

# Latent Trajectory Classes for Alcohol-Related Blackouts from Age 15 to 19 in ALSPAC

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**Background:** Alcohol-related blackouts (ARBs) are reported by ~50% of drinkers. While much is known about the prevalence of ARBs in young adults and their cross-sectional correlates, there are few prospective studies regarding their trajectories over time during mid-adolescence. This paper reports latent trajectory classes of ARBs between age 15 and 19, along with predictors of those patterns.

**Methods:** Latent class growth analysis (LCGA) was used to evaluate the pattern of occurrence of ARBs across 4 time points for 1,402 drinking adolescents from the Avon Longitudinal Study of Parents and Children (ALSPAC). Multinomial regression analyses evaluated age-15 demography, substance-related items, externalizing characteristics, and estimated peer substance use as predictors of latent class membership.

**Results:** ARBs were reported at age 15 in 30% and at age 19 in 74% of these subjects. Four latent trajectory classes were identified: Class 1 (5.1%) reported no blackouts; for Class 2 (29.5%), ARBs rapidly increased with age; for Class 3 (44.9%), blackouts slowly increased; and for Class 4 (20.5%), ARBs were consistently reported. Using Class 2 (rapid increasers) as the reference, predictors of class membership included female sex, higher drinking quantities, smoking, externalizing characteristics, and estimated peer substance involvement (pseudo  $R^2 = 0.22$ ).

**Conclusions:** ARBs were common and repetitive in these young subjects, and predictors of their trajectories over time involved multiple domains representing diverse characteristics.

**Key Words:** Alcohol, Blackouts, Predictors, Latent Trajectories.

PATTERNS OF ALCOHOL intake vary dramatically over the lifespan, with the heaviest drinking and steepest trajectory of increasing alcohol problems typically observed in the mid-teens to mid-20s (Brown et al., 2008; Mason and Spoth, 2012; Schuckit et al., 2014). In the United States, a person's first drink is likely to occur at about age 15, and by age 18, 70% of people have consumed alcohol, 35% were ever intoxicated, and 24% admitted to consuming 5 or more drinks on an occasion (Johnston et al., 2013). It has been estimated that the first drink in the United Kingdom may occur closer to age 14, with 70% of students in that age range having consumed alcohol (Bremner et al., 2011; Gould,

2009; Hibell et al., 2004). Thus, heavy drinking during adolescence may be especially prominent in the United Kingdom, which ranks near the top among 35 European countries regarding several measures of drunkenness (Hibell et al., 2004).

A common alcohol-related adverse consequence is an alcohol-related blackout (ARB), defined as not being able to remember parts (fragmentary) or entire periods (en bloc) of events that occurred while drinking and awake (Hartzler and Fromme, 2003; Rose and Grant, 2010). Almost 50% of drinkers, including college students, have ever experienced an ARB (Barnett et al., 2014; Mundt and Zakletskaia, 2012; Nelson et al., 2004), as have 80% of individuals with alcohol use disorders (AUDs) (Raimo et al., 1999). The high rate of blackouts in people with AUDs prompted the inclusion of these phenomena in alcohol questionnaires and interviews (Seltzer, 1990), but their prevalence in non-AUD drinkers resulted in their omission from most AUD diagnostic criteria (American Psychiatric Association, 1994).

Blood alcohol concentrations (BACs)  $>0.300$  g/dl are associated with a 60% rate of ARBs, especially for en bloc events, although fragmentary blackouts are observed with BACs as low as  $\geq 0.06$  g/dl (Hartzler and Fromme, 2003; Rose and Grant, 2010; Wetherill and Fromme, 2009). Higher drinking frequencies also relate to blackouts, perhaps reflecting their association with higher quantities (Jennison and Johnson, 1994; LaBrie et al., 2011; Mundt et al., 2012). In addition, the rate of ARBs may be higher in individuals

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consuming other drugs that affect brain functioning (Hartzler and Fromme, 2003). Thus, alcohol quantities and frequencies and the use of substances other than alcohol are important characteristics to consider as predictors of ARBs.

Individuals with prior ARBs are more likely to demonstrate similar phenomena when administered alcohol in a laboratory (i.e., might have a predisposition toward experiencing memory lapses with alcohol), and ARBs are more common in individuals with alcoholic relatives, with estimated heritabilities of ~50% (Goodwin, 1971; Nelson et al., 2004; Pressman and Caudill, 2013). The genetic component of ARBs may operate through several intermediate characteristics including the genetically influenced phenotype of a low level of response (low LR) to alcohol (Schuckit, 2014; Schuckit et al., 2008, 2011), which is associated with higher drinking quantities per occasion. The low LR, a genetically influenced characteristic that predates heavy drinking and associated ARBs, has been noted to potentially relate to blackouts (Heath et al., 1999; Schuckit, 2014; Wetherill and Fromme, 2009), but has not been extensively evaluated as a predictor of future alcohol-related memory lapses.

Additional characteristics potentially correlated with ARBs include: male sex (Jennison and Johnson, 1994), externalizing behaviors (e.g., impulsivity, sensation seeking, and a lack of conscientiousness) (Jennison and Johnson, 1994; Sher et al., 2000; Wetherill et al., 2012; White et al., 2002), and having friends who engage in heavy drinking and drug use (LaBrie et al., 2011; Rose and Grant, 2010). Thus, a person's demography, externalizing personality characteristics, and substance use among peers are also characteristics to consider when studying the onset and course of blackouts.

