The Impact of Drinking History on Alcohol Response

by

Jessica Hartman

A Dissertation Presented in Partial Fulfillment
of the Requirements for the Degree
Doctor of Philosophy

Approved December 2020 by the
Graduate Supervisory Committee:

William Corbin, Chair
Laurie Chassin
Leah Doane
Kevin Grimm

ARIZONA STATE UNIVERSITY

May 2021

ABSTRACT

Alcohol use remains a major public health concern and economic burden. Extant literature suggests that young adulthood is a particularly high-risk developmental period for heavy drinking. Given this, it is imperative to understand possible risk and protective factors for heavy drinking and related consequences during this risky developmental period. Prior research has shown that both drinking history and alcohol response (AR) are consistent predictors of future drinking outcomes. However, it is unclear how they may work together to confer this risk. The current study aimed to fill this gap in the literature by examining how alcohol use trajectories across adolescence and early adulthood impacted relations between AR after an alcohol challenge and drinking outcomes over a 2-year period in a sample of young adult moderate to heavy drinkers. Results showed that both drinking history and AR were independently predictive of alcohol outcomes at the 6-month follow-up such that a more extensive drinking history, greater high arousal positive effects, and lesser low arousal negative effects predicted greater drinking and alcohol-related problems 6-months later. However, drinking history and AR were largely not predictive of change in drinking outcomes over time. Finally, AR did not mediate the relationship between drinking history and later alcohol-related outcomes. This is the first study to address relations among drinking history, AR, and later drinking outcomes using a longitudinal alcohol challenge design with a full account of early drinking history. Future research would benefit from inclusion of a broad range of drinkers and longer follow-up assessments to better understand the complex pathways of risk from early drinking history and AR to future drinking outcomes. Such efforts may

increase the understanding of who is at greatest risk and/or would benefit most from specific intervention programs.

TABLE OF CONTENTS

Page

CHAPTER Page

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

Alcohol use remains a major public health concern and economic burden. According to the 2015 National Survey on Drug Use and Health (NSDUH), approximately 15 million adults and over 620,000 adolescents have met criteria for a diagnosis of alcohol use disorder (AUD) in their lifetime. Further, alcohol is the third leading cause of preventable death in the United States and the fifth worldwide, with just under 90,000 people dying from alcohol-related causes annually (Mokdad, Marks, Stroup, & Gerberding, 2004; World Health Organization, 2014). Globally, alcohol use contributes to more than 200 diseases and injury-related health conditions including cancer, liver cirrhosis, and alcohol dependence (World Health Organization, 2014). Further, alcohol misuse in the United States was associated with $249 billion in costs in 2010 and approximately three-quarters of that cost was related to binge-drinking (Sacks, Gonzales, & Bouchery, 2015).

A large body of research suggests that young adulthood is a particularly high-risk developmental period for heavy drinking (National Institute of Alcohol Abuse and Alcoholism, 2006). According to the National Survey on Drug Use and Health (NSDUH), almost 40% of young adults reported binge drinking in the last 30 days (Substance Abuse and Mental Health Services Administration, 2015). Further, extreme binge drinking, consuming 10 or more drinks per occasion, occurs in approximately 20% of college students/young adults (Johnston, O'Malley, Bachman, Schulenberg, & Miech, 2016). This is concerning given the numerous consequences that are associated with binge drinking. Binge drinking occasions are associated with greater risk for

experiencing physical injury or engaging in risky sexual behavior (Cranford, McCabe, & Boyd, 2006). Further, binge drinking has been linked to greater depressive symptoms, less positive mood, and higher endorsement of suicidality (Bell et al., 2014; Cranford et al., 2006; Townshend & Duka, 2005). Finally, binge drinking puts young adults at risk for AUDs. Binge drinking young adults have double the AUD symptoms of their non-binge drinking counterparts (Fillmore & Jude, 2011), and both occasional and frequent binge drinkers are at significantly higher risk for developing an AUD than those that never binge drink (Chou, Liang, & Mackenzie, 2011). Given, the health and financial consequences of heavy alcohol use, it is imperative to understand possible risk and protective factors for heavy drinking and related consequences, particularly in young adulthood.

