CAMBRIDGE
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Regular Article

Polygenic and environmental influences on the course of African Americans' alcohol use from early adolescence through young adulthood

Jill A. Rabinowitz[1], Rashelle J. Musci[1], Beth Reboussin[2], Adam J. Milam[1], Kelly S. Benke[1], George R. Uhl[3],
Danielle Y. Sisto[1], Nicholas S. Ialongo[1] and Brion S. Maher[1]

[1]Bloomberg School of Public Health, Department of Mental Health, Johns Hopkins University, Baltimore, MD, USA; [2]School of Medicine, Wake Forest University, Winston-Salem, NC, USA and [3]New Mexico VA Health Care System, Albuquerque, New Mexico, USA

Abstract

The study examined (a) whether alcohol use subgroups could be identified among African Americans assessed from adolescence through early adulthood, and (b) whether subgroup membership was associated with the interaction between internalizing symptoms and antisocial behavior polygenic risk scores (PRSs) and environmental characteristics (i.e., parental monitoring, community disadvantage). Participants ($N = 436$) were initially recruited for an elementary school-based prevention trial in a Mid-Atlantic city. Youths reported on the frequency of their past year alcohol use from ages 14–26. DNA was obtained from participants at age 21. Internalizing symptoms and antisocial behavior PRSs were created based on a genome-wide association study (GWAS) conducted by Benke et al. (2014) and Tielbeek et al. (2017), respectively. Parental monitoring and community disadvantage were assessed at age 12. Four classes of past year alcohol use were identified: (a) early-onset, increasing; (b) late-onset, moderate use; (c) low steady; and (d) early-onset, decreasing. In high community disadvantaged settings, participants with a higher internalizing symptoms PRS were more likely to be in the early-onset, decreasing class than the low steady class. When exposed to elevated community disadvantage, participants with a higher antisocial behavior PRS were more likely to be in the early-onset, increasing class than the early-onset, decreasing and late-onset, moderate use classes.

Keywords: alcohol use classes, antisocial behavior polygenic risk score, community disadvantage, internalizing symptoms polygenic risk score, parental monitoring

(Received 16 February 2018; revised 24 January 2019; accepted 31 March 2019)

Excessive alcohol use is a significant public health problem, with higher levels of use associated with psychological disorders (e.g., anxiety), motor vehicle accidents, risky sexual behaviors, and physical illnesses (e.g., heart disease) (CDC, 2016). Experimentation with alcohol may occur during adolescence, with over 18% of adolescents nationwide reporting alcohol consumption prior to age 13 (Kann et al., 2014). Although infrequent and low levels of alcohol use among adolescents may have no untoward effects, more frequent and heavy alcohol consumption may result in structural and functional neurocognitive deficits that persist into adulthood (Clark, Thatcher, & Tapert 2008; Zeigler et al., 2005). Moreover, while heavier alcohol use during adolescence and young adulthood may be temporally limited for some, other youth who use alcohol during these developmental periods may develop serious alcohol use problems and impairments (Danielsson, Wennberg, Tengström, & Romelsjö, 2010; Englund, Egeland, Oliva, & Collins, 2008; Pitkänen, Kokko, Lyyra, & Pulkkinen, 2008). Given that variations in alcohol use likely occur across

development, it is important to identify the nature of such variation, along with individual and contextual factors that contribute to the development of heavy use and ultimately abuse and dependence. Such knowledge could be used to inform the development of effective preventive interventions directed at curtailing harmful drinking and its consequences.

Developmental course of alcohol use across adolescence and young adulthood

The use of alcohol during adolescence and young adulthood can be best understood through a developmental lens. Alcohol use shows age-related patterns which can be attributed to sociocultural differences, individual differences in vulnerability to using alcohol, and the developmental tasks (e.g., forming new friendships) and transitions (e.g., entering high school or the work force) associated with adolescence and young adulthood (Masten, Faden, Zucker, & Spear, 2009). Among Western societies, average trajectories of alcohol consumption involve increases in use in adolescence, peak levels of use in the early twenties, and declines in use in later adulthood (Chassin, Sher, Hussong, & Curran, 2013). However, heterogeneity likely exists in these average trajectories given individual differences in opportunities

to use alcohol and the ability to adapt to the numerous changes that occur during adolescence and young adulthood.

Studies examining alcohol use during adolescence and early adulthood have identified between three and eight trajectories (Chassin et al., 2002; Flory, Lynam, Milich, Leukefeld, & Clayton, 2004; Nelson, Van Ryzin, & Dishion, 2015; Su, Supple, Leerkes, & Kuo, 2018; Tucker, Orlando, & Ellickson, 2003; Zucker, Hicks, & Heitzeg, 2016). Differences in study findings may be due to the baseline assessment of alcohol use, frequency of alcohol use assessments, and the questions used to assess alcohol use (i.e., monthly vs. annual accounts of alcohol use). Across these studies, parallels in the trajectories identified can be observed, with subgroups characterized by (a) low alcohol use during adolescence and young adulthood; (b) moderate alcohol use that is developmentally limited to middle adolescence and the early twenties; (c) alcohol use that begins in early adolescence that persists and intensifies in young adulthood; (d) alcohol use that begins in early adulthood with moderate use over time; and (e) alcohol use that begins in early adulthood characterized by heavier, more frequent alcohol use over time. These trajectories of alcohol use, however, reflect primarily European Americans that are socioeconomically diverse (e.g., Flory et al., 2004). Low-income, African American youth may experience different contextual stressors (e.g., higher levels of community disadvantage) that influence their alcohol use behaviors in a different manner than their European American, same-aged peers (Wallace & Muroff, 2002; Wallace, Neilands, & Phillips, 2017), warranting an examination of alcohol use behaviors in this population.

Internalizing and externalizing pathways to alcohol use trajectories

Internalizing symptoms, a broad band category encompassing anxious and depressive symptoms (Achenbach, 1991), represent an individual-specific factor that has been robustly associated with alcohol use among predominantly European adolescents and young adults (Fite, Colder, & O'Connor, 2006; Hussong, Jones, Stein, Baucom, & Boeding, 2011; Stice, Myers, & Brown, 1998). Whereas some work has indicated that phenotypic (i.e., observable) internalizing problems are positively related to alcohol and illicit drug use among late adolescents and young adults (e.g., Steele, Forehand, Armistead, & Brody, 1995; Stice et al., 1998), other work has linked higher internalizing symptoms to less frequent alcohol use during early and middle adolescence (e.g., Colder et al., 2013; Fite et al., 2006). Differences in study findings may be due to the timing in which alcohol use was assessed (e.g., early adolescence vs. late adolescence), as it is possible that internalizing symptoms may confer differential risk for alcohol consumption depending on the developmental stage. For example, youth experiencing internalizing symptoms in early adolescence may begin drinking heavily as a way of self-medicating (Chassin et al., 2013; Crum Storr, Ialongo, & Anthony, 2008; Hussong et al., 2011). However, the untoward consequences of alcohol use in the form of parent/peer disapproval or impaired academic performance may result in declines in alcohol consumption over the late adolescent and young adult years (Crosnoe, Benner, & Schneider, 2012; Mrug & McCay, 2013).

Considerable evidence also indicates that externalizing problems, particularly antisocial behaviors, are associated with alcohol use (Armstrong & Costello, 2002; Cook, Pflieger, Connell, & Connell, 2015; King, Iacono, & McGue, 2004). Higher levels of antisocial behaviors and behavioral disorder symptoms (e.g.,

conduct disorder, oppositional defiant disorder) predict early adolescent alcohol use (King et al., 2004), and heavy alcohol use and disorders in adulthood (Armstrong & Costello, 2002; Lee, Winters, & Wall, 2010; Trim et al., 2015). It has been suggested that externalizing disorders and substance use problems are a part of a larger externalizing syndrome, which is supported by work indicating strong, positive correlations between these conditions (King et al., 2004; Krueger, Markon, Patrick, & Iacono, 2005).