Relatively few prospective studies have evaluated predictors of the pattern of occurrence of ARBs over time. We reported a 10-year follow-up of 230 drinking 20-year-old nonalcoholic males, noting that those who subsequently developed ARBs drank more heavily and frequently at baseline and were more likely to develop AUDs during the follow-up (Anthenelli et al., 1994). Jennison and Johnson (1994) evaluated data at 2 points over 4 years for drinking 19- to 26-year-old men and women, reporting that ARBs were related to earlier onsets of drinking, higher alcohol quantities, alcoholic relatives, and smoking. Subjects who had blackouts at baseline had a 68% chance of experiencing ARBs during the follow-up, with chronicity related to male sex and higher baseline alcohol intake and problems. A third longitudinal study of heavy drinkers reported that a history of 6+ lifetime ARBs was related to a 2-fold higher future risk of seeking treatment in emergency rooms (Mundt et al., 2012).

While there are plentiful data regarding the high prevalence and retrospective correlates of blackouts, few studies have followed the course of these problems over multiple time points or have used latent trajectory analyses to search for predictors of patterns of ARBs over time. Also, few studies have focused on ARBs during a period of rapidly increasing heavy drinking and problems, the mid- to late-teens. The

current study prospectively evaluated patterns of ARBs and their predictors from age 15 to 19 to test 4 hypotheses: (i) the proportion of subjects reporting alcohol-related memory lapses will increase with age; (ii) there will be multiple trajectories of the occurrence of blackouts over time; (iii) characteristics from multiple domains will predict different latent ARB trajectories; and (iv) reflecting how a low LR relates to heavier drinking, a low LR will predict a greater likelihood of reporting ARBs.

## MATERIALS AND METHODS

### *Subjects*

Following approval from the Avon Longitudinal Study of Parents and Children (ALSPAC) Ethics Committee and a local Research Ethics Committee, in 1991, the protocol was initiated to identify and follow a population cohort born in the Avon valley near Bristol, England (Boyd et al., 2013; Fraser et al., 2013; Heron et al., 2013). The goal was to enroll singleton children of 14,541 pregnant women between April 1, 1991, and December 31, 1992. Eight thousand children were randomly selected at age 7 to continue with face-to-face evaluations approximately every 18 months. The current analyses focus on offspring who had ever consumed at least 1 full alcoholic drink by age 15, completed the Self-Report of the Effects of Alcohol (SRE) questionnaire to measure LR, and participated in at least 2 assessments between age 15 and 19. Among these, 552 had data at all 4 assessments, 509 had 3, and 341 completed 2 assessments.

### *Baseline Measures*

Demographic characteristics and alcohol-related data at baseline (age 15) were gathered through questions from the overall ALSPAC protocol, using queries that were not specifically designed for the current analyses. The structured questionnaire included items from the Semi-Structured Assessment for the Genetics of Alcoholism interview (Hesselbrock et al., 1999), including alcohol quantities (8 g of ethanol [EtOH] per U.K. standard drink) and frequencies (recording the number reported), as well as the occurrence of ARBs. Baseline drug-related items included the times having smoked tobacco and times used cannabis. Blackouts were defined as a drinking situation "where you couldn't remember things" or being "unable to remember what happened the night before," with answers coded in some assessments as 0, 1 (1 to 2 times), or 2 (3+ times), and in other assessments on a 5-point scale of 0 (never), 1 (1 to 2 times), 2 (monthly), 3 (weekly), or 4 (almost daily). The measure common across the diverse scales used at different assessments is whether or not ARBs had occurred, which is the focus of our analyses.

Baseline externalizing measures included a Conduct Scale of 15 prior-year childhood antisocial items from the Edinburgh Study of Youth Transitions and Crime (Cronbach  $\alpha = 0.82$  in these analyses) scored 1 (not at all) through 4 (6+ times) (Barker and Maughan, 2009). Extroversion and Conscientiousness subscales of the International Personality Item Pool form of the NEO 5-Factor Personality Inventory (IPIP-NEO) ( $\alpha = 0.84$  and 0.76, respectively) were scored from 1 (not like me) through 5 (very like me) (Heron et al., 2013), and the modified 11-item Arnett Sensation Seeking Scale ( $\alpha = 0.65$ ) was scored from 1 (not like me) to 4 (very like me) (Arnett, 1994). Finally, in 3 separate questions, subjects estimated the proportions of current peers using alcohol, drugs, and tobacco, with possible scores for each substance of 1 (none), 2 (some peers), or 3 (most or all peers), as adapted from the Important People and Activities Scale (Longabaugh et al., 2001).

The LR to alcohol was measured from the SRE questionnaire. The scores used in these analyses reflected the subject's estimate of the number of standard drinks needed for up to 4 effects they actually experienced the first 5 times of drinking. These included the following: drinks required to first feel any effect; drinks needed to slur speech; drinks to produce gait unsteadiness; and the number of drinks associated with unwanted falling asleep (Schuckit et al., 2008, 2009). The SRE5 score for the first 5 times of drinking is the sum of the number of drinks for up to 4 effects, divided by the number of effects experienced (i.e., the average number drinks across the effects). For the SRE, Cronbach  $\alpha$  is 0.81 (all 4 items) to 0.91 (for the first 3 items only), 1-year retest reliability = 0.82, while SRE and alcohol challenge-based LRs overlap 0.60 in predicting future drinking problems (Schuckit et al., 2009).

### Analyses

Class membership probabilities were generated by the computer program for latent class growth analysis (LCGA) based on the maximum likelihood estimates approach in Mplus (Muthén and Muthén, 2006). Regarding identifying the appropriate number of classes, this decision process was guided by the following criteria for when to stop adding another class: stop when the bootstrap likelihood ratio test (BLRT) became noncontributory, and/or the Bayesian information criterion (BIC) stopped decreasing, and the classes became difficult to interpret (Jung and Wickrama, 2008; Nagin and Tremblay, 2001; Schwartz, 1978). Next, consistent with a recent report (Schuckit et al., 2014), baseline characteristics were used as predictors of class membership, rather than as covariates, by evaluating differences in predictors across latent trajectory classes using chi-square test ( $\chi^2$ ) and analysis of variance (ANOVA) in a process carried out outside the LCGA. Finally, baseline items that were different across classes were entered into a simultaneous entry multinomial logistic regression analysis, with continuous items  $z$ -scored to facilitate comparisons of odds ratios (ORs) across items.

