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Investigating Progression in Substance Use Initiation Using a Discrete-Time Multiple Event Process Survival Mixture (MEPSUM) Approach

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Abstract

The order and timing of substance initiation has significant implications for later problematic patterns of use. Despite the need to study initiation from a multivariate framework, survival analytic methods typically cannot accommodate more than two substances in one model. The Discrete-Time Multiple Event Process Survival Mixture (MEPSUM; Dean, Bauer, & Shanahan, 2014) model represents an advance by incorporating more than two outcomes and enabling establishment of latent classes within a multivariate hazard distribution. Employing a MEPSUM approach, we evaluated patterns of tobacco, alcohol, and cannabis initiation in the National Longitudinal Study of Adolescent to Adult Health (*N*=18,923). We found four classes that differed in their ages and ordering of peak initiation risk. Demographics, externalizing psychopathology, and personality significantly predicted class membership. Sex differences in the association between delinquency and initiation patterns also emerged. Findings support the utility of the MEPSUM approach in elucidating developmental pathways underlying clinically relevant phenomena.

Keywords

Substance use initiation; development; multivariate survival analysis; latent class analysis

Tobacco, alcohol, and cannabis are the three most commonly used substances among adolescents in the United States. Results from the Monitoring the Future study indicate that among high school seniors, lifetime prevalence of alcohol, cigarette, and marijuana use is 69.4%, 39.5% and 45.2%, respectively (Johnston, O'Malley, Bachman, & Schulenberg, 2013). Youth polysubstance involvement is also increasingly common; a recent analysis of the National Longitudinal Study of Adolescent to Adult Health indicated that 34.1% of adolescents reported using alcohol and marijuana or alcohol, marijuana, and cigarettes prior

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Authorship

L.S.R. and K.A.F. developed the study concept. All authors contributed to the study design. L.S.R. and K.A.F. performed the data analysis and interpretation and prepared tables and figures under the supervision of W.S.S. L.S.R. drafted the paper, and K.A.F. and W.S.S. provided critical revisions. All authors approved the final version of the paper for submission.

to age 16 (Moss, Chen, & Yi, 2014). The *order* of substance use initiation, in addition to the *type* of substance used, is also important. Adolescents have been shown to exhibit a normative sequence of drug use onset, during which they progress from tobacco and alcohol use to cannabis and other illicit drug involvement (Degenhardt et al., 2009). This has been termed the "gateway theory" (Huizink et al., 2010; Kandel & Yamaguchi, 2002).

Significant debate surrounds the extent to which associations between the initiation of different substances reflect causal factors. Proposed causal influences include the influence of initial drug experiences on later involvement. Many individuals describe their first experiences with tobacco, alcohol, and cannabis as pleasurable, which may facilitate subsequent use (de Wit & Phillips, 2012). Further, seemingly safe or successful first experiences with a drug may reduce perceived barriers to subsequent use (Lynskey et al., 2003) and initiation of one drug may facilitate access to other drugs via drug using peers or other mechanisms of provision (Hall & Lynskey, 2005). Finally, pharmacological mechanisms may mediate causal relationships. For instance, common receptor sensitization may lead exposure to one drug to increase sensitivity to the effects of subsequent substances (Agrawal et al., 2006; Tanda, Pontieri, & DiChiara, 1997).

With regard to non-causal explanations, it has been proposed that early-onset substance involvement reflects a general liability to deviant behavior (Hopfer, Crowley, & Hewitt, 2003; Young, Stallings, Corley, Krauter, & Hewitt, 2000). Considering the ordering of substance use onset, individuals have argued that the “gateway” pattern is the result of greater availability of legal than illegal drugs and differing background prevalence of substance use (Degenhardt et al., 2010).

Regardless of whether the mechanisms underlying substance use uptake are causal or non-causal, initiation of one substance may be associated with previous drug use experiences. This requires an analytic approach for simultaneously modeling the occurrence of multiple interrelated events. Multivariate survival methods, such as recurrent event and parallel data approaches, relax the requirement that all outcomes are univariate and independent (Hougaard, 2000). Until now, however, such models have not accounted for the fact that outcomes may occur at the same point in time. For instance, with regard to initiation, individuals may use multiple drugs in combination. For the purpose of the current study, we were interested in (1) examining the order and timing of initiation of multiple substances of abuse, and (2) identifying classes of individuals who differ in their patterns of progression from abstinence to initiation. Available multivariate trajectory modeling techniques have not allowed for use of time-to-event data to examine latent classes of individuals who adopt different initiation patterns. For instance, latent transition analysis predicts individuals’ movement between latent subgroups from their responses to manifest variables administered longitudinally. This can help identify the antecedents and correlates of transition between categories or stages (Collins & Lanza, 2010; Collins & Wugalter, 1992). Growth mixture modeling identifies latent subgroups that adopt different patterns of inter- and intra-individual change over time. This approach can provide insight into the mechanisms underlying change across classes (Ram & Grimm, 2009). Although these methods offer useful information regarding progression, they cannot speak to (1) whether and why multiple, interrelated outcomes occur at specific times, and (2) whether the timing of

multiple events can be used to characterize latent subgroups. Such questions require integration of multivariate time-to-event analyses with a mixture modeling approach. Recently, the Multiple Event Process Survival Mixture (MEPSUM) model (Dean, Bauer, & Shanahan, 2014) was developed to accomplish these aims.

Identifying different patterns underlying substance use initiation has significant public health implications. Of particular importance is the timing of initiation, as robust associations exist between early first use of tobacco, alcohol, and cannabis and increased risk for substance use problems (Dawson, Goldstein, Chou, Ruan, & Grant, 2008; Hu, Davies, & Kandel, 2006; Lynskey et al., 2003). Adolescent substance use onset is also of concern as heavy drug use during this period of neurodevelopmental "plasticity" may exert lasting impact on brain functioning (Lubman, Yücel, & Hall, 2007). Establishing different patterns of substance use uptake and relating them to health-related outcomes may inform prevention efforts by clarifying risk factors for different pathways of polysubstance involvement.

The primary goal of the current study was to present a novel, sophisticated method for examining different latent subgroups using multivariate time-to-event data. This method was applied to evaluate latent pathways of substance use initiation in a longitudinal, nationally representative sample of adolescents. We hypothesized that classes would be primarily differentiated by (a) their *timing* of onset of tobacco, alcohol, and cannabis use and (b) the *order* in which they initiated each substance. As a secondary aim, we investigated the relationship between class membership and individual-level variables that have been robustly associated with adolescent substance involvement: sex, race/ethnicity, externalizing psychopathology, and the Big Five personality traits. Finally, we explored interactions between demographic characteristics and externalizing psychopathology in predicting class membership. These predictors were selected for moderation analyses as previous work has demonstrated clinically relevant demographic differences in substance involvement and externalizing psychopathology. Research has documented sex and racial/ethnic differences in the age of substance use initiation and the rate of progression toward problems (Alvanzo et al., 2011; Keyes et al., 2010; Lopez-Quintero et al., 2011), as well as sex-differentiated outcomes of delinquency, including greater likelihood for substance abuse among males than females (Moffitt, Caspi, Rutter, & Silva, 2001).[1]

Method

Participants

Participants were drawn from the National Longitudinal Study of Adolescent to Adult Health (Add Health), a nationally representative sample of individuals surveyed about health and risk behaviors (Harris, 2011). A random sample of high schools was selected in the United States, which were stratified by geographic region, school size and type, and racial composition. A random subsample of students completed an in-home interview in 1994–

[1]Personality factors are well associated with substance involvement; however, there is limited evidence for sex differences in these associations. Research typically finds no differences in the relation between five-factor personality structure and substance use (e.g., Chassin, Flora, & King, 2004; Malouff, Thorsteinsson, Rooke, & Schutte, 2007) across men and women. Therefore, in order to (1) explore the most robust and clinically relevant differences in class membership and (2) maintain analytic parsimony, only interactions between demographics and externalizing psychopathology were explored.