The role of genetics in alcohol use trajectories

Although internalizing and externalizing phenotypes have been associated with alcohol involvement across the developmental course, less is known about whether genetic variants underpinning these conditions are related to alcohol use behaviors. In samples of predominantly European adult twins, small to moderate positive correlations between internalizing disorders (i.e., depression) and alcohol use frequency and dependence have been observed (r's ranging from .001 to .60) (Andersen et al., 2017; Kendler et al., 1993; Tambs et al., 1997; Torvik et al., 2017). Other work has indicated that greater genetic propensity for externalizing symptoms is associated with membership in trajectories characterized by heavier alcohol use in adolescence and young adulthood among majority European adult twins (Alati et al., 2014; Kendler et al., 2003; McAdams, Rowe, Rijsdijk, Maughan, & Eley, 2012; Wichers, Gillespie, & Kendler, 2013). Findings from twin studies thus support the notion that genetic variants linked to internalizing symptoms and antisocial behaviors also underpin alcohol use.

There is increasing evidence, however, that substance use outcomes are influenced by numerous genetic variants that have very small effect sizes (McGue & Carey, 2016). One frequently used approach to capturing these polygenic influences is through the use of polygenic risk scores (PRSs). PRS are generated by identifying single nucleotide polymorphisms (SNPs) associated with a phenotype and weighting these SNPs based on the magnitude and strength of their association with a specific phenotype (Maher, 2015). Despite empirical evidence that suggests polygenic contributions to the development of problematic alcohol use (Dick et al., 2017), few studies have investigated whether polygenic influences are associated with alcohol use subgroups among youth in adolescence and early adulthood. In a notable exception, Li et al. (2017) examined whether a PRS for alcohol abuse and dependence predicted the intercept and slope of alcohol use trajectories among a majority European sample assessed from ages 15 to 28. The authors found that, among males, a higher PRS for alcohol abuse and dependence predicted both greater alcohol use at age 15.5 and greater increases in drinking between the ages of 15.5 and 21.5 relative to males with a lower alcohol PRS (Li et al., 2017).

Similar to the findings above, variations in an internalizing symptoms PRS may be associated with alcohol use over time. Youth higher in polygenic load for internalizing symptoms may experience (a) higher levels of negative affect and stress reactivity, and (b) rejection by mainstream peers due to poorer interpersonal skills, so they may subsequently seek out deviant peers to gain acceptance (Chassin et al. 2013; Hussong et al. 2011). Higher levels of negative emotional states and/or involvement with deviant peers may increase the likelihood that youths with a higher internalizing symptoms PRS will use alcohol more frequently during early and middle adolescence. However, potential negative ramifications of alcohol use (e.g., parental reprimands, reduced scholastic performance) may result in a reduction in alcohol consumption later in adolescence and young adulthood given

that youths with a higher internalizing symptoms PRS may be more affected by negative repercussions. Another possibility is that individuals with a higher internalizing symptoms PRS use alcohol in early adolescence and continue to use alcohol in young adulthood. These youths may reap the affective or interpersonal benefits of using alcohol and thus continue using this substance across developmental periods.

Variations in an antisocial behavior PRS may also be associated with alcohol use behaviors over time. During adolescence, increased autonomy from parents, greater centrality of the peer group, and normative increases in risk taking may set the stage for increased alcohol involvement (Steinberg, 2007), and this may be particularly true among youths with a greater genetic propensity for antisocial behaviors. Individuals with a higher polygenic load for antisocial behaviors may be more prone to using alcohol during adolescence, as they may be (a) higher in novelty seeking, (b) higher in behavioral disinhibition, and (c) more likely to disregard negative consequences, all of which may exacerbate risk for experimenting with alcohol (Maneiro, Gómez-Fraguela, Cutrín, & Romero, 2017; Mann et al., 2017). Higher polygenic load for antisocial behaviors may also confer risk for more frequent alcohol use during young adulthood, though research is insufficient to support this claim.

Contextual factors and alcohol use patterns

Although polygenic markers of internalizing symptoms and antisocial behavior may be associated with alcohol use over time, genetic loading for these problems likely interacts with environmental factors to influence risk for alcohol use. Consistent with bioecological models, the consideration of individual-specific features and proximal contextual influences, such as parental monitoring, is necessary to elucidate patterns of alcohol use behaviors that unfold across development (Bronfenbrenner & Ceci, 1994). Parental monitoring, defined as parental knowledge and supervision of children's activities (Dishion & McMahon, 1998), has a substantial effect on the children's alcohol use across adolescence and young adulthood (Becker et al., 2012). For example, lower levels of parental monitoring are associated with alcohol use trajectories characterized by higher levels of alcohol use during early and middle adolescence (Becker et al., 2012). Higher levels of parental knowledge and monitoring have been associated with less favorable attitudes towards using drugs and higher self-efficacy in refusing drugs (Chuang, Ennett, Bauman, & Foshee, 2009; Donaldson, Handren, & Crano, 2016; Lac, Alvaro, Crano, & Siegel, 2009; Nash, McQueen, & Bray, 2005). Parental monitoring may also insulate children from affiliating with deviant peers and/or being exposed to illicit drug use, which may contribute to reduced adolescent alcohol use (Handren, Donaldson, & Crano, 2016; Nash et al., 2005). Although parental monitoring is an important contextual factor that may protect against heavy alcohol use among youths, it is unclear whether this parenting behavior influences the alcohol use patterns of individuals varying in polygenic load for internalizing symptoms and antisocial behavior.

The consideration of distal contextual factors (e.g., community disadvantage) in relation to alcohol use over time is also paramount. Community disadvantage has been predictive of alcohol use among adolescents, with higher levels of neighborhood disorder and disadvantage positively predictive of alcohol involvement (Anderson, Sabatelli, & Kosutic, 2007; Cambron, Kosterman, Catalano, Guttmannova, & Hawkins, 2017; Lambert, Brown, Phillips, & Ialongo, 2004). Neighborhood disadvantage may be particularly important to consider during adolescence, given

that parents often grant their children more autonomy during this developmental period, resulting in greater exposure to extrafamilial influences such as the neighborhood and peers (Steinberg & Morris, 2001). Exposure to neighborhoods characterized by residential segregation, lower community supervision of children's behaviors, and greater access to alcohol and illicit drugs may increase the likelihood of youths using alcohol at an earlier age and continuing to use alcohol into adulthood (Ross & Mirowsky, 2001; Wallace & Muroff, 2002). Children residing in more disadvantaged communities may also experience demoralization and hopelessness (Ross & Mirowsky, 2001) and use alcohol during adolescence and young adulthood to reduce their negative cognitive and affective states (Rhodes & Jason, 1990).

No studies to our knowledge have considered whether community disadvantage intensifies risk for prolonged, heavy alcohol use among children varying in internalizing symptoms and antisocial behavior polygenic load. However, one study found that the effect of a conduct disorder PRS on marijuana use disorders was only significant when its interaction with community disadvantage was included in the analytic model (Rabinowitz et al., 2018). In particular, individuals with a higher conduct disorder PRS were more likely to have a marijuana use disorder when exposed to higher levels of community disadvantage (Rabinowitz et al., 2018). Given the role of community disadvantage among individuals with higher polygenic load for conduct disorder, it is possible that community disadvantage may similarly confer risk for problematic alcohol use over time among individuals with higher polygenic load for internalizing symptoms and antisocial behavior.

The current study

In the present study, we sought to identify subgroups of alcohol use in adolescence and early adulthood (ages 14–26) among urban African Americans. This population of young people may experience environmental stressors (i.e., higher community disadvantage) that contribute to earlier and more frequent alcohol use over time relative to socioeconomically advantaged peers. Grounded in the theoretical and empirical scholarship regarding the developmental course of alcohol use, we expected to observe five subgroups of alcohol use: (a) an early-onset, increasing class characterized by heavy alcohol use in early adolescence that escalated in young adulthood; (b) an early-onset, decreasing alcohol use group characterized by increases in alcohol use in middle to late adolescence followed by declines in use in the mid-twenties; (c) a late-onset, moderate alcohol use group that exhibited low alcohol use in adolescence and moderate alcohol use in the early- and mid-twenties; (d) a late-onset, heavy alcohol class characterized by heavier and more frequent alcohol use beginning in late adolescence that extended to young adulthood; and (e) a subgroup of individuals that exhibited low alcohol use over time.