## RESULTS

The sample from the age-15 evaluation included 5,180 individuals who were part of the core follow-up sample, after excluding siblings. Among these, 2,609 did not indicate drinking before age 15 and did not fill out an SRE. Of the remaining 2,571 subjects, 578 did not have at least 1 of the 3 possible follow-up assessments age 16 to 19; 367 gave incomplete or uninterpretable answers on the SRE; 224 were missing 1 or more key baseline predictors. This created a sample of 1,402 individuals. As shown in the first data column of Table 1, 60% were female and 98% had a European ethnicity. At baseline, they estimated an average of 3 U.K. standard drinks with a maximum of 10, consuming alcohol an average of 18 times annually. The average SRE5 score was 4.9 U.K. drinks (3.9 U.S. drinks). Almost 20% had used cannabis, and 44% had ever smoked tobacco. Externalizing characteristics included an average score of 22.3 on the Conduct Scale (range 15 to 60), and while the table lists average IPIP-NEO Externalizing scale scores, these are not standardized. Finally, the subjects reported 1.85 to 2.82 average values (possible scores of 1 to 3) as estimates of peer alcohol, drugs, and tobacco use.

The proportions of subjects who had experienced ARBs at baseline and during each follow-up interval are presented

in Table 2. In the 2 years prior to age 15, almost 30% experienced an ARB, with the proportion per interval increasing over the subsequent years. Increases over time were observed for the 991 subjects who reported no baseline blackouts, including higher rates from 16 through 19. The only exception to this pattern was seen for the 411 individuals who had at least 1 ARB at baseline, for whom the proportion with blackouts decreased from age 15 to 16, but then increased from age 16 to 19. While not shown in the table, between age 15 and 19, the usual drinks per occasion increased 68.6%,  $F(3, 4,203) = 510.64$ ,  $p < 0.001$ .

Figure 1 presents the results of an LCGA that identified 4 latent trajectory classes for the occurrence of ARBs across time. The 71 subjects (5.1%) in Class 1 consistently reported no blackouts; in Class 2, 414 individuals (29.5%) demonstrated a rapidly increasing trajectory of ARBs; the 630 adolescents (44.9%) in Class 3 had a gradual increasing trajectory; the 287 members of Class 4 (20.5%) were likely to report ARBs at every time point. The LCGA fit statistics were as follows: for a 1-class solution, BIC = 5,733 and mean posterior probability = 1.00; for a 2-class solution, BIC = 5,269 with mean posterior probabilities of 0.95 for Class 1 and 0.85 for Class 2, and BLRT = 458.23,  $p < 0.0001$ ; for a 3-class solution, BIC = 5,287, mean posterior probabilities = 0.65 for Class 1, 0.80 for Class 2, and 0.92 for Class 3, and BLRT = 30.10,  $p < 0.0001$ ; for a 4-class solution, BIC = 5,273, mean posterior probabilities were 0.56 for Class 1, 0.77 for Class 2, 0.79 for Class 3, and 0.75 for Class 4, and BLRT = 8.46,  $p < 0.0001$ ; and evaluation of a 5-class solution created a fifth class with only 18 members and BLRT = 0.29,  $p = 1.00$ . These fit statistics supported 4 classes.

The remaining columns of Table 1 describe how baseline characteristics related to the 4 latent classes. Focusing on age-15 items for which the  $F$ -test or the chi-square test indicated differences across the 4 classes, members of Class 1 (no ARBs) reported lower baseline alcohol quantities and frequencies and the need for the fewest drinks for effects on the SRE (i.e., had high LRs per drink). The teens in Class 1 were the least likely to smoke or use cannabis, had the lowest values for Conduct, Extroversion, and Sensation Seeking, as well as the highest Conscientiousness, and reported the lowest peer substance use. Class 4 members (consistent ARBs) had the highest: proportion of females, drinking quantities and frequencies, SRE5 scores (lowest LR per drink), personal substance use, and externalizing characteristics, as well as the highest peer substance use. At age 15, having had an ARB correlated with maximum drinks at 0.33 ( $p < 0.001$ ).

Class 2 (rapid increase) is of interest because the rate of ARBs resembled Class 1 at baseline, but thereafter members of this class had an ARB trajectory similar to Class 4. At age 15, Class 2 subjects differed from members of Class 1 by demonstrating higher alcohol quantities, alcohol frequencies, SRE values (lower LRs per drink), proportion of smokers, Conduct scores, Extroversion scores, and estimated peer

**Table 1.** Baseline (Age-15) Characteristics for the Full Sample of 1,402 Drinking ALPSAC Adolescents and for Each Latent Trajectory Class Regarding Alcohol-Related Blackouts (ARBs) from Age 15 to 19