Prior research has identified a variety of important risk factors for later alcohol outcomes including a family history of alcohol problems, various parental factors, mood disorders, and impulsivity (Chartier, Hesselbrock, & Hesselbrock, 2010; Foulds, Adamson, Boden, Williman, & Mulder, 2015; Hartman, Corbin, Curlee, & Fromme, 2019; Loree, Lundahl, & Ledgerwood, 2015). Alcohol response (AR) has also been shown to be related to later risk. Currently there are two leading models regarding patterns of AR that confer risk for heavy drinking and AUDs. The low level of response (LLR) model posits that high-risk drinkers (e.g. those with a family history of alcohol use disorders, etc.) are more likely to display an overall blunted response to alcohol (Schuckit, 1980; 1984; 1985). Studies supporting the link between LLR and future alcohol outcomes have primarily been conducted by Schuckit and colleagues. For example, in one of the first alcohol-challenge studies that followed a high-risk population

(sons of alcoholics) over several decades, a LLR in 20-year old's was associated with approximately 4 times greater likelihood of developing alcoholism almost 10 years later (Schuckit, 1994). This was true for both the high-risk group and control participants (sons of non-alcoholics). It is also important to note that, for sons of alcoholics, 56% of those with a LLR at age 20 went on to develop alcoholism compared to only 14% of those who had a high level of response to alcohol. These results have been supported across numerous studies. For example, in a different sample of male participants, Trim, Schuckit, and Smith (2008) found that LLR at age 20 was related to maximum number of drinks per occasion and drinking to cope 15 years later. Further, this pattern continued such that LLR at age 20 predicted drinking outcomes at age 40 through deficient coping mechanisms (Schuckit et al., 2011). In a multigenerational study, Schuckit and colleagues (2012a) found that, in an original sample of men who completed an alcohol-challenge, LLR predicted a variety of outcomes 5-years later. They found similar results when offspring retrospectively reported on their level of AR.

LLR has also been examined in relation to other important indicators of future risk. Schuckit, Smith, Pierson, Danko, and Beltran, (2006) found that LLR was significantly positively correlated with the number of relatives with alcohol problems. Further, while both family history and LLR contributed to a range of drinking outcomes including alcohol-related problems and abuse and dependence symptoms, only LLR significantly predicted maximum quantity and frequency across 20-years. Additionally, when participants retrospectively reported on their AR, low risk drinkers reported a high level of response, while problem drinkers reported even lower AR than heavy drinkers (Schuckit et al., 2018). This was true even when age, sex, and drinking and drug use

histories were accounted for. In another alcohol challenge study, heavy drinking young adult men demonstrated reduced AR, such that they reported significantly less stimulant effects and slightly less sedative effects than lighter drinkers (Gilman, Ramchandani, Crouss, & Hommer, 2012). fMRI results from this study demonstrated that heavy drinkers also showed a blunted brain reward system response.

While most of the research on LLR has been conducted with men, studies suggest that LLR is a risk factor for women as well. For instance, in an alcohol challenge study that examined AR in both family history positive and negative women, family history positive women were more likely to demonstrate a LLR to alcohol (Eng, Schuckit, & Smith, 2005). Another study found that family history positive men and women did not significantly differ in level of response to alcohol (Schuckit, Smith, & Kalmijn, 2004). Further, Schuckit et al. (2012b) found that the link between LLR and future alcohol-related outcomes may be even stronger in women than in men. In this study, while invariance analyses indicated that there were few differences between men and women, when analyzed separately, only women showed a significant association between LLR and alcohol outcomes through positive alcohol expectancies and drinking to cope. Taken together, results suggest that level of response to alcohol is an important marker of future risk for both men and women.

Although the LLR model has received considerable support, there is also a significant body of research suggesting that the relationship between AR and future risk is more nuanced. Newlin and Thomson (1990) introduced the differentiator model (DM), a novel model to explain risk associated with AR. The DM posits that sensitivity to alcohol is dependent on the limb of the blood alcohol curve. Newlin and Thomson found

that those at risk for heavy drinking displayed acute sensitization on the ascending limb and acute tolerance on the descending limb of the blood alcohol curve. In other words, high-risk individuals were more sensitive to the positive and rewarding aspects of initial alcohol consumption, but less sensitive to the more negative effects of alcohol when alcohol concentration was decreasing. This increased stimulant response and decreased sedative response is not something that is captured by the LLR model. This could be because most LLR studies have focused more heavily on sedating effects of alcohol and/or only assessed AR on the descending limb.