We also examined whether antisocial behavior and internalizing symptoms polygenic load (assessed via polygenic risk scores) were associated with alcohol use subgroup membership. We hypothesized that individuals with a greater PRS for antisocial behaviors would be more likely to belong to the early-onset, increasing subgroup relative to the (a) low use subgroup; (b) late-onset, moderate use subgroup; (c) late-onset, heavy use subgroup; and (d) early-onset, decreasing subgroup. These hypotheses are grounded in past research (Crum et al., 2008) that has linked higher levels of phenotypic antisocial behaviors to membership in classes characterized by heavy, frequent alcohol use during early adolescence and young adulthood relative to other

subgroups (e.g., early-onset, decreasers; low users; late-onset, increasers) (e.g., Alati et al., 2014; Becker et al., 2012; Wichers et al., 2013). In terms of our expectations regarding the interaction between the antisocial behavior PRS and the contextual factors, we hypothesized that the higher the level of community disadvantage and the lower the level of parental monitoring, the greater the increase in the association between the antisocial behavior PRS and membership in the early onset, increasing class.

Despite the ambiguity in the literature with respect to the direction of the relationship between phenotypic internalizing symptoms and alcohol use, we expected that a higher internalizing symptoms PRS would be positively associated with membership in classes characterized by early alcohol use. These hypotheses are grounded in our past research using an African American sample, which revealed that higher levels of internalizing symptoms in late childhood were associated with increased alcohol use in adolescence (Crum et al., 2008), and other research that has linked internalizing symptoms to heavy alcohol and drug use among young adults (e.g., Steele et al., 1995). We hypothesized that individuals with a higher internalizing symptoms PRS would be more likely to be a member of the early-onset, increasing class relative to the low use subgroup. We expected that exposure to low parental monitoring and high community disadvantage would increase the likelihood of membership in the early-onset, increasing subgroup relative to the low use class among youth with a higher internalizing symptoms PRS.

In addition, we anticipated that a higher internalizing symptoms PRS would increase the likelihood of an individual belonging to the early-onset, decreasing class compared to the low use class. This hypothesis is based on the premise that early adolescent engagement in alcohol use may result in a number of negative consequences that individuals with a higher internalizing symptoms PRS may be more sensitive to. In line with this hypothesis, we expected that when exposed to low parental monitoring or high community disadvantage, individuals with a higher internalizing symptoms PRS would be more likely to be a member of the early-onset decreasing class compared to the low use subgroup.

Method

Participants

The analytic sample for this study consists of 436 African Americans who were originally recruited as first grade students in the fall of 1993 as part of a randomized controlled, universal preventive intervention trial in nine mid-Atlantic urban elementary schools (Ialongo et al., 1999). These 436 participants provided a successfully assayed DNA sample and completed at least one assessment of alcohol use over the course of annual assessments when participants were 14–26 years of age (see supplementary materials for more information on the alcohol use assessments). Demographic data for this study, including participant sex and free- or reduced-price lunch status (described in more detail below), were drawn from the baseline assessment conducted in the fall of first grade or when the participants were approximately 6 years old. Parental monitoring and community disadvantage data were assessed when participants were in sixth grade (i.e., ≈12 years old). The alcohol use data were derived from annual assessments that began at age 14 and continued to age 26. DNA data was collected from participants when they were approximately 21 years old. Thus, we drew on 15 waves of assessment data. A table regarding the number of alcohol use

Table 1. Sample characteristics

Characteristic	n (%)
Sex	
Males	222 (50.9)
Females	214 (49.1)
Free/reduced priced lunch status	
Yes	313 (72.3)
No	120 (27.7)
Intervention status	
Yes	290 (66.5)
No	146 (33.5)
Education	
High school	50 (12.8)
High school or GED[a]	136 (34.7)
Some college/vocational training	145 (37.1)
Associates or Bachelor's degree	50 (12.8)
Masters or professional degree	10 (2.5)
Income	
No income reported	10 (2.9)
<$10,000	34 (9.8)
$10,000–$20,000	39 (11.2)
$20,000–$35,000	69 (20.0)
$35,000–$50,000	62 (17.9)
$50,000–$70,000	50 (14.5)
$70,000–$100,000	48 (13.9)
>$100,000	34 (9.9)

[a]GED=General Education Degree.

assessments that participants completed can be found in the supplementary materials.

With respect to the demographic characteristics of the analytic sample (i.e., 436 participants) (Table 1), 50.9% were male, 72.3% received free/reduced priced lunch, and 66.5% were assigned to an intervention condition. The analytic sample generally reflects the characteristics of the larger sample of 585 African American participants recruited in first grade with respect to participant sex (whole sample, 52.8% vs. analytic sample, 50.9%), free/reduced priced lunch status (whole sample, 70.6% vs. analytic sample, 72.5%), and percentage assigned to an intervention condition (whole sample, 67.9% vs. analytic sample, 66.5%).

Measures

Frequency of alcohol use

Frequency of alcohol use in the past year was assessed using questions adapted from the Monitoring the Future (MTF) survey (Bachman, Johnston, Lloyd, & O'Malley, 1998) when participants were between the ages of 14 and 26. Participants reported on their frequency of alcohol use in the past year on a 0–7 Likert scale: 0 (*no use*), 1 (*once*), 2 (*twice*), 3 (*3-4 times*), 4 (*5-9 times*), 5 (*10–19 times*), 6 (*20–39 times*), and 7 (*40 or more occasions*). The MTF

survey has been used in a number of studies to model alcohol use over time (e.g., Pokhrel, Unger, Wagner, Ritt-Olson, & Sussman, 2008; Wagenaar, O'Malley, & LaFond, 2001).

Parental monitoring

When participants were 12 years old, the Structured Interview of Parent Management Skills and Practices Youth-Version (SIPMSP) was used to assess parental monitoring (Capaldi and Patterson, 1989). Sample items are "How often would your parents or a sitter know if you came home late or on weekends?" and "How often before you go out do you tell your parents when you will be back?" Seven items were rated on a scale from 1 (*all of the time*) to 5 (*never*). Items were reverse scored. An average parental monitoring score was calculated with higher scores reflecting more monitoring. Capaldi and Patterson (1989) report adequate internal consistency and test-retest reliability for the monitoring subscale.

Community disadvantage

Neighborhood disadvantage was assessed by geocoding census data when participants were approximately 12 years old. Community disadvantage as assessed via census data has been extensively used in the literature, with higher levels of disadvantage significantly associated with increased marijuana use offers and heavy marijuana use (Reboussin et al., 2015). In addition, higher levels of community disadvantage have been associated with a greater concentration of alcohol outlets (e.g., Furr Holden et al., 2018; Milam et al., 2014), which have been linked to higher levels of violent crime, decreased life expectancy, and increased substance use (Furr-Holden et al., 2018; Jennings et al., 2013; Reboussin et al., 2018).

Using ArcMap, a spatial join (appends data from two map layers using geographic location) was conducted to determine the census tract for each participant. A community disadvantage score was calculated using census-tract level items from the 1990 and 2000 Decennial census (U.S. Census, 2009). The items used to create the index include the percentages of (a) adults 25 years or older with a college degree, (b) owner-occupied housing, (c) households with incomes below the federal poverty threshold, and (d) female-headed households with children. We used Ross & Mirowsky's (2001) formula to generate the following index: $\{[(c / 10 + d / 10) - (a / 10 + b / 10)] / 4\}$. The score has a possible range of −5 to +5, where -5 reflects low disadvantage and +5 reflects high disadvantage.

DNA and genotyping

At approximately age 21, blood or buccal samples were obtained from participants and DNA was extracted. Genotyping was carried out using the Affymetrix 6.0 microarray, which provides coverage of approximately one million SNPs across the genome (Affymetrix Inc.). Standard quality control steps were implemented to ensure that accurate genotypes were included in subsequent analyses. Subjects with >5% missing genotype data were removed. Single nucleotide polymorphisms were also removed from further analysis when they had a minor allele frequency <.01, missingness >0.05, or departures from Hardy–Weinberg equilibrium at $p < .0001$ (Anderson et al., 2010). These steps were performed using PLINK 2.0 (Chang et al., 2015). Genotypes were imputed to the 1000 Genomes Phase 3 reference panel (1000 Genomes Project Consortium et al., 2010) using IMPUTE2 (Howie, Donnelly, and Marchini, 2009) with prephasing performed in SHAPEIT (Delaneau, Zagury, and Marchini, 2013). Resulting variants imputed with an INFO (quality) score

<0.8 were removed. Uncertainty adjusted dosage data, instead of called alleles, were used to generate the PRSs.