Variables	All subjects 1,402	Class 1 "no ARBs" 71 (5.1%)	Class 2 "rapid increase" 41.4 (29.5%)	Class 3 "gradual increase" 630 (44.9%)	Class 4 "consistent ARBs" 287 (20.5%)	Tukey's HSD <i>p</i> -values															
						1 vs. 2	1 vs. 3	1 vs. 4	2 vs. 3	2 vs. 4	3 vs. 4										
<b>Demographics</b>																					
Sex (female %)	59.7	60.6	56.0	57.1	70.4																
Age mean $\pm$ SD	15.5 (0.29)	15.5 (0.32)	15.5 (0.24)	15.5 (0.28)	15.6 (0.33)																
European (%)	98.0	97.2	99.5	97.1	97.9																
Alcohol mean $\pm$ SD																					
Usual quantity (6 months)	3.4 (2.71)	2.3 (1.86)	3.2 (2.40)	3.0 (2.45)	5.0 (3.26)																
Maximum drinks (2 years)	9.9 (6.42)	6.5 (4.50)	9.1 (5.88)	9.1 (6.30)	13.4 (8.50)																
Usual frequency (2 years)	36.3 (32.52)	21.0 (23.44)	33.0 (29.85)	31.2 (30.51)	56.1 (34.49)																
LR (SRE5)	4.9 (2.07)	4.0 (1.89)	4.7 (1.96)	4.7 (2.14)	5.7 (1.91)																
Drugs (% lifetime)																					
Cannabis	19.1	5.6	12.5	15.1	39.0																
Tobacco	44.0	23.9	37.2	39.1	71.8																
Externalizing mean $\pm$ SD																					
Conduct scale	22.3 (6.42)	19.6 (3.91)	22.1 (6.72)	21.7 (5.94)	24.7 (6.86)																
NEO: Extroversion	36.6 (6.37)	35.2 (6.55)	37.33 (6.20)	35.6 (6.48)	38.2 (5.85)																
NEO:	31.1 (5.72)	32.7 (5.55)	31.5 (5.34)	31.4 (5.72)	29.3 (5.93)																
Conscientiousness																					
Arnett sensation seeking	29.9 (4.93)	28.5 (4.93)	30.0 (4.96)	29.5 (4.85)	30.7 (4.92)																
Peer substance use mean $\pm$ SD																					
Number used alcohol	2.82 (0.40)	2.69 (0.50)	2.84 (0.39)	2.77 (0.43)	2.93 (0.26)																
Number used drugs	1.85 (0.66)	1.51 (0.61)	1.76 (0.62)	1.79 (0.66)	2.18 (0.63)																
Number used tobacco	2.22 (0.59)	1.92 (0.57)	2.18 (0.56)	2.17 (0.60)	2.47 (0.54)																

ALPSAC, Avon Longitudinal Study of Parents and Children; honestly significant difference; SD, standard deviation; LR, level of response to alcohol, as measured by SRE5; SRE5, Self-Report of Effects of Alcohol Scale, first -5 times drunk.

NEO = International Personality Item Pool (IPIP) Representation of the NEO PI-R questionnaire. Conduct Scale = Conduct Problem Subscale of the Strengths and Difficulties Questionnaire (15 items on 4-point scale from not at all to 6+ times). Peer substance use = Perceptions of proportion of peers who use alcohol, illicit drugs, and tobacco (3-point scale where 1 = none, 2 = some, 3 = most or all).

<sup>c</sup>*p* < 0.001.

**Table 2.** Percentage with Blackouts for 1,402 Subjects at Each Age

	Age				Cochran's <i>Q</i> comparing ages		
	15	16	18	19	15 to 19	16 to 19	15 to 16
All subjects <i>N</i> = 1,402	29.3	57.4	69.3	74.2	926.77 <sup>c</sup>	168.08 <sup>c</sup>	267.65 <sup>c</sup>
No baseline blackout <i>N</i> = 991	00.0	49.1	64.0	69.8	1350.16 <sup>c</sup>	163.41 <sup>c</sup>	487.00 <sup>c</sup>
Yes baseline blackout <i>N</i> = 411	100.0	77.4	82.2	84.7	128.13 <sup>c</sup>	12.50 <sup>b</sup>	93.00 <sup>c</sup>

<sup>b</sup>*p* < 0.01, <sup>c</sup>*p* < 0.001.

substance use. Members of Class 2 and 3 only differed regarding higher Extroversion and peer drinking for Class 2.

We next evaluated how each of the most relevant 14 baseline predictors of class membership performed in the context of the others, using simultaneous entry multinomial regression analyses with all other classes compared to the rapidly increasing trajectory of Class 2. Table 3 demonstrates that Class 4 (consistent ARBs) had the greatest number of differences from Class 2, with higher ORs for female sex, baseline alcohol-use patterns and smoking, lower Conscientiousness, and higher estimated peer drug use. Compared to Class 2, Class 3 (gradual increase) demonstrated lower Extroversion and assumed peer drinking. The only item to enter the regression for predicting Class 1 (no ARBs) compared to Class 2 (rapid increase) was lower Extroversion for Class 1.

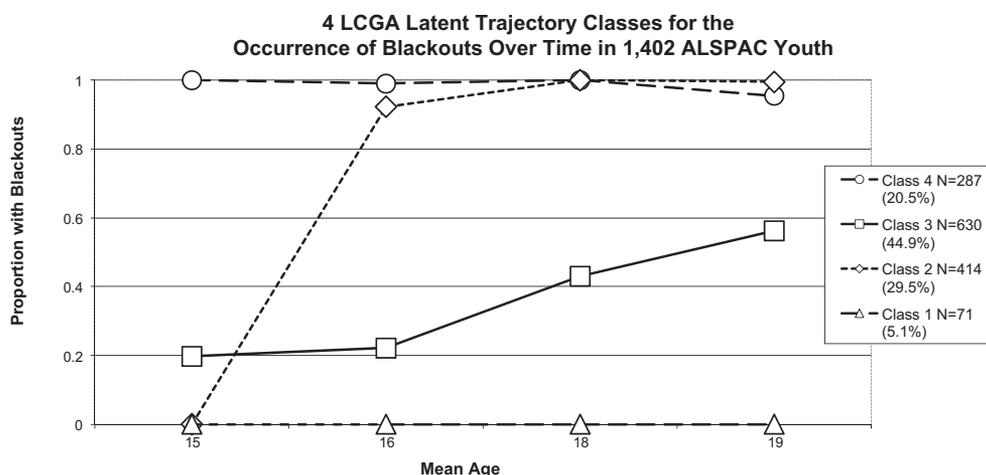
Regarding Hypothesis 4, LR did not add to the regression. However, recognizing the close link between LR and baseline drinking quantities, we repeated the regression analysis after deleting alcohol quantity measures. The result was LR now contributed to the regression (*p* = 0.003), with OR = 1.32

(1.10 to 1.57) for Class 4 (consistent ARBs) versus Class 2 (rapid increase).