1995 (Wave I; *n*=20,745, age=11–20 years (*M* age=15.9), response rate=79.0%). In addition, the biological mother (or other female head-of-household) was interviewed regarding their own health behavior, the family environment, and neighborhood characteristics. The second panel of interviews was conducted in 1996 with a sample drawn primarily from Wave I respondents (Wave II; *n*=14,738, response rate=88.6%), who were surveyed again in 2001–2002 (Wave III; *n*=15,197, response rate=77.4%), and 2008–2009 (Wave IV; *n*=15,701, response rate=80.3%). The mean household income for participants at Wave I was $45,728 (*standard deviation (SD)*=$51,617).

Data for the current study come from all four waves. Add Health incorporates sampling weights that account for the unequal probability of selection; for proper weighting when conducting time-to-event analyses, weights from the first wave are used, and individuals with missing weights must be removed (Chen & Chantala, 2014). After removing individuals with missing Wave I weight variables (8.8% of the sample), we were left with a sample size of 18,923.

Given the differences in response rates across waves, potential bias due to non-response and/or dropout was explored. A large-scale analysis (Brownstein et al., 2010) examined bias due to non-response in Wave IV of Add Health using characteristics from Wave I. Bias was minimal for nearly all variables, including baseline variables included in the current analysis, substance use, and psychopathology. In addition, results indicated that differences in measurements between respondents and non-respondents were most likely due to random variation. Therefore, procedures employing full information maximum likelihood (FIML) can appropriately account for missing data attributable to non-response and/or dropout in the current sample. A description of FIML procedures and treatment of missing data is presented in the *Statistical Analysis* section.

Measures

Age of alcohol initiation—At Waves I and II, participants were asked if they had had a drink of beer, wine, or liquor–not just a taste of someone else's drink–more than two or three times, and if they ever drank alcohol when they were not with parents or other adults in their family. If they responded yes to both, they were asked to report the age at which they first had a drink of beer, wine, or liquor when they were not with their parents or other adults in their family. At Wave IV, participants were asked whether they had had a drink of beer, wine, or liquor more than two or three times. If yes, respondents were asked to report the age at which they first had an alcoholic drink (defined as a glass of wine, can or bottle of beer, glass of liquor, or a mixed drink). To limit the risk of bias due to retrospective reporting, respondents' age of onset was taken from the earliest wave at which they reported having tried alcohol. 17,243 participants reported on their drinking, of which 3.5% had not tried alcohol by Wave IV. Mean age of alcohol initiation for the sample was 15.4 years (*SD*=3.0).

Age of tobacco initiation—At Waves I and III, participants were asked whether they had ever tried cigarette smoking, and if so, the age at which they first smoked a whole cigarette. At Wave IV, they were asked if they had ever smoked an entire cigarette, and if so, the age at which they first smoked a whole cigarette. Respondents' age of onset was taken from the

earliest wave at which they reported having tried smoking. 16,569 participants reported on their smoking behavior, of which 10.1% had not tried smoking as of Wave IV. Mean age of tobacco initiation was 14.8 years (*SD*=3.3).

Age of cannabis initiation—At Waves I and IV, participants were asked to report the age at which they first used cannabis. Their age of onset was taken from the earliest wave at which they reported having tried cannabis. 14,511 respondents reported on their cannabis use, of which 21.8% had not tried cannabis by Wave IV. Mean age of cannabis initiation was 15.9 years (*SD*=3.1).

Demographics—Males report greater substance involvement and initiate substance use earlier, on average, than females (Becker & Hu, 2008). Additionally, increased rates of abstention are observed among African-Americans compared with Caucasians and other racial/ethnic groups (Johnston et al., 2013). Sex and race/ethnicity were therefore included as predictors of latent class membership. Both variables were assessed at Wave I; sex was measured as a binary category of male (49.1%) and female (50.9%), and race/ethnicity was coded as four categories: Caucasian (51.0%), African-American (21.7%), Hispanic (17.1%), and other (10.2%).

Alcohol use disorder—Individuals with an alcohol use disorder (AUD) report initiating alcohol use earlier than individuals without alcohol problems (DeWit, Adlaf, Offord, & Ogborne, 2000). We thus investigated the association between class membership and lifetime AUD. At Wave IV, individuals were asked to report how many drinks per day they typically consumed during the past 12 months or during their period of heaviest drinking. If men endorsed typically drinking five or more drinks per day and women four or more drinks per day, they were queried about lifetime symptoms of DSM-IV alcohol abuse and dependence. Individuals were coded as positive for a DSM-IV alcohol use disorder if they met criteria for abuse or dependence. 21.7% of the sample met criteria for a lifetime AUD (*M* age at Wave IV interview=28.5 years (*SD*=1.8)).

Cannabis use disorder—Increased risk for cannabis use disorder (CUD) is related to early-onset cannabis use (Lynskey et al., 2003). We therefore evaluated the association between class membership and lifetime CUD. At Wave IV, respondents were asked similar questions regarding cannabis use as those regarding alcohol use; individuals who reported using cannabis once per week or more were asked to report on lifetime symptoms of DSM-IV cannabis abuse and dependence. Individuals were coded as positive for a DSM-IV cannabis use disorder if they met criteria for abuse or dependence. 9.7% of the sample met criteria for a lifetime CUD.

Nicotine dependence—Nicotine dependence is well associated with early-onset tobacco use (Breslau, Fenn, & Peterson, 1993). Nicotine dependence (ND) was thus included as a predictor of class membership. At Wave III and Wave IV, participants were administered the Fagerström Test for Nicotine Dependence (FTND), a six-item questionnaire composed of two items assessing the physiological and four items assessing the behavioral aspects of smoking (Heatherton, Kozlowski, Frecker, & Fagerström, 1991). At Wave III, individuals who had ever smoked daily and had smoked in the past 30 days were administered the

FTND items pertaining to current smoking. Current smokers and individuals not administered the current FTND questions were administered FTND items pertaining to their heaviest period of smoking if they indicated that there was a period in their life in which they smoked more heavily. At Wave IV, if individuals reported smoking in the past 30 days, they were administered the FTND items and were asked to report on symptoms that occurred during their heaviest period of smoking. Individuals were coded as positive for current or past nicotine dependence if they scored a six or more on the FTND (range=0–10) at the Wave III and/or Wave IV assessment. 12.5% of the sample met criteria for nicotine dependence.

Delinquency—Early antisocial behavior is robustly associated with adolescent substance involvement (Hawkins, Catalano, & Miller, 1992) and was therefore examined as a predictor of class membership. Delinquent behaviors were assessed at all waves. The Wave I assessment was used to capture early life conduct problems most proximate to the peak period of risk for substance use initiation. Participants were asked to report how often they had engaged in 15 delinquent activities in the past year: *Never* (0), *One or two times* (1), *Three or four times* (2), or *Five or more times* (3). Examples of symptoms assessed include damaging property, stealing, lying to parents or guardians, and physical fighting. Delinquency scores were created by summing across individuals' responses to all 15 items and then standardizing the variable. This was done in order to preserve the continuous nature of the measure while providing meaningful units (deviations from the mean) for logistic regression analyses (see *Statistical Analysis* below). 18,788 individuals completed the delinquency assessment.