When exploring genetic associations, it is important to identify and control for population stratification or genetic differences between subpopulations so that any significant associations observed are not confounded by ancestry (Hellwege et al., 2018). We used principal components analysis in PLINK 2.0 to create the population stratification control variables (Chang et al., 2015). This process uses an orthogonal transformation to reduce the multidimensional genome-wide SNP data into a smaller number of principal components. All the available measured SNPs (roughly 900,000) were used to generate these components. Although these were not a priori identified ancestry information markers, it has been shown that "randomly" selected SNPs perform equally as well (Pritchard & Rosenberg, 1999). We included the first ten principal components in our analyses to sufficiently account for population stratification in the sample.

Discovery sample for internalizing symptoms

The discovery sample results used to generate the internalizing symptoms PRS were provided by a genome-wide meta-analysis of internalizing symptoms among preschool-aged children that was conducted by the Early Genetics and Lifecourse Epidemiology Consortium (EAGLE) (Benke et al., 2014). To date, this is the only GWAS to our knowledge that has been conducted on internalizing symptoms among children or adolescents. Though the authors of the GWAS examined internalizing symptoms in early childhood, a number of studies have shown that early childhood internalizing symptoms often persist into adolescence (Beyer, Postert, Müller, & Furniss 2012; Mesman & Koot, 2001; Pihlakoski et al. 2006).

The genome-wide meta-analysis of internalizing symptoms was performed using three separate cohorts drawn from the Generation Rotterdam (Generation R) study, Netherlands Twin Registry, and Western Australian Pregnancy (Raine) Cohort study. Internalizing symptoms were measured using 34 items found in common from different versions of the Child Behavior Checklist (Achenbach, 1991) collected across the three samples. This study evaluated 4,596 total children across >2.4 million imputed SNPs. No genome-wide statistically significant SNPs were identified. The discovery sample SNP names and association results are available for download here: http://www.tweelingenregister.org/EAGLE.

Discovery sample for antisocial behavior

The antisocial behavior PRS was created based on a GWAS for antisocial behavior conducted by Tielbeek et al. (2017). This analysis included participants from five cohorts including the Avon Longitudinal Study of Parents and Children, Collaborative Studies on the Genetics of Alcoholism, Generation R, the Twins Early Development Study, and a population-based study conducted by the Queensland Institute of Medical Research (Tielbeek et al., 2017). Participants ($N = 16,400$) were ethnically diverse children and adults. Antisocial behaviors (e.g., conduct disorder symptoms, rule-breaking) were assessed differently (e.g., questionnaires, interviews) depending on the cohort (Tielbeek et al., 2017). The discovery sample SNP names and association results can be downloaded here: http://broadabc.ctglab.nl/documents/p12/BroadABC_METALoutput_Combined.tbl.

PRS generation

Our GWAS panel contained 741,174 (26.30%) directly genotyped SNPs from the internalizing symptoms discovery sample list and

736,488 (7.73%) SNPs from the antisocial behavior discovery sample list. After imputation, 2,554,305 (90.50%) SNPs from the internalizing symptoms and 6,193,047 (65.00%) from the antisocial behavior discovery datasets were available for the current sample. Palindromic (A/T or C/G) SNPs were excluded, as methods for properly orienting strand from discovery to test datasets require precise knowledge of the true minor allele frequency and haplotype structure of the test sample. To account for linkage disequilibrium (LD), two rounds of LD-based results clumping were run in PLINK 2.0 (Chang et al., 2015) against the HapMap Phase III Release 2 Build 36 reference panel (The International HapMap 3 Consortium, 2010), resulting in 219,312 and 168,617 available SNPs for the internalizing symptoms PRS and antisocial behavior PRS, respectively. Based on our chosen *p*-value threshold of 0.001, the number of SNPs included in the internalizing symptoms PRS was 549 and the number of SNPs included in the antisocial behavior PRS was 393. There was no overlap in the SNPs included in the internalizing symptoms PRS and antisocial behavior PRS. Raw scores were generated in the imputed dosage dataset in PLINK 2.0 (Chang et al., 2015). We used mean imputation for missing genotypes, and alleles were weighted by the effect sizes from the discovery GWAS. The raw PRSs were regressed on the ten ancestry principal components. The z-scored residuals from these regressions were the continuous ancestry-corrected scores used in the primary analyses. A list of the SNPs included in both the internalizing symptoms and antisocial behavior PRSs can be found in the supplementary materials.

Statistical analyses

Bivariate correlations and descriptive statistics were conducted in SPSS Version 25 (IBM, 2016). A longitudinal latent class analysis (LCA) was used to categorize individuals into homogeneous subgroups of past year alcohol use. The frequency of alcohol use variables are considered count data and accordingly, a Poisson model was used to estimate our latent models. To handle missing data, we used Full Information Maximum Likelihood (FIML) estimation in Mplus (Muthén & Muthén, 2017), although the count variables were skewed. In simulation studies that have evaluated the effect of non-normality on FIML estimation in latent models, FIML may result in negatively biased standard errors and inflated model rejection rates (Enders, 2001). However, FIML has been shown to be superior to other approaches (e.g., multiple imputation) for handling non-normal missing data, and it has generally yielded more accurate estimates relative to other methods (Enders, 2001). All predictor variables were *z*-scored ($M = 0$, $SD = 1$).

Consistent with the procedures outlined by Masyn et al. (2017), we employed a three-step procedure that included class enumeration and involved the examination of the predictors of class membership. The first two steps centered on class enumeration and involved determining the number of latent classes without the covariates included in the model in the first step. LCA begins with a one-class (unconditional) model, and the number of classes is increased until there is no additional improvement in model fit (Nylund, Asparouhov, & Muthén, 2007). Several model fit indices were examined, including the Akaike Information Criterion (AIC) (Akaike, 1987), the Bayesian Information Criterion (BIC) (Schwartz, 1978), sample-size adjusted BIC (ABIC) (Sclove, 1987), and the Bootstrap Likelihood Ratio Test (BLRT) (Nylund et al., 2007). The size of the smallest class was also considered as small class sizes

(less than 5% of the sample) may indicate overfitting of the data and create potential problems with replication and generalizability of the LCA solution. Further, we considered entropy, a measure of classification uncertainty, with higher values (e.g., >.7) indicating better participant classification. Models were also examined to determine whether classes were distinct and conceptually meaningful.

The second step involved assigning individuals into classes based on their most likely class membership. The estimated values of participants' probabilities of membership in each class were calculated, which were based on the maximum likelihood parameter estimates from the model and participants' responses on the latent class indicators (Masyn, 2017). These probabilities were saved using the "cprobabilities" command in Mplus and were used in the third step.

The third step involved entering the covariates and predictors while accounting for the classification error rate of participants. The first set of the multinomial logistic regressions involved regressing latent class membership on each of the covariates (participant sex, intervention status, free/reduced priced lunch status), the PRSs (internalizing symptoms, antisocial behavior), and the contextual variables (parental monitoring, community disadvantage). In these regressions, both PRSs were included (i.e., internalizing symptoms PRS and the antisocial behavior PRS). Separate regressions were run for parental monitoring and community disadvantage. We controlled for free/reduced priced lunch status; this variable is often considered a proxy for family income (Hobbs & Vignoles, 2010; Huang & Barnidge, 2016), and it has been robustly associated with psychological impairments and substance use problems among youth (Goodman, 1999; Hanson & Chen, 2007). Although individuals and families with low incomes may be more likely to live in disadvantaged neighborhoods, there still may be variation in family incomes in these neighborhoods. As such, we controlled for free/reduced priced lunch status to ensure that our results were driven by the neighborhood context and not family income.