To facilitate testing of the DM, Martin, Earleywine, Musty, Perrine, & Swift (1993) sought to validate a novel measure of AR (Biphasic Effects of Alcohol Scale; BAES) across two populations; college students and a community sample. Results of these studies showed support for differential effects on the ascending and descending limb of the blood alcohol curve. On the ascending limb, participants showed greater stimulant than sedative effects. In contrast, on the descending limb, they exhibited greater sedative effects. While this study did not include high-risk drinkers, it supported the DM such that AR appeared to be limb dependent. Further, when AR was examined after alcohol consumption in light and moderate/heavy drinkers across two samples, moderate/heavy drinkers in both samples experienced significantly more stimulant effects than light drinkers (Holdstock, King, & de Wit, 2000). In one of the samples, the moderate/heavy drinkers also experienced significantly fewer sedative effects.

Although early studies provided support for the DM, other research has called specific aspects of the DM into question. For example, Thomas, Drobes, Voronin, and Anton (2004) found only partial support for the model when comparing non-treatment

seeking alcoholics and social drinkers. Alcoholics reported significantly greater stimulant effects of alcohol relative to light drinkers, particularly on the ascending limb. However, the two groups did not differ in their reports of sedative effects. In a separate study that sought to determine whether recent drinking impacted the relation between family history and AR, the investigators found that recent heavy drinkers experienced greater stimulating effects on the ascending limb while recent light drinkers felt stronger stimulating effects on the descending limb (Wetherill et al., 2012). This was true for both family history positive and negative participants. Interestingly, this study did not find reduced sedative effects on the descending limb among heavier drinkers. Collectively, these studies only partially support the DM.

Other studies suggest the DM should be amended to be less limb specific. King and colleagues (2002) found that, when compared to light drinkers, heavy drinkers experienced significantly more stimulant effects, particularly on the ascending limb. In contrast, heavier drinkers experienced fewer sedative effects than light drinkers on *both* the ascending and descending limb of the BAC curve. Prior studies have also demonstrated that heavy drinkers experience greater stimulant effects and lesser sedative effects of alcohol at peak breath alcohol concentrations (BrAC), suggesting that this pattern of response may not be limb dependent (King, de Wit, McNamara, & Cao, 2011). Further, greater stimulation and less sedation at peak BAC was associated with significantly greater binge drinking, quantity/frequency of alcohol use, alcohol-related consequences, and rates of AUD's across a two-year follow-up.

Additional support for an amended DM was found in a placebo-controlled alcohol challenge study demonstrating that higher stimulation and lower sedation at peak BrAC

were predictive of an increase in AUD symptoms across 6 years (King, McNamara, Hasin, & Cao, 2014). These effects were not predictive when measured on the ascending or descending limb. Finally, in a study that followed high and low risk individuals across 5-6 years, heavy drinkers at baseline showed greater stimulant response and lesser sedative responses at peak BrAC (King, Hasin, O'Connor, McNamara, & Cao, 2016). Light drinkers had an opposite pattern of response. In a follow-up alcohol challenge, heavy drinkers who had persistent AUD symptoms at follow-up showed increased stimulation and decreased sedation at peak BAC. In contrast, heavy drinkers with few AUD symptoms showed reduced stimulant response at re-examination. This suggests that maintained sensitivity to the rewarding aspects of alcohol is a risk factor for the maintenance of AUD symptoms.