Finally, we noted that the pattern of predictors in Tables 1 and 3 may reflect quantitative differences across classes regarding baseline alcohol-related characteristics, externalizing measures, and assumed peer substances use patterns. To evaluate this further, separate factor analyses yielded single factor solutions for each of these domains with eigenvalues (and variance percentage) of 2.34 (58.6%) for drinking measures, 1.27 (42.4%) for externalizing, and 1.78 (59.2%) for estimated peer substance use. These 3 factors were correlated (*p* < 0.001): alcohol with externalizing = 0.35, alcohol with peer = 0.40, and externalizing with peer = 0.40. A second-order factor analysis yielded a single factor with eigenvalue = 1.77 (59.0%). A 1-way ANOVA across the 4 trajectory classes with the second-order factor scores as the dependent variable yielded, *F*(3, 1,398) = 85.62, *p* < 0.001, with *z*-score means and standard deviations (SD) of: Class 1 = -0.73 (0.70), Class 2 = -0.10 (0.91), Class 3 = -0.19 (0.97), and Class 4 = 0.73 (0.87). Tukey's HSD post hoc values were *p* < 0.001 for all pairs except for Classes 2 and 3.

## DISCUSSION

These evaluations focused on prospective latent trajectory analyses of patterns and predictors of ARBs over time beginning at age 15. Here, 75% of the drinkers reported blackouts at age 19, a prevalence higher than the 50% lifetime rate in U.S. general population and college samples (Barnett et al., 2014; Mundt and Zakletskaia, 2012; Nelson et al., 2004; White et al., 2002). This high ARB prevalence in ALSPAC is consistent with a report that the United Kingdom ranks high regarding the proportion of adolescents who have been intoxicated 20+ times (Hibell et al., 2004). Results may also reflect our requirement that subjects drank alcohol by age 15, as earlier onset drinking is associated with higher rates of



**Fig. 1.** The resulting latent class trajectory analysis (LCGA), 4 latent trajectory classes based on blackouts over time. Class 1 (no ARBs) *N* = 71 (5.1%), Class 2 (rapid increase) *N* = 414 (29.5%), Class 3 (gradual increase) *N* = 630 (44.9%), and Class 4 (consistent ARBs) *N* = 287 (20.5%). ALSPAC, Avon Longitudinal Study of Parents and Children; ARB, alcohol-related blackouts.

**Table 3.** Odds Ratios (with 95% Confidence Intervals) Using Age-15 Predictors of Trajectory Classes and Simultaneous Entry Multinomial Regression: Comparing Class 1, 3, and 4 with Class 2 as the Reference<sup>e</sup>

	1	3	4
Demography			
Sex			2.31 (1.59 to 3.37) <sup>c</sup>
Alcohol			
Usual quantity (6 month)			1.23 (1.03 to 1.47) <sup>a</sup>
Maximum drinks (2 years)			1.26 (1.02 to 1.56) <sup>a</sup>
Usual frequency (2 years)			1.36 (1.12 to 1.64) <sup>b</sup>
LR (SRE5)			
Drugs (% Lifetime)			
Cannabis 5+ times Smoke			1.65 (1.10 to 2.46) <sup>a</sup>
Externalizing			
Conduct scale			
NEO: Extroversion	0.78 (0.60 to 1.00) <sup>d</sup>	0.76 (0.66 to 0.87) <sup>c</sup>	
NEO: Conscientiousness			0.84 (0.70 to 0.99) <sup>a</sup>
Sensation seeking			
Peer substance use			
Number used alcohol		0.87 (0.76 to 0.99) <sup>a</sup>	
Number used drugs			1.36 (1.09 to 1.70) <sup>b</sup>
Number used tobacco			
Pseudo $R^2 = 0.22$			

LR, level of response; SRE5, Self-Report of Effects of Alcohol Scale, first ~5 times drank.

Items are as defined in Table 1.

<sup>e</sup>Continuous variables were z-scored, so Odds Ratios are comparable.

<sup>a</sup> $p < 0.05$ , <sup>b</sup> $p < 0.01$ , <sup>c</sup> $p < 0.001$ , <sup>d</sup> $p = 0.06$ .

later alcohol problems (Grant and Dawson, 1997); although by age 14, 70% of U.K. students reported drinking (Bremner et al., 2011; Hibell et al., 2004).

Our current results support Hypothesis 1 (proportions of subjects with ARBs will increase over time). As shown in Table 2, the proportions with ARBs increased over the 4 years for both subjects with and without ARBs at baseline. Such increases parallel the rapid increase in consumption levels likely to begin in mid-adolescence reported in most epidemiological studies (e.g., Brown et al., 2008; Johnston et al., 2013; Mason and Spoth, 2012; Schuckit et al., 2014). The current report and prior studies (Jennison and Johnson, 1994; Rose and Grant, 2010; Wetherill and Fromme, 2009) indicate a close link between higher quantities and ARBs, with some moderation through genetic influences and other characteristics (Goodwin, 1971).