The second set of multinomial regressions involved regressing latent class membership on the interaction terms involving the PRS and relevant contextual variables while controlling for the covariates. Significant interactions and slopes were plotted using an automated spreadsheet (Dawson, 2014). Post hoc probing involved creating new moderator variables at the mean and ±1 *SD* from the z-scored values of the moderator (i.e., parental monitoring or community disadvantage) (Aiken & West, 1991; Cohen & Cohen, 1983). Interaction terms were created that included these variables. For significant interactions, the post hoc regressions involved entry of the covariates considered in the original regression, the internalizing symptoms and antisocial behavior PRSs, the moderator (at the mean and ±1 *SD* from the mean of the contextual variable), and the Contextual Variable × PRS interaction (Aiken & West, 1991; Cohen & Cohen, 1983). In graphing the interactions, we included the unstandardized betas that were at the mean and ±1 *SD* from the mean of the moderator (Holmbeck, 2002).

In total, we planned to carry out 4 sets of planned comparisons and 14 exploratory analyses. For the antisocial behavior PRS, the planned, hypothesis-driven analyses included comparisons between the early-onset, increasing subgroup and the (a) low use group; (b) early-onset, decreasing class; (c) late-onset, moderate use class; and (d) late-onset, heavy use class. The planned, hypothesis-driven analyses for the internalizing symptoms PRS involved comparisons between the low use subgroup and (a)

early-onset, increasing class, and (b) early-onset, decreasing class. To test for significance of the exploratory analyses, we employed a Bonferroni correction (.05/14 tests) which yielded a p-value of .003. A list of the planned and exploratory analyses can be found in Table 2.

Results

Bivariate correlations and descriptive statistics of study variables are presented in Table 3. There were no correlations among the predictors that were significant at $p < .05$. Results from the primary analyses are presented below.

Latent class analysis results

Following the three-step procedure described above, a longitudinal LCA was conducted using raw scores for frequency of past year alcohol use from ages 14–26. The AIC, BIC, and ABIC decreased with the addition of each class (Table 4). Entropy remained relatively high across models. Although the ABIC and BLRT decreased in the five-class model, this model included a very small class, potentially indicating model overfitting and a class that was not distinct from another subgroup. Thus, we selected the four-class model.

Class 1 was named "early-onset, increasing" ($n = 114$, 26.2%), as individuals in this class showed greater mean levels of past year alcohol use in early adolescence and higher mean levels of alcohol use in young adulthood relative to the other classes. Class 2 was named "late-onset, moderate use" ($n = 93$, 21.3%), as individuals in this class exhibited low mean levels of past year alcohol use until age 20 and showed increases in mean levels of past year alcohol use from ages 21 to 26. Class 3 was named "low steady" ($n = 136$, 31.2%), as participants in this class displayed low mean levels of past year alcohol use from ages 14–26. Class 4 was named "early-onset, decreasing" ($n = 93$, 21.3%), as individuals in this profile reported moderate to high mean levels of past year alcohol use during early and middle adolescence followed by a decline in mean levels of alcohol use in late adolescence and young adulthood. Given that our Bonferroni correction was based on the exploratory analyses, if a five-class solution was found, we recalculated our Bonferroni correction based on a four-class solution, which yielded a p-value of .007 (.05/7 tests), and then we applied this p-value to the exploratory analyses that we conducted.

Planned comparisons

Main effect results

There was a significant main effect of the internalizing symptoms PRS on class membership. Consistent with our hypotheses, participants with a higher internalizing symptoms PRS were more likely to be in the early-onset, decreasing class compared to the low steady class, OR = 1.34, $p = .013$, 95% CI [1.06, 1.69]. There was a trend for significance such that youth with a higher internalizing symptoms PRS were less likely to be in the early-onset, increasing class relative to the low steady class, OR = 0.80, $p = .057$, 95% CI [0.63, 1.01]. None of the antisocial behavior PRS planned comparisons were significant (Tables 5 and 6).

Interaction results

Consistent with our hypotheses, there was a significant interaction between the internalizing symptoms PRS and community

Table 2. Expected and actual planned and exploratory analyses

Expected planned comparisons:
Antisocial behavior PRS[a]
early-onset, increasing class vs. low use class
early-onset, increasing class vs. early-onset, decreasing class
early-onset, increasing class vs. late-onset, moderate use class
early-onset, increasing class vs. late-onset, heavy use class
Internalizing symptoms PRS
early-onset, increasing class vs. low use class
early-onset, decreasing class vs. low use class
Expected exploratory comparisons:
Antisocial behavior PRS
early-onset, decreasing class vs. low use class
early-onset, decreasing class vs. late-onset, moderate use class
early-onset, decreasing class vs. late-onset, heavy use class
late-onset, moderate use class vs. low use class
late-onset heavy use class vs. low use class
late-onset, heavy use class vs. late-onset, moderate use class
Internalizing symptoms PRS
early-onset, decreasing class vs. late-onset, moderate use class
early-onset, decreasing class vs. late-onset, heavy use class
early-onset, decreasing class vs. early-onset, increasing class
early-onset, increasing class vs. late-onset, moderate use class
early-onset, increasing class vs. late-onset, heavy use class
late-onset, heavy use class vs. low use class
late-onset, heavy use class vs. late-onset, moderate use class
late-onset, moderate use class vs. low use class
Actual planned comparisons:
Antisocial behavior PRS
early-onset, increasing class vs. low use class
early-onset, increasing class vs. early-onset, decreasing class
early-onset, increasing class vs. late-onset, moderate use class
Internalizing symptoms PRS
early-onset, increasing class vs. low use class
early-onset, decreasing class vs. low use class
Actual exploratory comparisons:
Antisocial behavior PRS
early-onset, decreasing class vs. low use class
early-onset, decreasing class vs. late-onset, moderate use class
late-onset, moderate use class vs. low use class
Internalizing symptoms PRS
early-onset, increasing class vs. early-onset, decreasing class
early-onset, increasing class vs. late-onset, moderate use class
late-onset, moderate use class vs. early-onset, decreasing class
late-onset, moderate use class vs. low use class

Note: A Bonferroni correction was applied to the exploratory analyses.
[a]PRS = polygenic risk score.

Table 3. Bivariate correlations, means, standard deviations, ranges, and *n*'s of study variables

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Age 14 AU	–																
2. Age 15 AU	.21**	–															
3. Age 16 AU	.16**	.54**	–														
4. Age 17 AU	.14**	.39**	.54**	–													
5. Age 18 AU	.12*	.32**	.39**	.49**	–												
6. Age 19 AU	.04	.20**	.31**	.29**	.32**	–											
7. Age 20 AU	−.01	.08	.18**	.20**	.25**	.73**	–										
8. Age 21 AU	.08	.12*	.19**	.12*	.20**	.27**	.32**	–									
9. Age 22 AU	−.01	.17**	.22**	.15**	.21**	.32**	.33**	.36**	–								
10. Age 23 AU	−.08	.09	.11*	.05	.14*	.34**	.36**	.33**	.48**	–							
11. Age 24 AU	−.10	.11*	.20**	.04	.11*	.28**	.21**	.37**	.44**	.46**	–						
12. Age 25 AU	−.05	.14*	.18**	.09	.13*	.31**	.29**	.33**	.46**	.52**	.59**	–					
13. Age 26 AU	−.12*	.08	.06	.06	.08	.22**	.24**	.32**	.40**	.40**	.44**	.55**	–				
14. Disadvantage	−.01	−.03	.001	−.003	.01	−.003	−.03	.07	−.08	−.01	−.04	−.04	−.04	–			
15. Monitoring	.12*	.04	.01	−.02	.02	.14*	.12*	.05	.12*	.10	.08	.09	.02	−.07	–		
16. INT PRS[a]	−.02	.03	.05	.11*	−.02	.05	.04	.09	.10	−.02	−.05	.06	.02	−.002	.05	–	
17. ASB PRS[a]	−.06	−.07	−.00	−.02	−.05	.05	.07	.05	−.02	.09	.04	.04	.02	.07	.05	−.09	–
M	0.32	0.65	1.07	1.44	1.25	1.16	1.19	1.22	1.91	1.58	1.59	2.11	2.06	−1.27	2.02	−0.05	0.01
SD	0.82	1.46	1.72	2.07	1.91	1.95	1.98	2.05	2.53	2.39	2.40	2.53	2.57	0.71	0.66	1.09	1.00
Range	0–7	0–7	0–7	0–7	0–7	0–7	0–7	0–7	0–7	0–7	0–7	0–7	0–7	−3.24–1.21	1–4.43	−2.11–4.17	−2.97–3.15
n	367	360	344	353	387	375	377	393	394	395	397	389	391	327	353	436	436

Note: AU = frequency of alcohol use; INT PRS = internalizing symptoms polygenic risk score; ASB PRS = antisocial behavior polygenic risk score.
[a]Bivariate correlations and descriptive statistics are presented for the residualized polygenic risk scores.
*p < .05 **p < .01.