Both the LLR and DM models typically work under the assumption that patterns of AR identified in the lab reflect innate individual differences in alcohol response. Many of these studies have examined risk related to family history, suggesting possible genetic underpinnings of subjective effects of alcohol. Indeed, there is a growing body of literature examining the heritability of alcohol response (Enoch, 2014). Several studies have addressed this question using the Self-Rating of the Effects of Alcohol (SRE) questionnaire, which assesses predominately sedative effects of alcohol during early drinking experiences (Schuckit, Smith, & Tipp, 1997). For example, Schuckit et al., (2005) found significant correlations between the SRE scores of participants and their first-degree relatives and non-significant correlations between SRE scores and those of unrelated participants. Further, in a study utilizing sibling adult social drinkers, SRE scores were shown to be 67% heritable (Kalu et al., 2012). Heritability of similar

measures assessing sedative effects of alcohol has also been shown to be approximately 60% (Heath et al., 1999; Viken, Rose, Morzorati, Christian, & Li, 2003). Moving beyond estimates of heritability, studies have searched for specific areas of the genome associated with a low level of response to alcohol, showing the strongest potential for chromosomes 10, 11 and 22 (Wilhelmsen et al., 2005), the 5-HTTLPR high activity variant (Hinckers et al, 2006), and minor alleles of SNPs within the distal GABRA2 haplotype block (Enoch, 2008). Thus, there is considerable evidence for a genetic basis for subjective alcohol effects.

However, much of the research on the heritability of alcohol response outlined above has focused on more sedative effects of alcohol, so there is less evidence supporting genetic influences on stimulant response. Further, there is considerable evidence that stimulant alcohol response is associated with drinking history, such that heavier drinkers experience more positive stimulant effects than do lighter drinkers (King et al., 2002; Corbin, Gearhardt, & Kim Fromme, 2008; Morean & Corbin, 2008; Quinn & Fromme, 2011). Therefore, it is possible that sedative response to alcohol is more of an innate characteristic, whereas stimulant response may be more impacted by drinking history, a possibility that has received little attention in the literature. This is a bit surprising as early drinking history is a well-known predictor of later drinking outcomes, and it is possible that negative consequences of early alcohol exposure operate, at least in part, through changes in AR. The lack of prior work in this area may be a function of the lack of comprehensive information about the drinking histories of individuals participating in alcohol challenge studies. Most studies capture early drinking history with one or two items about age of onset of drinking and/or regular or heavy drinking.

Although minimal assessments of age of first use or regular/heavy drinking provide an incomplete understanding of drinking history, research has consistently shown that an earlier age of onset is a risk factor for alcohol use and problems (Morean, Corbin, & Fromme, 2012). For example, those who consumed their first drink before age 18 engaged in significantly more heavy drinking than those who did not start drinking until age 21 (Liang & Chikritzhs, 2015). Further, individuals who had an earlier age of onset reported significantly more occasions of driving while under the influence and alcohol-related motor vehicle accidents (Hingson, Heeran, Levenson, Jamanka, & Voas, 2002). An earlier age of onset is also associated with higher rates of alcohol abuse and dependence (Dawson, Goldstein, Chou, Ruan, & Grant, 2008). One longitudinal study found that, after 10 years, approximately 14% of participants who initiated alcohol use between 11 and 14 years old met diagnostic criteria for alcohol abuse, and 16% met criteria for an alcohol dependence diagnosis (DeWit, Adlaf, Offord, & Ogborne, 2000). In contrast, rates of abuse and dependence for those who started drinking after the age of 19 were 2.0% and 1.0% respectively.

Research has also shown that age of first intoxication is an important indicator of early alcohol exposure and predicts drinking outcomes over and above age of onset (Warner & White, 2003; Warner, White, & Johnson, 2007). For instance, college students who reported an age of first intoxication of 13 or under were approximately three times as likely to be diagnosed with an alcohol use disorder relative to those who reported an age of first intoxication of 19 or above (Hingson, Heeren, & Winter, 2006). Additionally, a shorter delay from first use to first intoxication accounts for unique

variance in the prediction of later heavy drinking and related problems (Morean, Corbin, & Fromme, 2012).