Personality—Early substance use initiation and substance use disorder are associated with elevated levels of neuroticism and disinhibition (Kotov, Gamez, Schmidt, & Watson, 2010). Personality was therefore included as a predictor of class membership. At Wave IV, participants were administered the Mini-IPIP, a 20-item inventory designed to assess the Big Five factors of personality (Donnellan, Oswald, Baird, & Lucas, 2006). For each item, individuals were asked, "How much do you agree with each statement about you as you generally are now, not as you wish to be in the future?" Responses followed a 5-point Likert scale ranging from 1 (*Strongly agree*) to 5 (*Strongly disagree*). Each of the Big Five domains (Conscientiousness (C), Extraversion (E), Agreeableness (A), Neuroticism (N), and Openness (O)) was assessed via four items. Individuals' scores for each domain were computed by summing across domain-specific items and then standardizing the variables.

Statistical Analysis

The MEPSUM model integrates multivariate, discrete-time survival modeling with latent class analysis. A finite mixture is used to approximate the multivariate hazard distribution, and components of the mixture–or latent classes–represent different patterns of event occurrence over time. That is, classes within the mixture distribution are composed of individuals with a similar hazard for multiple outcomes. For the purpose of the current study, different classes would be indicative of different patterns in the rates of progression of substance use initiation. Although this approach aims to detect different classes, it is often

the case that the actual multivariate hazard distribution is continuous, and different classes represent patterns underlying this dimensional distribution.

Add Health is organized by wave of assessment, with variability in chronological age at each wave. Data were therefore restructured to provide age-based measurement for discrete-time survival analyses. Restructuring data from wave to age creates a special case of missing data termed "missing by design," which is well handled by methods employing full information maximum likelihood (FIML; Bollen & Curran, 2006). For restructuring, participants' age at interview was coded as their age at the last wave of data collection that they completed. Event processes (ages of initiation of tobacco, alcohol, and cannabis use) were then coded according to whether an individual reported having tried a substance at each age between 10 and 30 years.[2] Individuals with an unknown event time (i.e., individuals who did not report having tried a substance at interview) were considered censored and assumed to be missing at random. In addition, individuals were considered censored for all time periods following their reported ages of initiation. This type of non-informative censoring allows us to assume that non-censored individuals at any given time point are representative of individuals who would have remained in the study if censoring had not occurred (enabling generalization to the entire dataset). For demonstration, the following represents the event history, from ages 10 to 15, for an individual who reports having first tried tobacco at age 13. "999" indicates censoring:

0 0 0 1 999 999

Models were conducted in Mplus version 7 (Muthén & Muthén, 1998–2012), which employs FIML to accommodate missing data. Sampling weights were included in analyses. Unstructured hazards were used and approximated with a logit link function. Although unstructured hazard functions are more computationally intensive than parametric functions, they allow for better approximation of the hazard if it is nonparametric and the shape changes over time.[3] Model estimation proceeded as follows: First, multivariate MEPSUM models were estimated. The first model was run on the three event processes, without covariates, including one to six latent classes with unstructured hazard functions. To ensure a global maximum likelihood solution, random start values were employed, with the best values obtained for final optimization. In addition, the resulting solutions were monitored to ensure that the final log-likelihood was replicated. When determining the number of classes to retain in mixture analyses, it is recommended that researchers examine fit statistics (such as the Akaike information criterion (AIC) and the Bayesian information criterion (BIC)) and classification indices indicating the separation between clusters and degree of certainty of class assignment (Akaike, 1974; Bozdogan, 1987; Fraley & Raftery, 1998). We therefore examined the AIC, BIC, and log-likelihood values, as well as entropy values and model-estimated probabilities of accurate class assignment. In addition, we visually inspected the

[2]A small number of individuals reported having initiated tobacco (5.9%), alcohol (4.0%), and cannabis (2.7%) before age 10 and after age 30 (tobacco: 0.01%, alcohol: 0.03%, cannabis: 0.01%). These outlying values led to numerous sparse cells at the tails of the onset distribution, contributing to model convergence problems. Therefore, individuals who reported initiating substance use before age 10 were recoded to age 10, and those who reported initiating substance use after age 30 were recoded to age 30.

[3]Dean and colleagues (2014) note that although it is possible to use results from unstructured hazard functions as a guide to possible parametric (e.g., quadratic) forms, this should be done with extreme caution, as it is likely that this parametric shape will not hold within or across latent classes.

hazard curves across models to determine whether the addition of a class provided unique information.

Following determination of the number of classes to retain, the influence of covariates (sex, race/ethnicity, externalizing psychopathology, and personality) on class membership was examined using logistic regression. For ease of interpretation, all covariates were first examined independently. The effect of covariates can be interpreted as indicating how the odds of experiencing each pattern of event histories (the odds of being in a specific class) are influenced. Subsequently, we explored interactions between demographics and externalizing psychopathology in predicting class membership.

Several steps were taken to reduce multiple testing and ensure we probed the most robust class differences. First, we only examined class comparisons within models with significant omnibus interaction effects. Second, we limited reference groups to the middle school and high school classes. Recent work has indicated that early and late adolescent substance exposure may confer differential risk and effects on the developing brain (Spear, 2015). The current approach allowed for direct comparison of all classes whose periods of peak initiation risk occurred at different stages of adolescence (middle school, high school, and early adulthood). Survey analysis procedures in SAS version 9.3 (SAS Institute Inc., Cary, NC) were employed to analyze the clustered, weighted data using Taylor series variance estimation to obtain correct sampling errors.

Results

Determination of the Class Solution

We determined the appropriate number of classes to retain by investigating various information criteria (see Table 1) and examining the hazard and distribution functions for each class solution. All information criteria showed an appreciable decrease as the number of classes increased from one to six with the exception of the BIC, which increased slightly in the six class solution relative to the five class solution. The five class solution included a class that represented only 13% of the sample and investigation of the hazards and distributions of this class indicated that the parameter estimates were unstable and likely not reliable due to the small sample size. Therefore, it was determined that a four class solution was best able to describe the underlying heterogeneity in tobacco, alcohol, and cannabis initiation risk in this sample. Average posterior probabilities of assignment for all classes exceeded the recommended threshold of 0.70 (Nagin, 2005), indicating that individuals were well matched to their respective classes and an adequate solution was achieved (class 1=0.76; class 2=0.84; class 3=0.77; class 4=0.86).

Hazard Functions in Latent Classes

Unstructured hazard functions and lifetime distribution functions for the four classes in the retained model are presented in Figure 1. Hazard functions represent the unique risk of substance initiation, or the probability that initiation of a particular substance occurs at a certain age, given that initiation has not yet happened. The lifetime distribution functions display the cumulative probability of substance initiation by a given age.

The first class in the four class solution was characterized by a relatively high early risk of initiating alcohol, tobacco, and cannabis. Risk increased sharply from age 11 to age 13 for alcohol ($\hat{h}_{11}$=0.12, $\hat{h}_{13}$ =0.48), tobacco ($\hat{h}_{11}$=0.18, $\hat{h}_{13}$ =0.50), and cannabis ($\hat{h}_{11}$=0.05, $\hat{h}_{13}$ =0.31). Risk for alcohol initiation began lower than risk for tobacco initiation but caught up by age 13, at which time the risk for initiating both substances was nearly identical. Risk for cannabis initiation in this class also peaked at age 13, but remained stable until age 15 and was relatively lower than peak risk for tobacco or alcohol. The cumulative probability of substance use initiation by age 30 was high for alcohol ($\hat{D}_{30}$=0.91), tobacco ($\hat{D}_{30}$=0.94), and cannabis ($\hat{D}_{30}$=0.84). Because this class was characterized by high risk of early initiation (i.e., peak risk before age 14), it is labeled as the “middle school” (MS) initiation class.