Table 4. Fit indices for longitudinal latent class analysis models with 1-5 classes

Number of profiles	Number of free parameters	Log likelihood	AIC	BIC	ABIC	BLRT	Entropy
1	13	−9973.30	19972.60	20025.61	19984.35	–	–
2	27	−8405.30	16864.59	16974.69	16889.00	<.005	.94
3	41	−7939.38	15960.76	16127.95	15997.84	<.005	.93
4	55	−7619.20	15348.39	15572.66	15398.12	<.005	.93
5	69	−7470.25	15078.51	15359.87	15140.90	<.005	.92

Note: AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion, ABIC = Sample-size Adjusted BIC, BLRT = Bootstrap Likelihood Ratio Test. BLRT and entropy are not calculated for the 1-class model.

disadvantage when comparing likelihood of class membership between the early-onset, decreasing class and the low steady class, OR = 1.53, p = .013, 95% CI [1.09, 2.14], (Table 5). In the context of higher community disadvantage, individuals with a higher internalizing symptoms PRS were more likely to be in the early-onset, decreasing class (B = 0.65, p = .002) compared to the low steady class (Figure 2). The slopes for average and low community disadvantage were not significant. No interactions between the internalizing symptoms PRS and community disadvantage (or parental monitoring) were found when considering likelihood of membership in the early-onset increasing class vs. the low steady group. However, there was a trend for significance for the internalizing symptoms PRS and parental monitoring interaction when comparing likelihood of class membership in the low steady class versus the early-onset, increasing class (p = .081) (Table 6).

As shown in Table 5, a significant interaction was observed between the antisocial behavior PRS and community disadvantage when comparing likelihood of class membership in the early-onset, increasing class to the early-onset, decreasing class, OR = 0.68, p = .041, 95% CI [0.46, 0.98], in line with our hypotheses (Figure 3a). Individuals with a higher antisocial behavior PRS were more likely to be in the early-onset, increasing class relative to the early-onset, decreasing class when exposed to higher (B = 0.78, p = .003) and average (B = 0.39, p = .038) levels of community disadvantage. The slope for low community disadvantage was not significant.

Consistent with our hypotheses, there was also a significant interaction between the antisocial behavior PRS and community disadvantage when comparing likelihood of class membership between the early-onset, increasing class and the late-onset, moderate use class, OR = 0.72, p = .045, 95% CI [0.52, 0.99], (Figure 3b). In the context of higher community disadvantage, individuals with a higher antisocial behavior PRS were more likely to be in the early-onset, increasing class relative to the late-onset, moderate use class (B = 0.48, p = .050). The slopes for average and low community disadvantage were not significant. Paralleling the Internalizing Symptoms PRS × Parental Monitoring interaction results, none of the planned comparisons involving the Antisocial Behavior PRS × Parental Monitoring interactions were significant (Table 6).

Exploratory comparisons

Main effect results

None of the main effects of the PRSs were significant at our Bonferroni-corrected p-value (Tables 5 and 6).

Interaction results

None of the interactions between the PRSs and contextual variables were significant at our Bonferroni-corrected p-value (Tables 5 and 6).

Discussion

The present study examined whether subgroups of alcohol use in adolescence and early adulthood could be identified in an urban African American sample. Most of the available work that has identified subgroups of alcohol use during these developmental periods has been conducted among predominantly European youth of varying socioeconomic status (Chassin et al., 2002; Flory et al., 2004). Thus, it is uncertain whether the patterns of alcohol use identified in these samples are relevant to low-income African Americans residing in an inner-city. Moreover, it is unclear whether genetic propensity for internalizing symptoms and antisocial behavior, as measured via polygenic risk scores, is associated with alcohol use during adolescence and young adulthood. Consistent with compelling evidence that genes and environmental features interact with each other (Shanahan & Hofer, 2005), we also examined whether alcohol use subgroup membership could be explained by the interplay between contextual factors (i.e., parental monitoring, community disadvantage) and genetic propensity for internalizing symptoms and antisocial behaviors.

Four subgroups of alcohol use were identified, including an early-onset, increasing class characterized by higher mean levels of past year alcohol use in early adolescence and young adulthood. This subgroup mirrors previous work that identified an early-onset, heavy alcohol use group that used alcohol frequently in early adolescence and continued on a trajectory towards increased use in adulthood (Chassin et al., 2002; Flory et al., 2004; Su, Supple, Leerkes, & Kuo, 2018; Zucker et al., 2016). A late-onset, moderate use class was also identified that displayed low mean levels of past year alcohol use in adolescence followed by moderate mean levels of alcohol use from ages 20 through 26. The individuals identified in this subgroup also parallel the characteristics of subgroups identified in previous studies (Chassin et al., 2002; Nelson et al., 2015). A low steady group was also observed that reported very low mean levels of past year alcohol use over time, mirroring previous findings regarding low alcohol consumption across developmental periods (Chassin et al., 2002; Nelson et al., 2015). We also observed an early-onset, decreasing class that exhibited higher mean levels of past year alcohol consumption from early to late adolescence, followed by decreases in mean levels of alcohol use into young adulthood. In contrast to our expectations, a late-onset, heavy alcohol use class was not found in our sample. As noted previously, studies that

Table 5. Multinomial logistic regression results involving the PRS and community disadvantage

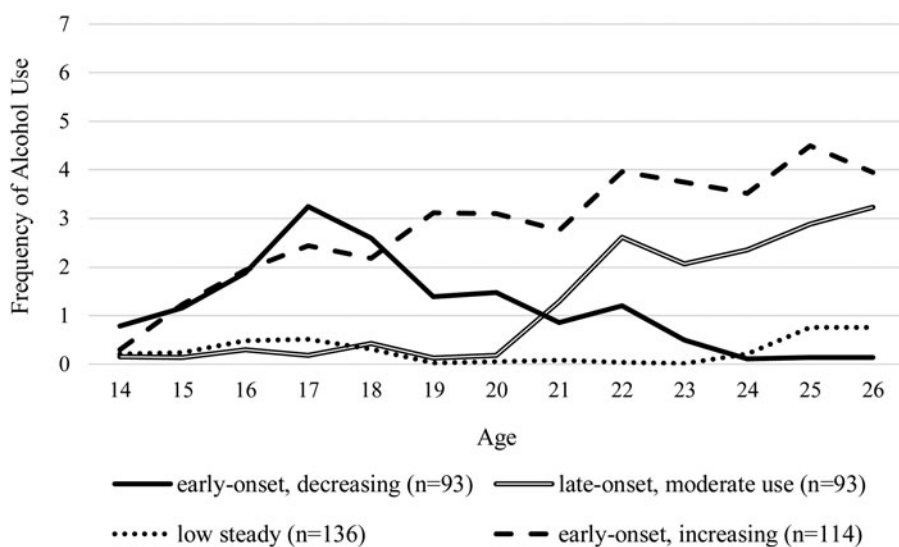|	Early-onset, decreasing vs. low steady (ref)	Early-onset, increasing vs. low steady (ref)	Early-onset, decreasing vs. early-onset, increasing (ref)	Late-onset, moderate use vs. early-onset, increasing (ref)	Late-onset, moderate use vs. low steady (ref)	Late-onset, moderate use vs. early-onset, decreasing (ref)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Step 1						
Sex	0.51 (0.25–1.04)*	1.01 (0.56–1.81)	0.51 (0.23–1.10)	0.90 (0.47–1.70)	0.90 (0.49–1.68)	1.77 (0.82–3.84)
Intervention status	1.08 (0.49–2.34)	1.10 (0.57–2.12)	0.98 (0.40–2.37)	0.82 (0.41–1.64)	0.90 (0.47–1.72)	0.83 (0.37–1.89)
Lunch status	0.97 (0.39–2.40)	0.60 (0.30–1.20)	1.61 (0.61–4.25)	0.72 (0.36–1.45)	0.43 (0.22–0.87)**	0.45 (0.18–1.10)*
Internalizing PRS	1.32 (1.02–1.69)**	1.15 (0.89–1.49)	1.14 (0.88–1.49)	0.84 (0.61–1.16)	0.97 (0.71–1.32)	0.74 (0.54–1.01)*
Antisocial PRS	0.75 (0.52–1.07)	1.06 (0.78–1.44)	0.70 (0.48–1.04)*	0.92 (0.68–1.24)	0.97 (0.74–1.28)	1.30 (0.91–1.87)
Disadvantage	1.10 (0.79–1.53)	0.95 (0.71–1.27)	1.16 (0.83–1.64)	0.99 (0.72–1.37)	0.94 (0.69–1.28)	0.85 (0.60–1.22)
Step 2						
Internalizing PRS × Disadvantage	1.53 (1.09–2.14)**	1.14 (0.83–1.55)	1.35 (1.00–1.81)*	1.12 (0.80–1.55)	1.27 (0.89–1.82)	0.83 (0.59–1.16)
Antisocial PRS × Disadvantage	0.79 (0.54–1.17)	1.18 (0.84–1.65)	0.68 (0.46–0.98)**	0.72 (0.52–0.99)**	0.84 (0.60–1.18)	1.06 (0.74–1.51)