Although measures of age of onset have predictive utility, they are not optimal, as early drinking experiences are known to be more variable compared to drinking in later adulthood. Numerous trajectory studies have demonstrated diverse drinking patterns during adolescence and into young adulthood (Wills, McNamara, Vaccaro, & Hirky, 1996; Stice, Myers, & Brown, 1998). For example, Colder, Campbell, Ruel, Richarson, and Flay (2002) found five distinct drinking patterns in adolescence (grades 7 through 12). The first pattern consisted of occasional very light drinkers; the second included those who had a moderate escalation of quantity and frequency of alcohol use; the third identified adolescents who drank infrequently, but drank heavily when they did drink; the fourth displayed a rapid increase in both quantity and frequency throughout adolescence; and the final pattern started with high levels of alcohol use in grade 7 but rapidly decreased in frequency by grade 12. Those who showed rapid escalation in alcohol use were at greatest risk for alcohol-related problems.

Several studies have found four distinct alcohol use trajectories across adolescence. Shamblen, Ringwalt, Clark, and Hanley (2014) examined trajectories across a three-year time period (grade 6 through grade 8), and identified abstainers, small increasers, light users, and rapid increasers. Danielsson and colleagues (2010) also found four drinking classes based on patterns of consumption from ages 14 to 19; low consumers, gradually increasing, high consumers, and rapidly increasing. Interestingly, both high consumers and rapid increasers were more likely to have experienced alcohol-related problems. Similarly, in a large sample of over 13,700 adolescents, Su, Supple,

Leerkes, and Kuo (2019) identified four classes including persistent heavy alcohol users, developmentally limited alcohol users, late-onset heavy alcohol users, and non/light alcohol users. The National Longitudinal Study of Adolescent Health also found four alcohol use patterns from 7th to 9th grade, including abstainers, early starters, late starters, and de-escalators (Martineau & Cook, 2017). Finally, Brunborg and colleagues (2018) examined drinking trajectories in a long-term longitudinal study across the ages of 13-27. Participants were classified into stably high, early increasers, later increasers, or stably low drinker categories. Those classified as either stably heavy drinkers or early increasers were more likely to experience alcohol-related problems at the last follow-up. Together, results of these studies suggest that relations between early use and later drinking outcomes may be complex and require more information than one or two items about age of onset.

In summary, research suggests that both AR and early drinking experiences are robust predictors of later drinking outcomes. Thus, it would be beneficial to better understand how they may work in concert to confer risk. It is important to acknowledge that as with AR, drinking history may also be an indication of heritability or genetic risk. Studies have shown that having a family history of problematic alcohol use is related to earlier age of onset of drinking and classification into heavier drinking trajectories (Harrington, Velicer, & Ramsey, 2014; Warner, White, & Johnson, 2007). Therefore, we are not able to truly differentiate between genetic and drinking history effects on AR. It is quite possible that there are both genetic effects of AR that run through drinking history and genetic effects that are independent of drinking history.

Interestingly, a recent meta-analytic review of the AR literature that examined over 30 years of research, suggests that there may be different pathways of risk which support this idea (Quinn & Fromme, 2011). On one hand, results suggested that those with a positive family history of alcohol problems were more likely to exhibit an AR pattern that is consistent with LLR model. More specifically, when collectively looking at data from family history positive individuals, they were more likely to display an overall blunted response to alcohol as opposed to a heighted stimulant response. This suggests that there may be more direct genetic component of sedative response.

However, when examining recent drinking histories, recent heavy drinkers were more likely to show an AR pattern consistent with the DM (Quinn & Fromme, 2011). These results suggest that drinking history, rather than, or in addition to inherited risk, may have an important impact on both sedative and stimulant responses to alcohol. The impact of drinking history can also be seen in the literature on tolerance and sensitization to alcohol with drinking experience. Tolerance refers to the need for more alcohol to feel the same effects as one did during earlier drinking experiences and results from heavy use (Schuckit, 1994). Greater tolerance has been shown to be a strong predictor of heavy drinking and alcohol-related problems (Schuckit et al., 2008). Further, tolerance has been shown to develop rapidly across adolescence due to the critical brain development that occurs during this time (Spear, 2013; Witt, 2010). Tolerance is particularly important with respect to the LLR model and the reduced sedative response predicted by the DM model. A low sedative/impairment response to alcohol may reflect a more direct innate risk factor and/or an acquired tolerance to alcohol effects as a result of drinking

experience. Together, these studies support distinct pathways of risk that could differentially impact stimulant and sedative response to alcohol.