The second class was characterized by relatively low early risk of substance use initiation in the preteen years that increased sharply between the ages of 13 to 16 for alcohol ($\hat{h}_{13}$ =0.17, $\hat{h}_{16}$ =0.36), tobacco ($\hat{h}_{13}$ =0.25, $\hat{h}_{16}$ =0.37), and cannabis ($\hat{h}_{13}$ =0.05, $\hat{h}_{16}$ =0.20). Risk for tobacco initiation was initially higher than risk for alcohol initiation until age 14, at which time alcohol initiation became the higher risk event for the next two years. Risk for cannabis initiation was lower than risk for tobacco or alcohol initiation overall, but followed the same basic hazard pattern as a function of age (i.e., increasing through the early teenage years to a peak at ages 15–16). Cumulative probabilities were comparable to those in the middle school class for alcohol ($\hat{D}_{30}$=0.91) and tobacco ($\hat{D}_{30}$=0.91), but were slightly lower for cannabis ($\hat{D}_{30}$=0.77). This class was labeled as the “high school” (HS) initiation class.

The third class was characterized by low risk of substance initiation through the early teen years that increased during the later teen years. Risk of initiating alcohol, tobacco, and cannabis was low throughout early adolescence ($\hat{h}_{15}$ =0.07, 0.12, and 0.03, respectively) and increased sharply through late adolescence. Peak risk for initiating came at age 18 for tobacco ($\hat{h}_{18}$ =0.32) and cannabis ($\hat{h}_{18}$ =0.28) and at age 19 for alcohol ($\hat{h}_{19}$ =0.45). In this class, risk for initiating all substances was fairly comparable until age 17, at which time the risk for alcohol initiation increased more rapidly and stayed much higher than tobacco or cannabis initiation, with this difference in relative risk remaining until the age of 23. Cumulative probabilities in this class were nearly identical to those in the high school class for alcohol ($\hat{D}_{30}$=0.92) and cannabis ($\hat{D}_{30}$=0.77), but were lower for tobacco ($\hat{D}_{30}$=0.83). This class is labeled the “early adulthood” (EA) initiation class.

The hazard functions in the fourth class differed a great deal from those in the previous three classes. Risk of initiation started very low and did not appreciably increase for either tobacco or cannabis with peak estimated risks of 0.07 and 0.12, respectively. Risk for alcohol initiation also started very low and continued to be low through the teenage and young adult years with the exception of a small relative increase in risk at age 21 ($\hat{h}_{21}$=0.22), which was the legal age for alcohol consumption for the large majority of participants in this study. Due to the relatively small cumulative probabilities of initiating alcohol ($\hat{D}_{30}$=0.58), tobacco ($\hat{D}_{30}$=0.38), and cannabis use ($\hat{D}_{30}$=0.11) in this group, it is labeled the “relative abstainer” (RA) class.

Substance Use Characteristics of the Four Latent Classes

Table 2 displays the prevalence of substance use and the average ages of tobacco, alcohol, cannabis onset among the four latent classes. Individuals in the middle school, high school, and early adulthood groups were significantly more likely to have tried all substances than people in the relative abstainer group; the greatest difference was observed for cannabis (MS vs. RA: odds ratio (OR)=59.9, 95% confidence interval (CI) [44.1, 81.5]; HS vs. RA: OR=25.5, 95% CI [20.4, 31.8]; EA vs. RA: OR=33.1, 95% CI [26.3, 41.6]). The mean ages of tobacco, alcohol, and cannabis initiation significantly varied across the four classes (tobacco: $F_{(1, 128)}$=1235.46, p<.0001; alcohol: $F_{(1, 128)}$=2124.97, p<.0001; cannabis: $F_{(1, 127)}$=584.49, p<.0001). Considered pairwise, all classes significantly differed from each other (tobacco: Fs$_{(1, 128)}$=7.40– 4334.84, p<.0001– p=.007; alcohol: Fs$_{(1, 128)}$=419.22–3632.95, ps<.0001; cannabis: Fs$_{(1, 127)}$=4.88–3036.49, p<.0001–p=.03).

Association of Demographic Characteristics with Class Membership

Prevalences of demographic characteristics among each latent class are displayed in Table 2, and odds ratios from logistic regression analyses predicting class membership from demographic variables are presented in Table 3. Confidence intervals for odds ratios were computed with a Bonferroni correction for multiple comparisons at α=.05. With regard to sex, males were significantly more likely than females to be in an earlier initiating class, relative to a later initiating class, for all comparisons. Considering race/ethnicity, with the exception of the high school and early adulthood vs. middle school comparisons, Caucasians were significantly more likely than other groups to adopt an earlier initiation pathway. The opposite pattern of results was observed for African-Americans, who were less likely to be in the earlier initiating classes. This effect was strongest when comparing the relative abstainer class to the middle school class (OR=2.64, 95% CI [1.93, 3.61]) and high school class (OR=2.48, 95% CI [1.88, 3.27]). Hispanic individuals were more likely to be in the relative abstainer group than the high school and early adulthood groups.

Association of Externalizing Psychopathology with Class Membership

Means and prevalences of the externalizing psychopathology measures are presented for each class in Table 2, and results from analyses predicting class membership from measures of psychopathology are displayed in Table 3. Confidence intervals for odds ratios were computed with a Bonferroni correction at α=.05. Odds ratios for delinquency indicate the likelihood of being in a specific class as a function of a one standard deviation change in delinquency. Participants with a lifetime AUD were significantly more likely than those without to be in the middle school, high school, and early adulthood groups compared with the relative abstainer group. Lifetime CUD and ND significantly differentiated all classes, such that individuals who met criteria for a disorder were significantly more likely to adopt an earlier initiation pathway. Concerning delinquency, across all class comparisons, individuals endorsing more delinquent behaviors were significantly more likely to fall into earlier initiating groups.

Association of Personality with Class Membership

Means for personality variables among each latent class are displayed in Table 2, and odds ratios indicating the relation between personality and class membership are presented in Table 3. Confidence intervals for odds ratios were computed with a Bonferroni correction at α=.05. These odds ratios indicate the likelihood of being in a specific class as a function of a one standard deviation change in personality. Individuals who were lower on extraversion were significantly more likely to be in the relative abstainer class than the other classes, with the greatest difference observed in comparison to the middle school class (OR=0.74, 95% CI [0.67, 0.81]). Agreeableness and conscientiousness had a similar effect, such that individuals higher in both domains were more likely to be in a later-initiating group compared to the middle school group. Individuals lower on neuroticism were significantly more likely to be in the relative abstainer group than the middle school and high school groups and to adopt the early adulthood and high school pathways compared to the middle school pathway. Respondents higher on openness were more likely to be in the early adulthood class than the high school (OR=1.15, 95% CI [1.05, 1.25]) and the middle school (OR=1.10, 95% CI [1.004, 1.21]) classes, and were less likely to be assigned to the relative abstainer class than the other three classes.