Note: Step 1 included Step 2 variables.
*p < .10 **p < .05.

**Table 6.** Multinomial logistic regression results involving PRS and parental monitoring

	Early-onset, decreasing vs. low steady (ref)	Early-onset, increasing vs. low steady (ref)	Early-onset, decreasing vs. early-onset, increasing (ref)	Late-onset, moderate use vs. early-onset, increasing (ref)	Late-onset, moderate use vs. low steady (ref)	Late-onset, moderate use vs. early-onset, decreasing (ref)
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Step 1						
Sex	0.57 (0.30–1.10)*	1.49 (0.85–2.61)	0.38 (0.20–0.75)***	0.76 (0.41–1.41)	1.13 (0.62–2.05)	1.97 (0.98–3.94)*
Intervention status	0.69 (0.35–1.38)	0.80 (0.43–1.49)	0.87 (0.43–1.75)	0.75 (0.40–1.42)	0.60 (0.32–1.13)	0.87 (0.43–1.76)
Lunch status	0.92 (0.43–1.97)	0.60 (0.32–1.13)	1.53 (0.72–3.26)	0.85 (0.44–1.63)	0.51 (0.27–0.99)**	0.55 (0.26–1.19)
Internalizing PRS	1.24 (0.94–1.63)	1.26 (0.97–1.64)*	0.98 (0.74–1.29)	0.85 (0.63–1.14)	1.07 (0.80–1.43)	0.87 (0.64–1.18)
Antisocial PRS	0.74 (0.54–1.03)*	1.02 (0.75–1.39)	0.72 (0.51–1.04)*	0.85 (0.63–1.14)	0.87 (0.66–1.14)	1.17 (0.86–1.60)
Monitoring	1.14 (0.84–1.56)	1.36 (1.01–1.82)**	0.84 (0.63–1.12)	0.87 (0.64–1.19)	1.18 (0.85–1.63)	1.03 (0.75–1.42)
Step 2						
Internalizing PRS × Monitoring	0.83 (0.62–1.11)	0.79 (0.61–1.03)*	1.05 (0.80–1.37)	1.13 (0.87–1.46)	0.89 (0.67–1.19)	1.08 (0.81–1.43)
Antisocial PRS × Monitoring	1.003 (0.73–1.37)	1.07 (0.77–1.47)	0.94 (0.68–1.31)	0.89 (0.66–1.20)	0.94 (0.72–1.25)	0.94 (0.71–1.25)

Note: Step 1 included Step 2 variables.
*p < .10 **p < .05 ***p < .01.

Figure 1. Frequency of past year alcohol use from ages 14 to 26 in the four-class model.
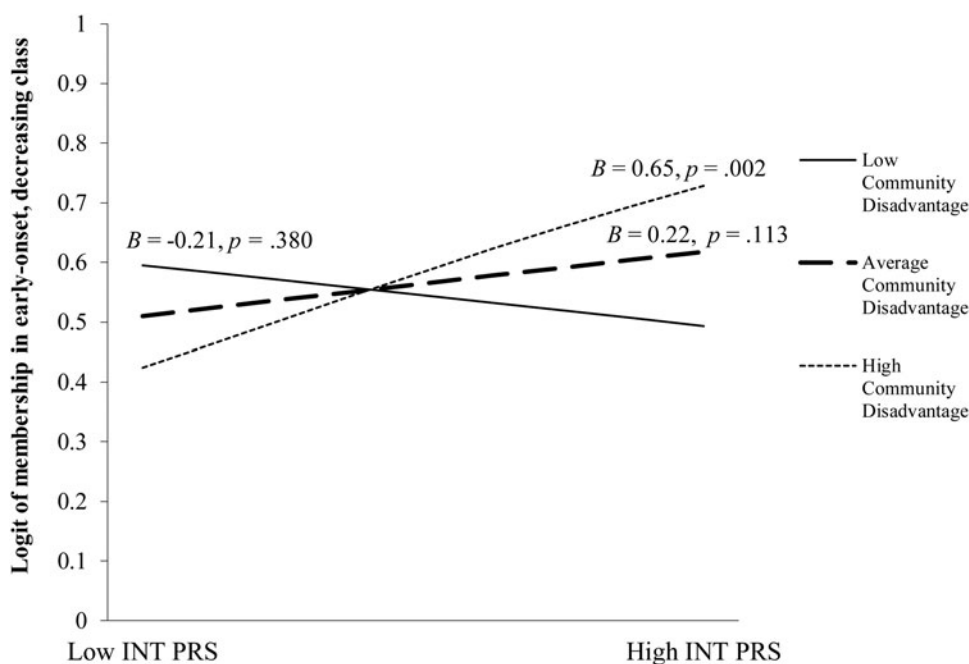
Figure 2. Relative to the low steady class, the log odds of membership in the early-onset, decreasing class based on participant internalizing symptom PRS levels and community disadvantage.

Note: INT PRS = internalizing symptoms polygenic risk score.

have examined longitudinal patterns of alcohol use have been conducted among predominantly European American samples, and not all of the classes identified in these samples may be relevant to inner-city African American youth. It is also possible that we may have observed this class in a larger African American sample.

Higher polygenic load for internalizing symptoms was associated with membership in the early-onset, decreasing class relative to the low steady class, consistent with our hypotheses. The contextual (e.g., transition to high school) and neurobiological changes (e.g., puberty) associated with early and middle adolescence may be particularly challenging for individuals with a higher internalizing symptoms PRS given that these individuals may exhibit greater reactivity towards stressors. These youths may subsequently seek out alcohol to reduce tension and negative

affective states (Kushner, Sher, Wood, & Wood, 1994). Early use of alcohol during early and middle adolescence may result in negative repercussions (e.g., arrests, parental discipline), to which individuals with a higher internalizing symptoms PRS may be more sensitive to (Fite et al., 2006). As a result, these individuals may attempt to avoid these or other negative consequences by decreasing their consumption of alcohol in later adolescence and early adulthood.