Although little research has addressed this question, Morean and Corbin (2008) assessed the role of early AR, measured retrospectively, and acquired tolerance, an indicator of drinking history, on alcohol outcomes. They found that a low level of early AR was significantly related to greater alcohol use and alcohol-related problems. Additionally, acquired tolerance predicted these outcomes over and above early AR. In a separate sample of young adult heavy drinkers, both retrospectively reported low early AR and acquired tolerance were significant predictors of weekly drinking (Corbin et al., 2013). Though similar to the previous study, acquired tolerance was a more robust predictor than early AR.

The incentive-sensitization theory also supports the role of alcohol use history in relation to level of response to various drugs (Berridge & Robinson, 1995; 1998; Robinson & Berridge, 1993; 2000). This theory posits that one of the ways addiction develops is through sensitization such that, with chronic use, the brain reward system becomes more sensitive to a particular drug. In other words, a more chronic or risky pattern of drinking may lead to sensitization to the rewarding effects of alcohol. Consistent with this possibility, Newlin and Thomson (1991;1999) showed that, across multiple drinking sessions, high-risk participants developed chronic sensitization to alcohol's effects across trials. Taken together with research on tolerance, drinking history could lead to an AR pattern similar to the DM through the development of sensitization to the rewarding aspects of alcohol and tolerance to the more negative effects. Collectively, studies of acquired tolerance and sensitization suggest that changes

in AR as a function of drinking history may be important in understanding risk for alcohol problems. These findings call into question the idea that patterns of risk associated with AR are primarily related to innate individual differences in alcohol response.

Although these studies suggest that AR may mediate the relation between drinking history and later problems, we are not aware of any longitudinal alcohol-challenge studies that have attempted to assess relations between early drinking history and AR, or the extent to which AR mediates effects of early drinking history on later outcomes. The current study aims to fill this gap in the literature by examining how alcohol use trajectories across adolescence and early adulthood impact relations between AR after an alcohol challenge and drinking outcomes over a 2-year period. Though it is possible that there may be interactive effects of early drinking history on early AR, given that we are assessing AR well into many participant's drinking experience, we felt it was more appropriate to assess a mediational pathway. In order to provide a full account of early alcohol exposure, we will use a novel measure, the Comprehensive Early Drinking History Form (CEDHF; Hartman, Corbin, Chassin, & Doane, 2019). This will allow for the creation of retrospective alcohol use trajectories beginning with individuals' earliest drinking experiences.

Based on the extant literature, we hypothesize 4 distinct consumption trajectories, (1) consistently heavy drinkers (HH), (2) consistently light/social drinkers (LL), (3) those that increase their alcohol use over time (LH), and (4) those that decrease their alcohol use over time (HL). Regarding AR, we hypothesize that those at highest risk for later negative drinking outcomes will show one of two patterns of response. The first is an

overall blunted response to alcohol (consistent with the LLR model), and the second is a heightened stimulant response and dampened sedative response to alcohol (consistent with the DM). Further, although drinking history has been shown to be related to both stimulant and sedative response, we hypothesize that it will have a greater impact on stimulant relative to sedative response. Finding support for this hypothesis would suggest that there may be both genetic and drinking history effects on sedative response whereas stimulant response may be more strongly influenced by risk through drinking experience.

With regard to which drinking trajectory classes will show a risky AR profile, there are three plausible hypotheses based on prior research. First, persistent high exposure to alcohol may be necessary to increase long-term risk for heavy drinking and related problems. If this is the case, the HH group would be expected to differ in AR from all other trajectory classes. Second, early exposure may be the critical risk factor. If that is the case, the HH and HL groups should show greater risk for later heavy drinking and problems relative to the other two trajectory classes. Third, there may be a critical threshold such that any extensive exposure to alcohol is associated with a high-risk pattern of AR. In this case, the HH, HL, and LH groups would all be expected to show a higher risk pattern of AR than the LL trajectory class. See Table 1 for a depiction of study hypotheses with respect to both AR model and drinking trajectory. Given the lack of prior work on this topic, each of these hypotheses is reasonable, making this a more exploratory study. However, research on alcohol consumption trajectories outside of the context of AR suggests that the HH and HL groups may be at the greatest risk for negative outcomes (Brunborg et al., 2017; Colder et al., 2002; Danielsson et al., 2010).