Hypothesis 2, predicting heterogeneous patterns of blackouts over time, was supported by the LCGA. This procedure yielded 4 classes, including subjects with close to no ARBs; those with blackouts at every evaluation; those, who despite no ARBs at 15, were likely to experience blackouts at all follow-ups; and subjects with few members who reported early alcohol-related memory impairments, for whom the propor-

tion gradually increased to 60%. This heterogeneity is similar to what has been reported for alcohol use and problems across mid- to late-adolescence and early adulthood (Colder et al., 2002; Schuckit et al., 2014), but the application of this pattern to blackouts has not been previously well studied in mid-adolescence.

As projected in Hypothesis 3, the prediction of these latent trajectory classes required information from multiple domains. Among the age-15 items relevant to 5 potential domains of predictors (demography, alcohol-related items [including LR], additional substance use, externalizing characteristics, and estimated peer substance use), 14 differentiated across the latent classes. The data in Table 1 indicated that members of Class 2 (rapid increase) and Class 3 (gradual increase) demonstrated 14 baseline characteristics midway between Class 1 (no ARBs) and Class 4 (consistent ARBs) regarding age-15 domains. When these 14 items were entered in the multinomial logistic regression analysis predicting latent class membership, a pseudo  $R^2$  of 0.22 was generated, with separate contributions from at least 1 characteristic from each of these predictor domains. These represent the types of items highlighted in the Introduction as reflected in prior cross-sectional analyses (LaBrie et al., 2011; Rose and Grant, 2010; Wetherill et al., 2012; White et al., 2002).

While Classes 2 and 3 had age-15 characteristics that distinguished them from the extreme high and low classes, few items differentiated between Class 2 and 3. However, the LCGA fit statistics supported a 4-class solution over a 3-class result. The data in Tables 1 and 3 point to higher Extroversion and estimated peer substance use at age 15 that may have contributed to the more rapid increase in the proportion of members with blackouts in Class 2. The combination of being outgoing and sociable with having many drinking friends may have made subjects in Class 2 especially vulnerable to heavy drinking episodes that contributed to the high BACs associated with ARB by age 16. However, the few items that contributed to Class 3 versus 2 membership, along with the modest pseudo  $R^2$  for the multinomial logistic regression analyses, highlight the fact that there may be other important age-15 predictors of the trajectories of blackouts that were not available through the ALSPAC protocol. These might include family histories of alcohol problems and/or ARBs, low levels of parental supervision, and/or the absence of positive feelings toward parents, high life stresses, and using alcohol to cope with stress, each of which might characterize Class 2.

Of special note was the high proportion of females in Class 4 (consistent ARBs). Contrary to most prior studies (Jennison and Johnson, 1994; White et al., 2002), the current data may reflect a secular trend for increasing alcohol use and problems in females compared to males, as well as reports that with similar alcohol intake females have higher BACs and potentially greater alcohol-related complications (Johnston et al., 2013; Mann et al., 2005).

Hypothesis 4 predicted that a low LR would relate to a pattern of higher ARBs, perhaps although the link between

a low LR and heavier drinking per occasion (Heath et al., 1999; Schuckit, 2014; Wetherill and Fromme, 2009). Support for this hypothesis is seen in the univariate analyses in Table 1 where the highest number of drinks needed for effects on the SRE (lowest LR per drink) was observed for Class 4 (consistent ARBs) and the lowest drinks needed for effects for Class 1 (no ARBs). However, in Table 3, LR did not add to the prediction of latent trajectory classes when considered in the presence of alcohol quantity measures. Prior studies indicated that the relationship between low LR and alcohol-related problems operates primarily through an effect of LR on drinking quantities, as observed in subjects as young as age 12 (Schuckit et al., 2011, 2014). In the absence of age-15 quantity measures, LR entered the regression equation without any change from the pseudo  $R^2$  reported in Table 3. Thus, it is likely that the impact of a low LR on future blackouts overlapped with drinking quantities.

There are several practical implications of the current findings. First, clinicians and parents should be aware that in the large majority of these young subjects, ARBs were not isolated events. Thus, caregivers and parents, as well as young drinkers themselves need to learn that ARBs indicate relatively high BACs that are in turn related to dangers of escalating alcohol problems. Because alcohol-related memory lapses can be seen so early in the drinking history, there may be potential benefits of using brief motivational interviewing (Terlecki et al., 2010) to attempt to decrease future alcohol-related problems. The link between ARBs and the low LR to alcohol in Table 1 may indicate that the LR-based prevention program recently described for 18-year-olds may be worth testing in young drinkers who demonstrate ARBs (Schuckit et al., 2012). Also, information about the high BACs associated with ARBs, the potential risks for embarrassing behaviors, and possible poor judgment regarding unsafe sex and alcohol-related accidents with intense intoxication should become prominent components of all alcohol education–prevention programs with young drinkers.

While the current sample is relatively large, the data prospective and latent trajectory classes for ARBs have not been previously studied in this age group, the results must be considered in light of relevant caveats. First, the data were gathered through a prospective study that was not originally structured to focus on ARBs. As a result, the ALSPAC blackout question was not consistently coded as the actual number of ARBs experienced, and there was no distinction between fragmentary and en bloc phenomena. Related problems include that only a limited number of predictors were available from the age-15 evaluation, and a family history of AUDs was not consistently recorded in ALSPAC. Second, while data were evaluated as standard drinks, these are only estimates, as the grams of EtOH per drink can differ in different beverages and settings. Third, the subjects were almost exclusively of European origin and came from a single region in the United Kingdom. Fourth, to be eligible for consideration of ARBs in these prospective analyses, partici-

pants had to have consumed alcohol by age 15, raising questions of whether similar results would be seen in other populations or if baseline nondrinkers are included in the follow-up. Fifth, LCGA was used because it is appropriate for binary outcomes, relatively easy to interpret, can be applied to modest sized populations and has relatively few problems with convergence and model stability, but this approach might unrealistically constrain variance within classes. In addition, questions have been raised regarding whether latent trajectory analyses can do more than just describe patterns of variation over time and they may not be able to identify groups that reflect inherent fundamental attributes (Sher et al., 2011). Furthermore, reflecting our desire to help clinicians better predict future patterns of alcohol problems in 15-year-olds, baseline characteristics that are often handled as covariates in LCGA were used as predictors of trajectories in the current analyses. Thus, the trajectories reported here may look different than those seen with the typical approach to LCGA. Finally, the pseudo  $R^2$  reported from the multinomial regression was modest, and pseudo  $R^2$ s are not historically as meaningful as  $R^2$ s generated from continuous outcomes.