Individuals with a higher internalizing symptoms PRS were also more likely to be in the early-onset, decreasing class compared to the low steady subgroup when exposed to higher levels of community disadvantage. During early and middle adolescence, greater time spent in more socioeconomically deprived communities characterized by prevalent drug use may enable
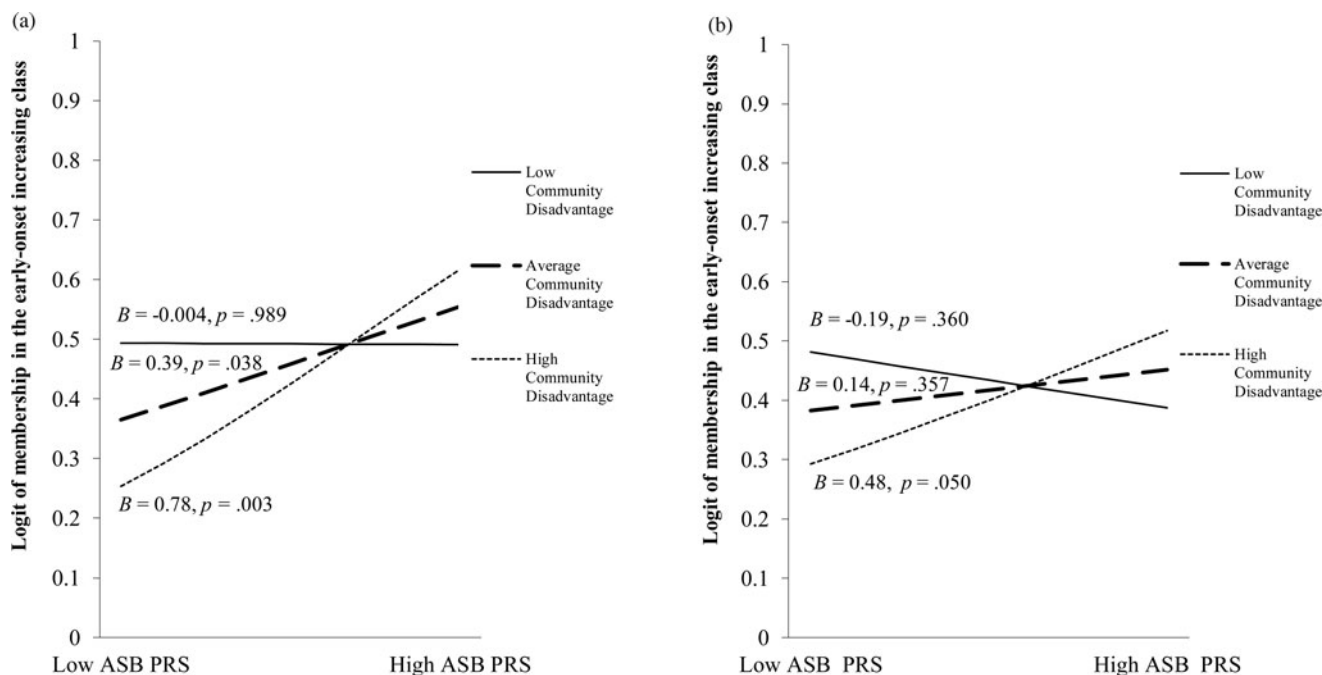
Figure 3. The log odds of membership in the early-onset, increasing class relative to the (a) early-onset, decreasing class, and (b) late-onset, moderate use class based on participant ASB PRS levels and community disadvantage.

Note: ASB PRS = antisocial behavior polygenic risk score.

alcohol use among individuals with a higher polygenic load for internalizing symptoms given that they may be more likely to experience negative emotional states (Chassin et al., 2013; Hussong et al., 2011; Wallace et al., 2017; Wallace & Muroff, 2002). Indeed, lower community supervision of youth behavior, coupled with increased alcohol outlets in these neighborhoods, may facilitate early alcohol use among individuals with a higher internalizing symptoms PRS (Milam et al., 2014). As noted above, frequent use of alcohol during early and mid adolescence may result in negative repercussions, and youth with a higher internalizing symptoms PRS may subsequently decrease their consumption of alcohol.

We also found that in the context of higher community disadvantage, individuals with a higher antisocial behavior PRS were more likely to be in the early-onset, increasing class relative to the early-onset, decreasing and late-onset, moderate use classes consistent with our hypotheses. Communities higher in disadvantage characterized by poverty and a greater concentration of alcohol outlets may enable alcohol use among adolescents higher in polygenic load for antisocial behavior, given greater sensation seeking behaviors and impulsivity that these youths may display (Mann et al., 2017; Maneiro et al., 2017). Adolescents with greater polygenic propensity for antisocial behaviors may also be lower in fearfulness, affiliate with substance using peers, and may be more inclined to use alcohol in disadvantaged communities where drugs are more available (Mann et al., 2017; Rosenberg & Anthony, 2001). Exposure to community disadvantage earlier in development may thus enable alcohol use over time among individuals with greater polygenic load for antisocial behavior.

Although interactive effects were found with regard to the antisocial behavior PRS and community disadvantage, the antisocial behavior PRS was not associated with class membership. This finding is consistent with limited work noted above that showed that genetic liability for conduct disorder was not associated

with substance use disorders (i.e., marijuana abuse and dependence) when neighborhood disadvantage was not included in the analytic model (Rabinowitz et al., 2018). It is possible that the predisposition for antisocial behavior only serves as a risk factor for elevated alcohol use in the context of environmental stressors, consistent with the diathesis-stress model (Zuckerman, 1999). Future research should examine other contextual factors (e.g., affiliation with deviant peers) that may influence the association between the antisocial behavior PRS and alcohol use patterns over time.

Parental monitoring did not moderate the relationship between polygenic load for internalizing symptoms and antisocial behavior and the alcohol use subgroups identified. However, there was a trend for significance involving the interaction between parental monitoring and the antisocial behavior PRS in predicting likelihood of class membership in the low steady vs. early-onset increasing class. Parental monitoring was assessed via participant self-report on a questionnaire; therefore, the pattern of findings may have been influenced by shared method variance or social desirability. Future work should consider assessing parental monitoring using other informants (e.g., siblings) and other methods (e.g., interviews).

There are limitations of the present study to acknowledge. We used results from a GWAS conducted in samples of largely European ancestry to inform the generation of PRSs in an African American sample. As of 2016, about 16% of individuals included in the GWASs are ethnic minority populations, and most of these individuals are of Asian ancestry (Popejoy & Fullerton, 2016). Although differences in linkage disequilibrium and ancestral markers have been observed across individuals of different ancestries, recent work has demonstrated using simulated data that PRSs maintain transferability across ancestry groups (Martin et al., 2017). Work across ethnic groups, such as that presented here, is needed to overcome the limitation of the field regarding the lack of

representation of African Americans in gene identification efforts and molecular genetics studies. Future research should attempt to replicate these findings in other African American samples and ethnic minority populations. Among the limitations of the study was the use of a single Likert item to capture frequency of alcohol use.

An additional limitation was that the discovery sample GWAS from which the internalizing symptoms PRS was derived included parent reports on their children's internalizing symptoms. While a number of studies have shown that childhood internalizing symptoms often persist into adulthood in both European and African American samples (e.g., Brody et al., 2005; Mesman & Koot, 2001; Musci et al., 2015; Pihlakoski et al. 2006), future GWASs should assess these symptoms during other developmental periods (e.g., adolescence, adulthood) using ethnically diverse samples and attempt to replicate findings from the current study. In addition, we only considered alcohol use in our latent models, as opposed to including other substances (e.g., marijuana, tobacco) that may co-occur with alcohol use over time (Armstrong & Costello, 2002; Banks, Rowe, Mpofu, & Zapolski, 2017). Although this decision enabled us to examine whether internalizing symptoms and antisocial behavior polygenic load were related specifically to patterns of alcohol consumption, polygenic load for these problems may also serve as a liability for other substance use behaviors, something future work should examine. Future research should also consider replicating findings from the current study using other indices of neighborhood disadvantage, such as self-reported neighborhood disadvantage and crime. An additional avenue for future research is to examine phenotypic internalizing symptoms and antisocial behaviors, genetic risk for these problems, and contextual risk and protective factors that may play a role in alcohol use across developmental periods. Such an approach may highlight processes involved in equifinality and multifinality and illuminate why individuals with higher polygenic risk for internalizing and externalizing symptoms may not display these phenotypes.

In terms of future directions, the field could benefit from identifying the pathways through which (a) higher internalizing symptom polygenic load resulted in an attenuation in alcohol use in late adolescence in more disadvantaged communities, and (b) higher antisocial behavior polygenic load resulted in an increase in alcohol use during adolescence and young adulthood in more disadvantaged neighborhoods. An additional avenue for future work is to examine whether spirituality (e.g., prayer, meditation) and specific coping practices (e.g., collective coping or support from extended family) influence alcohol use patterns among African Americans (Krentzman Farkas, & Townsend, 2010; Utsey, Bolden, Lanier, & Williams 2007). These factors have been associated with sobriety among individuals receiving alcohol abuse treatment and improved psychological and physical health among African Americans (Krentzman et al., 2010; Utsey et al., 2007).

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0954579419000701.

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