Interactions Between Demographics and Externalizing Psychopathology— Parameter estimates and odds ratios from all interaction models are presented in Table S1 and Table S2 in supplemental materials. No significant interactions were found between race/ethnicity and externalizing psychopathology. Concerning sex, a significant interaction was detected with delinquency, such that the effect of delinquency on class membership was stronger among women than men ($\chi^2_{(3)}$=18.56, p<.001). For every standard deviation increase in delinquency, women were more likely to be in the middle school class than the high school (OR=0.90, 95% CI [0.85, 0.95]), early adulthood (OR=0.73, 95% CI [0.67, 0.80]), and relative abstainer (OR=0.65, 95% CI [0.58, 0.72]) classes. They were also more likely to be in the high school than the early adulthood (OR=0.82, 95% CI [0.74, 0.89]) and relative abstainer (OR=0.72, 95% CI [0.65, 0.79]) classes.

Tests for Multicollinearity—To ensure that the effects of individual predictors were due to unique variance, we explored multicollinearity. Correlations across nearly all predictors were small, with the exception of AUD and CUD (r=0.52), CUD and ND (r=0.37), and agreeableness and conscientiousness (r=0.44; see Table S3 in supplemental materials). We therefore re-ran these models controlling for the effects of correlated predictors. All statistically significant effects for measures of psychopathology remained significant in the adjusted models. For agreeableness, the comparisons between the HS and MS classes and RA and MS classes were not significant after controlling for conscientiousness (HS vs. MS: OR=1.06, 95% CI [0.96, 1.17]; RA vs. MS: OR=1.08, 95% CI [0.96, 1.22]). For conscientiousness, the comparison between the EA and MS classes was not significant after controlling for agreeableness (OR=1.04, 95% CI [0.95, 1.15]).

Discussion

The current study employed a discrete-time multiple event process survival mixture (MEPSUM) approach to examine patterns of substance use initiation in a longitudinal, nationally representative sample of adolescents. Trajectory modeling approaches such as latent transition analysis and growth mixture modeling have offered insight into predictors of change over time. However, the MEPSUM method provides unique information by characterizing individuals according to the *timing* of multiple, interrelated events–something existing statistical models cannot do.

We hypothesized that the timing of substance use onset would significantly influence class assignment. This prediction was strongly supported, as results indicated a four class model in which groups were differentiated largely by their periods of peak initiation risk. Variation in multivariate hazard functions discriminated between groups of individuals whose periods of highest risk were in early adolescence ("middle school"), middle to late adolescence ("high school"), and early adulthood, respectively, as well as a group whose risk for initiating all substances remained low across all developmental periods ("relative abstainers"). Further, the earliest initiating classes (middle school and high school) differed from the latter two classes in the association between alcohol and tobacco initiation risk. For the youngest initiating classes, risk for alcohol and tobacco initiation followed virtually identical paths. By contrast, the early adulthood and relative abstainer classes were characterized by lower risks of initiating tobacco and cannabis at all time points, relative to alcohol. These findings suggest that risk for concurrent alcohol and tobacco initiation is greatest at younger ages and that co-initiation of these substances becomes less prevalent as the age of first substance initiation increases.

We also hypothesized that the order in which individuals initiated substances would differentiate groups. This prediction was moderately supported. Some group differences were observed in the relative risk of initiating one substance versus another; however, all classes appeared to follow the same general sequence of initiation (tobacco before alcohol before cannabis). This aligns with the commonly observed "gateway" pattern of first use of licit before illicit drugs (Kandel & Yamaguchi, 2002) and indicates that in this sample, the *period* of greatest risk for initiation, as opposed to the *sequence* of onset, more strongly differentiates groups of individuals. The current method provides an advance by allowing us to interpret findings regarding initiation of one substance in the context of initiation of prior substances. This can be considered a more "ecologically valid" approach to examining substance use progression–which is an inherently multivariate phenomenon–than univariate survival analytic approaches. Past studies of substance use trajectories (e.g., Agrawal et al., 2006; Behrendt et al., 2012) have focused primarily on predicting onset of one substance from another. Although these studies offer insight into relationships between drugs, they do not account for the fact that initiation of multiple substances may occur at the same time.

A previous analysis (Dean, Cole, & Bauer, 2015) applied a MEPSUM approach to examine patterns of substance use initiation in the National Survey on Drug Use and Health. Dean and colleagues (2015) examined the ages of initiation of nine substances and detected six classes, characterized by general abstention; early, late, and progressive soft drug use; and

early and late hard drug use. The timings of peak risk for initiation observed in the general abstention and soft drug use classes align reasonably well with what was observed for the four classes derived in the current analysis. Further, Dean and colleagues (2015) found that sex and race/ethnicity predicted class membership in a manner consistent with current findings. Females were more likely to be general abstainers than males, and African-Americans were less likely than Caucasians to adopt the Early Soft pattern. The current analysis extends beyond Dean and colleagues' approach by (1) utilizing a prospective rather than a retrospective design; (2) evaluating individuals surveyed across adolescence and young adulthood, when risk for substance use initiation is highest; and (3) characterizing latent classes using a much larger number of clinically relevant correlates. Continued research will assist in determining how the MEPSUM method's findings converge and differ across datasets employing different samples, assessment strategies, and substance-related phenotypes.

Relation to Demographic Characteristics

Women were more likely than men to be assigned to classes characterized by later first substance use (e.g., HS vs. MS: OR=1.29, 95% CI [1.09, 1.51]; EA vs. MS: OR=1.20, 95% CI [1.01, 1.42]) and to adopt the “relative abstainer” pathway (RA vs. EA: OR=1.18, 95% CI [1.04, 1.35]). This aligns with findings supporting greater male than female substance involvement and earlier substance use initiation among men than women (Kessler et al., 2005; Zilberman, Tavares, & el-Guebaly, 2003). How does this relate to sex differences in progression to other substance use milestones? Women may exhibit a more rapid trajectory to alcohol dependence than men (Schuckit, Daeppen, Tipp, Hesselbrock, & Bucholz, 1998), although recent research suggests this effect may not hold in general population samples (Keyes, Martins, Blanco, & Hasin, 2010). In addition, the effects of alcohol and cannabis use on subsequent drinking problems may be stronger among females than males (Buu et al., 2014). Future work employing the current method to investigate the rate of transition from initiation to heavier use will help elucidate potential sex differences in progression across substances.

Across nearly all class comparisons, African-Americans were significantly more likely than other racial/ethnic groups to be assigned to the later-initiating class (e.g., EA vs. MS: OR=1.60, 95% CI [1.23, 2.07]; EA vs. HS: OR=1.50, 95% CI [1.22, 1.85]). By contrast, Caucasians were more likely to adopt an earlier initiation pathway. This is consistent with results from national surveys (Johnston et al., 2013; Wu, Woody, Yang, Pan, & Blazer, 2011) documenting higher levels of substance use among Caucasians than African-Americans. However, racial/ethnic differences in substance involvement appear to be changing. Although African-Americans used to report lower rates of illicit drug use than Caucasians, this gap is narrowing, largely due to increased cannabis use among African-Americans (Johnston et al., 2013). Studies investigating racial/ethnic differences in *trajectories* of substance involvement produce mixed results. Some indicate that African-Americans report lower initial levels and lower increasing rates of substance use than Caucasians (Flory et al., 2006; White, Nagin, Replogle, & Stouthamer-Loeber, 2004), while others (e.g., Chen & Jacobson, 2012) indicate that racial/ethnic differences disappear in adulthood. Future studies

of racial/ethnic differences in polysubstance use trajectories would build on current results by incorporating measures of heavier use and problems.

