[b] Bolding denotes significance at the alpha = 0.05 level.