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## REFERENCES

- American Psychiatric Association (1994) Diagnostic and Statistical Manual of Mental Disorders. 4th ed. American Psychiatric Press, Washington, DC.

- Anthenelli RM, Klein JL, Tsuang JW, Smith TL, Schuckit MA (1994) The prognostic importance of blackouts in young men. *J Stud Alcohol* 55: 290–295.
- Arnett J (1994) Sensation seeking: a new conceptualization and a new scale. *Personality Individ Differ* 16:289–296.
- Barker ED, Maughan B (2009) Differentiating early-onset persistent versus childhood-limited conduct problem youth. *Am J Psychiatry* 166:900–908.
- Barnett NP, Clerkin EM, Wood M, Monti PM, Tevyaw TO, Corriveau D, Fingeret A (2014) Description and predictors of positive and negative alcohol-related consequences in the first year of college. *J Stud Alcohol Drugs* 75:103–114.
- Boyd A, Golding J, Macleod J, Lawlor DA, Fraser A, Henderson J (2013) Cohort profile: the children of the 90s — the index of the Avon Longitudinal Study of Parents and Children. *Int J Epidemiol* 42:111–127.
- Bremner P, Burnett J, Nunney F, Ravat M, Mistral W (2011) Young People, Alcohol and Influences: A Study of Young People and Their Relationship with Alcohol. Joseph Rowntree Foundation, York, UK.
- Brown SA, McGue M, Maggs J, Schulenberg J, Hingson R, Swartzwelder S, Martin C, Chung T, Tapert SF, Sher K, Winters KC, Lowman C, Murphy S (2008) A developmental perspective on alcohol and youths 16 to 20 years of age. *Pediatrics* 121(Suppl 4):290–310.
- Colder CR, Campbell RT, Ruel E, Richardson JL, Flay BR (2002) A finite mixture model of growth trajectories of adolescent alcohol use: predictors and consequences. *J Consult Clin Psychol* 70:976–985.
- Fraser A, Macdonald-Wallis C, Tilling K, Boyd A, Golding J, Davey Smith G, Henderson J, Macleod J, Molloy L, Ness A, Ring S, Nelson SM, Lawlor DA (2013) Cohort profile: the Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. *Int J Epidemiol* 42:97–110.
- Goodwin DW (1971) Two species of alcoholic “blackout.” *Am J Psychiatry* 127:1665–1670.
- Gould M (2009) Aged and matured? The Guardian roundtable in association with Drinkaware. The Guardian, Tuesday, June 16, 2009. Available at: [www.theguardian.com/society/2009/jun/17/young-people-alcohol](http://www.theguardian.com/society/2009/jun/17/young-people-alcohol). Accessed July 28, 2014.
- Grant BF, Dawson DA (1997) Age at onset of alcohol use and its association with DSM-IV alcohol abuse and dependence: results from the National Longitudinal Alcohol Epidemiologic Survey. *J Subst Abuse* 9:103–110.
- Hartzler B, Fromme K (2003) Fragmentary and en bloc blackouts: similarity and distinction among episodes of alcohol-induced memory loss. *J Stud Alcohol* 64:547–550.
- Heath AC, Madden PAF, Bucholz KK, Dinwiddie SH, Slutske WS, Bierut LJ, Rohrbach JW, Statham DJ, Dunne MP, Whitfield JB, Martin NG (1999) Genetic differences in alcohol sensitivity and the inheritance of alcoholism risk. *Psychol Med* 29:1069–1081.
- Heron J, Maughan B, Dick DM, Kendler KS, Lewis G, Macleod J, Munafò M, Hickman M (2013) Conduct problem trajectories and alcohol use and misuse in mid to late adolescence. *Drug Alcohol Depend* 133:100–107.
- Hesselbrock MN, Easton C, Bucholz KK, Schuckit M, Hesselbrock V (1999) A validity study of the SSAGA — a comparison with the SCAN. *Addiction* 94:1361–1370.
- Hibell B, Andersson B, Bjarnason T, Ahlström S, Balakireva O, Kokkevi A, Morgan M (2004) The ESPAD Report 2003: alcohol and other drug use among students in 35 European countries. The Swedish Council for Information on Alcohol and Other Drugs (CAN) and the Pompidou Group at Council of Europe, Stockholm, Sweden.
- Jennison KM, Johnson KA (1994) Drinking-induced blackouts among young adults: results from a national longitudinal study. *Int J Addict* 29:23–51.
- Johnston LD, O’Malley PM, Bachman JG, Schulenberg JE (2013) Monitoring the Future National Results on Adolescent Drug Use: Overview of Key Findings, 2012. Institute for Social Research, University of Michigan, Ann Arbor, MI.
- Jung T, Wickrama KAS (2008) An introduction to latent class growth analysis and growth mixture modeling. *Soc Psychol Compass* 2:302–317.
- LaBrie JW, Hummer J, Kenney S, Lac A, Pedersen E (2011) Identifying factors that increase the likelihood for alcohol-induced blackouts in the prepartying context. *Subst Use Misuse* 46:992–1002.
- Longabaugh R, Wirtz PW, Rice C (2001) Social functioning in Project MATCH: results and causal chain analyses, in *NIAAA Project MATCH Monograph Series*, Vol. 8 (Longabaugh R, Wirtz PW eds), p 285. NIH Publication No 01-4238. National Institutes of Health, Bethesda, MD.