Relation to Externalizing Psychopathology

Conduct disorder is robustly associated with adolescent substance use (Elkins, McGue, & Iacono, 2007; Hawkins, Catalano, & Miller, 1992). The current study's results were largely consistent with these findings, in that individuals with higher levels of delinquency were more likely to be assigned to earlier-initiating groups across all class comparisons (e.g., HS vs. MS: OR=0.68, 95% CI [0.62, 0.74]; EA vs. MS: OR=0.38, 95% CI [0.33, 0.44]; RA vs. MS: OR=0.23, 95% CI [0.20, 0.27]). The extent to which delinquency directly increases risk for early substance involvement remains unclear. Behavior genetic studies typically find that the overlap between conduct disorder and adolescent substance use is partially explained by genetic and family environmental factors (Hopfer, Crowley, & Hewitt, 2003; Young, Stallings, Corley, Krauter, & Hewitt, 2000), with little evidence for unique environmental overlap. This suggests that delinquency and adolescent substance use reflect a general risk for externalizing problems. The current study indicates that early substance use uptake tends to associate with externalizing behavior, and this occurs irrespective of the order of initiation. Future research using the current method with genetically informed data will help determine the extent to which polysubstance initiation patterns and early delinquency result from shared familial risk factors.

Individuals with a lifetime cannabis use disorder were significantly more likely to adopt an early initiation pathway across all class comparisons (e.g., HS vs. MS: OR=0.77, 95% CI [0.61, 0.96]; EA vs. MS: OR=0.41, 95% CI [0.31, 0.56]), and the same trend was found for nicotine dependence (e.g., HS vs. MS: OR=0.68, 95% CI [0.57, 0.81]; EA vs. MS: OR=0.40, 95% CI [0.31, 0.51]). The association between lifetime alcohol use disorder and class membership was less robust; lifetime AUD did not significantly differentiate between the middle school, high school, and early adulthood classes. This may be attributable to substance-specific and cross-substance processes. Some evidence supports stronger relations between early first use and problems for tobacco (Lopez-Quintero et al., 2011) and cannabis (Palmer et al., 2009) than alcohol. Buu and colleagues (2014) determined that after controlling for early alcohol initiation, early nicotine and marijuana initiation did not contribute to alcohol problems. Thus, our finding that AUD was more weakly related to class membership may partially reflect weaker associations with early alcohol use and/or early tobacco and cannabis use. Limited research, however, has compared multiple substances, and conflicting evidence exists. Some studies support stronger substance-specific and cross-substance relationships for alcohol than illicit drugs (Behrendt, Wittschen, Höfler, Lieb, & Beesdo, 2009; Wagner & Anthony, 2002). Greater exploration of cross-substance associations is needed.

Relation to Personality

The current data suggest that higher levels of neuroticism and lower levels of agreeableness and conscientiousness are associated with earlier ages of substance use initiation. For instance, levels of these personality traits significantly differed between the high school and middle school classes (neuroticism: OR=0.89, 95% CI [0.81, 0.99]; agreeableness:

OR=1.11, 95% CI [1.01, 1.22]; conscientiousness: OR=1.14, 95% CI [1.04, 1.26]). (It should be noted that variance shared between agreeableness and conscientiousness appeared to largely explain their effects). This is in line with evidence from previous studies. A meta-analysis of Big Five personality traits and alcohol involvement (Malouff et al., 2007) showed that low conscientiousness, low agreeableness, and high neuroticism were related to numerous dimensions of alcohol use; this mirrored findings from a meta-analysis examining tobacco use (Malouff, Thorsteinsson, & Schutte, 2006). Further, research on monozygotic twins discordant for cannabis involvement has shown cannabis initiation to be associated with higher levels of neuroticism (Vink, Nawijn, Boomsma, & Willemsen, 2007). Previous work has considered personality risk separately for these substances. The current study represents an advance by helping identify unique clusters of personality traits associated with initiation of multiple substances. The extent to which the current findings hold in different samples or across personality inventories should be explored.

Sex Differences in the Effects of Delinquency on Class Membership

Moderation models detected an interaction between sex and delinquency, such that increases in delinquency were associated with a greater likelihood of early substance use initiation among women than men (e.g., HS vs. MS: OR=0.90, 95% CI [0.85, 0.95]; EA vs. MS: OR=0.73, 95% CI [0.67, 0.80]). This is interesting in light of previous findings regarding sex differences in delinquency and substance use. Some (e.g., Moffitt et al., 2001) detect a greater likelihood of substance-related problems among delinquent boys than girls, while others (e.g., Elkins et al., 2007) find no sex differences. Some evidence also suggests that although delinquency and substance use are observed less frequently in girls, female delinquency rarely occurs in the absence of substance involvement (Federman et al., 1997). Far fewer studies, however, have explored sex differences in the link between conduct problems and early-onset substance use. It may be that sex-specific factors present in adolescence lead to a differential association between early-onset use and delinquency. For instance, girls' social-cognitive styles differ from boys' styles, such that they exhibit greater concerns regarding social judgment. This is generally protective against behavioral problems. However, for some girls, social-cognitive orientation may increase risk for externalizing behaviors (Rose & Rudolph, 2006). Connection-oriented goals may lead them to engage in delinquent behaviors or substance use to strengthen ties with boyfriends who behave this way (Caspi, Lynam, Moffitt, & Silva, 1993). Alternatively, they may integrate with opposite-sex peer groups, which diminish sex-typed social-cognitive styles and promote substance involvement (Rose & Rudolph, 2006). Thus, delinquency may occur at lower mean levels among girls due to lower exposure to risk factors (Moffitt et al., 2001). However, those girls who exhibit conduct problems may possess unique risk for other adolescent outcomes. To our knowledge, this is the first study to document sex differences in the relation between delinquency and polysubstance initiation. Future work will be necessary to replicate this finding and determine how it intersects with sex differences in the association between delinquency and later-onset substance involvement.

Interpretation of Latent Classes

Several considerations regarding interpretation of the latent classes derived in this analysis merit discussion. First, multiple classes may be required to capture different patterns of

association within the data; however, we do not assume that they represent qualitatively distinct groups. In addition, heterogeneity likely exists within classes. Of greater interest than defining discrete groups is understanding how group differences are influenced by theoretically driven predictors. This facilitates more meaningful exploration of the antecedents and outcomes of class membership (Nagin & Odgers, 2010). Finally, we do not contend that the present subgroups represent all possible multivariate pathways; there is likely remaining variance in progression patterns that remains unexplained and is accounted for by additional variables.

Applications of MEPSUM to Clinical Science

The current study represents one example of how the MEPSUM method can provide insight into multivariate time-to-event patterns. However, application of the method has implications for many areas of clinical science. For instance, epidemiologic studies indicate that "multimorbidity" is common; an analysis of the National Comorbidity Survey indicated that 23% of adults met criteria for three or more disorders in the past year (Kessler et al., 2005). In addition, individuals may arrive at disorders via multiple pathways (Krueger & Markon, 2006). The current method could help delineate patterns of multivariate comorbidity, as well as heterotypic and homotypic continuity in risk for psychiatric disorders. It could also assist in defining the risk associated with different ordering of symptom onsets within a disorder (e.g., Nelson, Heath, & Kessler, 1998) and the rapidity with which individuals progress toward problems (Hussong, Bauer, & Chassin, 2008).

The MEPSUM approach might also help define the topography of individuals' affect and experience. For example, studies of mood disorders focus on identifying antecedents and correlates of depressed and manic episodes (e.g., Judd et al., 2008). Better clarifying the timing and relationship between periods of mood disturbance could assist in understanding the course of affective disorders. Intensive longitudinal designs are also concerned with examining mood shifts. Ecological momentary assessment has been used to measure emotion dysregulation (Ebner-Priemer & Trull, 2009) and the relationship between affect and substance use (Shiffman, Stone, & Hufford, 2008). The current method could be applied to time- and event-based data to describe the natural history of a number of outcomes. This list is not meant to be exhaustive, but rather is intended to convey the large number of clinically relevant phenomena for which MEPSUM could prove valuable.

Limitations

This study has limitations. First, we could only determine the year in which initiation occurred. A more detailed assessment of the age of initiation would allow for a more finegrained analysis. It should be noted, however, that although age of initiation was only recorded on a yearly scale, measurement was likely more precise due to the longitudinal nature of assessment. In addition, the assumption of time as a discrete phenomenon (as opposed to continuous) must often be made in survival analytic frameworks, as it is typically untenable to gather specific event dates and models incorporating long time periods would have convergence problems if individual days were used as event measurements. Second, age of alcohol use initiation was assessed slightly differently across waves, such that at Wave IV, an alcoholic drink was more clearly defined ("glass of wine, can or bottle of beer,

glass of liquor, or a mixed drink") than at Waves I and II. This might lead to variability in interpretation across waves. However, there was consistency in the assessment procedure in that across waves, participants were required to endorse the same quantity and frequency of drinking to be queried regarding their age of initiation. In addition, at Waves I and II, participants were asked to report the age at which they first consumed alcohol when they were not with parents or other adults in their family. Although this question was intended to capture parental supervision, it might exclude individuals who first drank with other adult family members. Finally, this analysis did not incorporate intensive assessment of later-onset substance use phenotypes, thus limiting our ability to speak to progression from initiation toward heavier use and problems.

Notwithstanding limitations, the current study represents a significant advance in our understanding of progression in substance use uptake among adolescents and young adults. Employing a sophisticated analysis and a longitudinal, nationally representative sample, we identify specific patterns of substance use initiation characterized by unique multivariate time-to-event processes. Findings regarding predictors of class membership were consistent with prior research and support convergent validity of the current method. In addition, we detected a novel finding regarding sex differences in the association between delinquency and the timing of first substance use. Results demonstrate the utility of the MEPSUM approach in more fully elucidating developmental pathways of polysubstance involvement and other clinically relevant phenomena.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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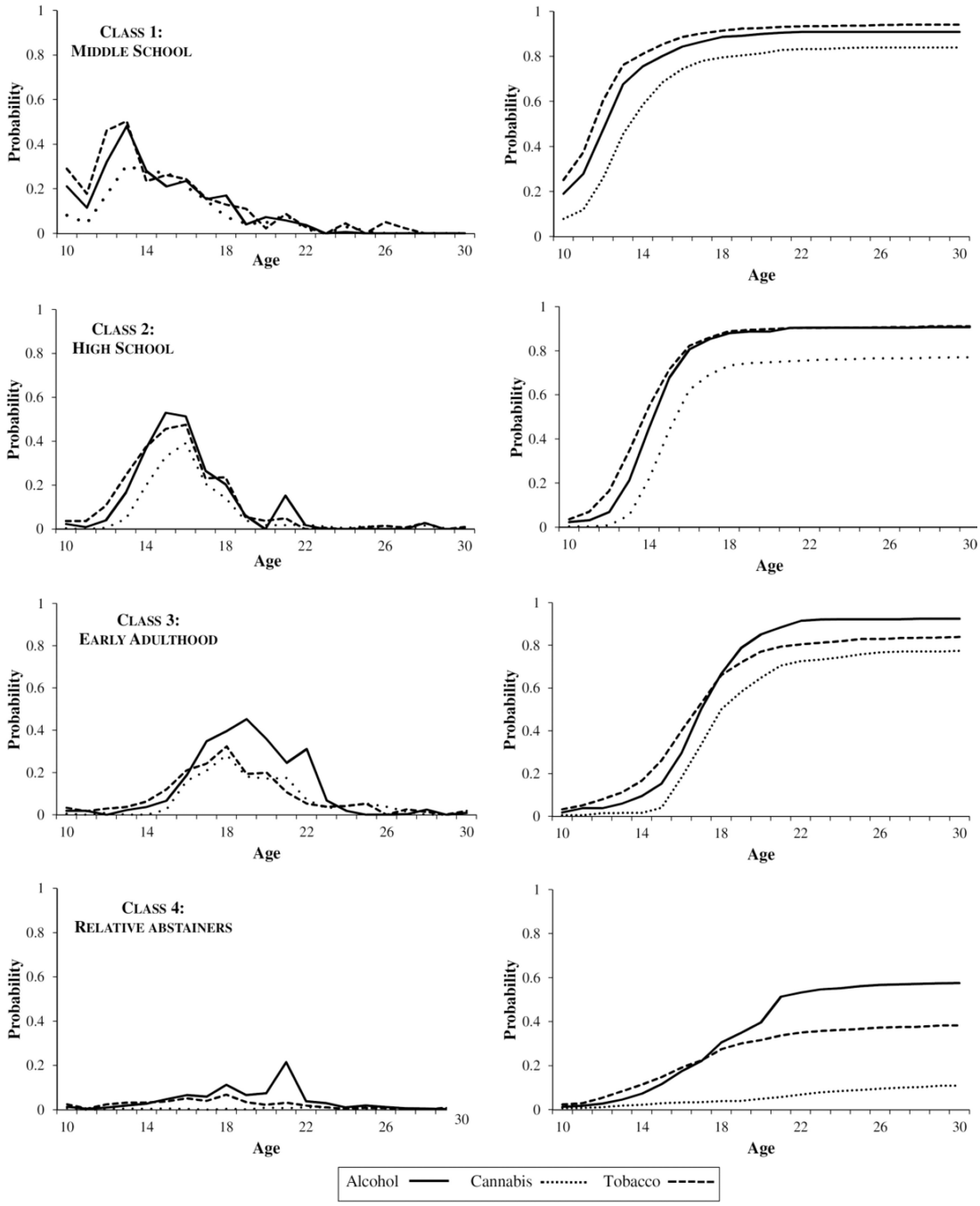

Fig. 1.

Hazard functions (left) and cumulative distributions (right) of substance use initiation as a function of latent class.

Table 1

Model Fit to Data

Latent Classes	-2LL	Free Parameters	AIC	BIC	Entropy
1	−125476.5	63	251079.06	251573.49	
2	−119854.4	127	239962.81	240959.53	0.71
3	−117996.2	191	236374.469	237873.46	0.68
4	−117264.0	255	235037.955	237039.23	0.65
5	−116794.3	319	234226.57	236730.13	0.64
6	−116555.0	383	233876.02	236881.86	0.64

Note. LL = log-likelihood, AIC = Akaike information criterion, BIC = Bayesian information criterion.