- Mann K, Ackermann K, Croissant B, Mundle G, Nakovics H, Diehl A (2005) Neuroimaging of gender differences in alcohol dependence: are women more vulnerable? *Alcohol Clin Exp Res* 29:896–901.
- Mason WA, Spoth RL (2012) Sequence of alcohol involvement from early onset to young adult alcohol abuse: differential predictors and moderation by family-focused preventive intervention. *Addiction* 107:2137–2148.
- Mundt MP, Zakletskaia LI (2012) Prevention for college students who suffer alcohol-induced blackouts could deter high-cost emergency department visits. *Health Aff* 31:863–870.
- Mundt MP, Zakletskaia LI, Brown DD, Fleming MF (2012) Alcohol-induced memory blackouts as an indicator of injury risk among college drinkers. *Inj Prev* 18:44–49.
- Muthén LK, Muthén BO (2006) *Mplus User’s Guide*. 4th ed. Muthén & Muthén, Los Angeles, CA.
- Nagin DS, Tremblay RE (2001) Analyzing developmental trajectories of distinct but related behaviors: a group-based method. *Psychol Methods* 6: 18–34.
- Nelson EC, Heath AC, Bucholz KK, Madden PAF, Fu Q, Knopik V, Lynskey MT (2004) Genetic epidemiology of alcohol-induced blackouts. *Arch Gen Psychiatry* 61:257–262.
- Pressman MR, Caudill DS (2013) Alcohol-induced blackout as a criminal defense or mitigating factor: an evidence-based review and admissibility as scientific evidence. *J Forensic Sci* 58:932–940.
- Raimo E, Daeppen J-B, Smith TL, Danko GP, Schuckit M (1999) Clinical characteristics of alcoholism in alcohol-dependent subjects with and without a history of alcohol treatment. *Alcohol Clin Exp Res* 23:1605–1613.
- Rose ME, Grant JE (2010) Alcohol-induced blackout: phenomenology, biological basis, and gender differences. *J Addict Med* 4:61–73.
- Schuckit MA (2014) A brief history of research on the genetics of alcohol and other drug use disorders. *J Stud Alcohol Drugs Suppl* 17:59–67.
- Schuckit MA, Kalmijn JA, Smith TL, Saunders G, Fromme K (2012) Structuring a college alcohol prevention program on the low level of response to alcohol model: a pilot study. *Alcohol Clin Exp Res* 36:1244–1252.
- Schuckit MA, Smith TL, Danko GP, Bucholz KK, Agrawal A, Dick DM, Nurnberger JI Jr, Kramer J, Hesselbrock M, Saunders G, Hesselbrock V (2014) Predictors of subgroups based on maximum drinks per occasion over six years for 833 adolescents and young adults in COGA. *J Stud Alcohol Drugs* 75:24–34.
- Schuckit MA, Smith TL, Heron J, Hickman M, Macleod J, Lewis G, Davis JM, Hibbeln JR, Brown S, Zuccolo L, Miller LL, Davey-Smith G (2011) Testing a level of response to alcohol-based model of heavy drinking and alcohol problems in 1,905 17-year-olds. *Alcohol Clin Exp Res* 35: 1897–1904.
- Schuckit MA, Smith TL, Trim R, Fukukura T, Allen R (2009) The overlap in predicting alcohol outcome for two measures of the level of response to alcohol. *Alcohol Clin Exp Res* 33:563–569.
- Schuckit MA, Smith TL, Trim R, Heron J, Horwood J, Davis JM, Hibbeln J, ALSPAC Study Team (2008) The self-rating of the effects of alcohol questionnaire as a predictor of alcohol-related outcomes in 12-year-old subjects. *Alcohol Alcohol* 43: 641–646.
- Schwartz G (1978) Estimating the dimension of a model. *Ann Stat* 6: 461–464.
- Seltzer ML (1990) The Michigan Alcoholism Screening Test: the quest for a new diagnostic instrument, in *Alcoholism: Theory and Treatment* (Ward DA ed), pp 250–257. Kendall-Hunt, Dubuque, IA.
- Sher KJ, Bartholow BD, Wood MD (2000) Personality and substance use disorders: a prospective study. *J Consult Clin Psychol* 68:818–829.
- Sher KJ, Jackson KM, Steinley D (2011) Alcohol use trajectories and the ubiquitous cat’s cradle: cause for concern? *J Abnorm Psychol* 120:322–335.

- Terlecki M, Larimer M, Copeland A (2010) Clinical outcomes of a brief motivational intervention for heavy drinking mandated college students: a pilot study. *J Stud Alcohol Drugs* 71:54–60.
- Wetherill RR, Fromme K (2009) Subjective responses to alcohol prime event-specific alcohol consumption and predict blackouts and hangover. *J Stud Alcohol Drugs* 70:593–600.
- Wetherill RR, Schnyer DM, Fromme K (2012) Acute alcohol effects on contextual memory BOLD response: differences based on fragmentary blackout history. *Alcohol Clin Exp Res* 36:607–617.
- White AM, Jamieson-Drake DW, Swartzwelder HS (2002) Prevalence and correlates of alcohol-induced blackouts among college students: results of an e-mail survey. *J Am Coll Health* 51:117–119, 122–131.