Table 2

Means and Prevalences of Substance Use, Demographic Characteristics, Externalizing Psychopathology, and Personality for the Four Latent Classes

	Class 1 (*n*= 2,761)		Class 2 (*n*= 4,585)		Class 3 (*n*= 3,845)		Class 4 (*n*= 7,732)	
	Prev. (%)	Mean (SD)	Prev. (%)	Mean (SD)	Prev. (%)	Mean (SD)	Prev. (%)	Mean (SD)
Substance Use								
Tobacco initiation	99.2	11.8 (1.8)	99.3	14.0 (1.8)	96.0	16.8 (2.9)	73.7	16.6 (4.0)
Alcohol initiation	99.7	12.1 (1.9)	99.5	14.4 (1.5)	99.7	16.3 (2.0)	90.9	18.0 (3.2)
Cannabis initiation	96.9	13.3 (2.2)	93.9	15.3 (1.6)	94.8	18.1 (2.3)	35.7	19.0 (5.5)
Demographics								
Female	44.6	--	50.8	--	48.7	--	54.3	--
Caucasian	60.7	--	60.1	--	53.7	--	40.7	--
Black	14.6	--	15.3	--	20.8	--	28.5	--
Hispanic	16.2	--	16.7	--	15.0	--	18.6	--
Other	8.3	--	7.9	--	10.5	--	12.1	--
Psychopathology								
AUD	34.3	3.5 (2.6)	31.3	3.1 (2.4)	28.7	2.7 (2.2)	5.7	1.7 (1.8)
CUD	21.6	2.6 (2.5)	16.0	2.3 (2.4)	9.8	2.0 (2.2)	0.6	1.8 (1.8)
ND: Overall	27.6	--	19.3	--	12.0	--	3.2	--
Delinquency	--	8.5 (7.6)	--	5.6 (5.5)	--	3.5 (3.8)	--	2.3 (3.1)
Personality								
Extraversion	--	13.6 (3.0)	--	13.5 (3.0)	--	13.3 (3.0)	--	12.7 (3.1)
Agreeableness	--	14.2 (2.9)	--	14.4 (2.8)	--	14.5 (2.8)	--	14.5 (2.7)
Conscientiousness	--	14.3 (2.8)	--	14.6 (2.7)	--	14.6 (2.8)	--	14.8 (2.6)
Neuroticism	--	10.8 (2.9)	--	10.6 (2.8)	--	10.3 (2.7)	--	10.2 (2.7)
Openness	--	14.6 (2.5)	--	14.4 (2.5)	--	14.7 (2.5)	--	14.2 (2.6)

Note. Class 1 = middle school, Class 2 = high school, Class 3 = early adulthood, Class 4 = relative abstainers. AUD = alcohol use disorder, CUD = cannabis use disorder, ND = nicotine dependence. Prev. = prevalence, SD = standard deviation. Prevalence estimates for tobacco, alcohol, and cannabis use indicate the number of individuals who reported having tried each substance. Means for tobacco, alcohol, and cannabis use indicate the age of initiation of each substance. Means for alcohol use disorder, cannabis use disorder, and nicotine dependence indicate the mean number of symptoms endorsed. Means for delinquency and personality variables derived from individuals' raw scores. An overall mean for nicotine dependence symptoms is not displayed as nicotine dependence diagnoses were derived from multiple assessments.

Table 3

Odds Ratios [and Confidence Intervals] of the Influence of Demographics, Externalizing Psychopathology, and Personality on Class Membership

	Sex	**Ethnicity**			
Class	**Female**	**Caucasian**	**Black**	**Hispanic**	**Other**
HS vs. MS	**1.29** [1.09, 1.51]	1.10 [0.88, 1.36]	1.06 [0.79, 1.43]	0.97 [0.73, 1.30]	0.69 [0.46, 1.03]
EA vs. MS	**1.20** [1.01, 1.42]	0.83 [0.65, 1.07]	**1.60** [1.23, 2.07]	0.88 [0.65, 1.21]	0.99 [0.60, 1.65]
RA vs. MS	**1.42** [1.19, 1.68]	**0.47** [0.37, 0.60]	**2.64** [1.93, 3.61]	1.36 [0.92, 2.01]	1.16 [0.73, 1.85]
EA vs. HS	0.93 [0.81, 1.07]	**0.76** [0.64, 0.90]	**1.50** [1.22, 1.85]	0.91 [0.73, 1.13]	**1.45** [1.01, 2.08]
RA vs. HS	1.10 [0.96, 1.27]	**0.43** [0.36, 0.52]	**2.48** [1.88, 3.27]	**1.39** [1.06, 1.83]	**1.69** [1.19, 2.41]
RA vs. EA	**1.18** [1.04, 1.35]	**0.57** [0.46, 0.69]	**1.65** [1.25, 2.20]	**1.53** [1.18, 2.00]	1.17 [0.82, 1.66]

Psychopathology

Class	AUD	CUD	ND	Delinquency
HS vs. MS	0.88 [0.72, 1.09]	**0.77** [0.61, 0.96]	**0.68** [0.57, 0.81]	**0.68** [0.62, 0.74]
EA vs. MS	0.82 [0.66, 1.03]	**0.41** [0.31, 0.56]	**0.40** [0.31, 0.51]	**0.38** [0.33, 0.44]
RA vs. MS	**0.13** [0.10, 0.17]	**0.02** [0.01, 0.04]	**0.10** [0.07, 0.13]	**0.23** [0.20, 0.27]
EA vs. HS	0.93 [0.75, 1.17]	**0.54** [0.41, 0.71]	**0.59** [0.46, 0.75]	**0.57** [0.50, 0.65]
RA vs. HS	**0.15** [0.12, 0.19]	**0.02** [0.01, 0.05]	**0.14** [0.11, 0.18]	**0.33** [0.28, 0.39]
RA vs. EA	**0.16** [0.12, 0.21]	**0.04** [0.02, 0.08]	**0.24** [0.18, 0.32]	**0.59** [0.52, 0.67]

Big Five Personality Dimensions

Class	Extraversion	Agreeableness	Conscientiousness	Neuroticism	Openness
HS vs. MS	0.97 [0.89, 1.07]	**1.11** [1.01, 1.22]	**1.14** [1.04, 1.26]	**0.89** [0.81, 0.99]	0.96 [0.87, 1.06]
EA vs. MS	0.92 [0.83, 1.01]	**1.15** [1.06, 1.23]	**1.10** [1.01, 1.20]	**0.82** [0.73, 0.91]	**1.10** [1.004, 1.21]
RA vs. MS	**0.74** [0.67, 0.81]	**1.15** [1.04, 1.28]	**1.21** [1.08, 1.34]	**0.82** [0.75, 0.90]	**0.85** [0.77, 0.95]
EA vs. HS	0.94 [0.87, 1.03]	1.03 [0.96, 1.11]	0.97 [0.89, 1.04]	**0.91** [0.84, 0.99]	**1.15** [1.05, 1.25]
RA vs. HS	**0.76** [0.70, 0.83]	1.04 [0.95, 1.13]	1.05 [0.98, 1.14]	**0.91** [0.86, 0.98]	**0.89** [0.81, 0.97]
RA vs. EA	**0.81** [0.74, 0.87]	1.00 [0.92, 1.09]	**1.09** [1.003, 1.19]	1.00 [0.93, 1.09]	**0.77** [0.71, 0.85]

Note. HS = high school, MS = middle school, EA = early adulthood, RA = relative abstainer. AUD = alcohol use disorder, CUD = cannabis use disorder, ND = nicotine dependence. Odds ratios for delinquency and the Big Five personality dimensions are calculated as a function of a one standard deviation change in delinquency and personality, respectively. Confidence intervals computed with a Bonferroni correction for multiple comparisons with $\alpha = .05$. Bold values indicate significant odds ratios at $\alpha = .05$.