To our knowledge, this is the first study to longitudinally assess AR in relation to participant's full drinking history and future alcohol-related outcomes.

CHAPTER 2

METHODOLOGY

Participants

This study utilized data from an ongoing alcohol challenge study investigating the effects of social and physical context on AR. The longitudinal parent study included 2 in-person sessions and 4 follow-up online/phone-interview sessions that took place across a 2-year period. The parent study had full Institutional Review Board approval from the university in which it was being conducted. Eligibility criteria included binge drinking (5 or more drinks in one sitting for men/4 or more for women) at least once a month. Individuals were excluded from the study if they reported current clinical levels of anxiety or depression, met criteria for alcohol dependence, had previously participated in abstinence-oriented treatment programs, and for women, pregnancy. Additionally, individuals who reported negative side effects of consuming alcohol were excluded to protect against undue discomfort. While the lightest and heaviest drinkers were excluded from the study, the sample is similar to nationally representative samples of young adults with respect to mean levels of alcohol use (Grant, Stinson, & Hartford, 2001; Kann et al., 2018). Recruitment consisted of flyers placed around campus and the surrounding community and online advertisements (e.g., Facebook, Craigslist).

Procedure

Participants first came into the lab for a series of surveys and interviews to determine eligibility. If they met inclusion criteria, participants returned to the lab within a few weeks to complete the alcohol administration session. Participants were randomly assigned to one of four contexts; individual lab, group lab, individual simulated bar,

group simulated bar. All participants were randomly assigned by context to either a placebo condition or alcohol condition. Only participants assigned to the alcohol condition will be included in the current study. Once age was verified and a zero blood alcohol concentration (BAC) was confirmed via breathalyzer, baseline alcohol response (AR) assessments were taken. For the participants assigned to the alcohol condition, the volume of alcohol in each drink was adjusted by gender, age, height, and weight, with a target BAC of .08 g%. Participants in both conditions were told that they were given alcoholic beverages.

Alcohol administration consisted of three drinks over 20 minutes (6 minutes per drink with a 1-minute resting period between each drink). Each drink in the alcohol condition contained 1-part alcohol to 3-parts mixer. Those in the placebo condition were given flat tonic water instead of alcohol in the same volume as those in the alcohol condition. Participants were instructed to consume the drinks at a steady rate across each 6-minute period. After an 8-minute absorption period, BACs were taken using a handheld breathalyzer at 10-minute intervals. Once the participant reached a BAC of at least .06 g%, the ascending limb measures of AR were taken. These measures were repeated at peak BAC and on the descending limb when BACs returned to levels that matched ascending limb assessments as closely as possible. Each placebo participant was yoked to an alcohol participant such that the timing of assessments was matched to an alcohol participant. Following the descending limb assessment, BAC readings were taken every 30 minutes until BACs fell below .03%, at which time participants were allowed to leave the laboratory. Following the beverage administration session,

participants completed online/phone interviews and web-based survey assessments every 6 months for a total of 2 years (4 follow-ups in all).

Measures

Demographics. Demographic variables included age and sex.

Lag between age of onset and other stages of drinking. Participants were asked the age at which they first consumed alcohol, the age at which they first consumed enough alcohol to feel intoxicated, and the age at which they began drinking regularly (one standard drink at least once a month). Given that age of first intoxication and age of regular use are both dependent upon age of first use, we calculated the lag between age of onset and both (1) age of first intoxication and (2) age of first regular use. Age of onset was subtracted from both age of first intoxication and age of first regular use such that higher scores reflected a longer delay between drinking milestones.

Family Tree Questionnaire (FTQ). The FTQ (Mann, Sobell, & Sobell, 1985) asked participants to categorize their biological mother, biological father, and maternal and paternal grandmother and grandfather into 1 of the following categories: (1) Never Drank: A person who (has) never consumed alcohol beverages (i.e., a lifelong abstainer; teetotaler). (2) Social Drinker: A person who drinks moderately and is not known to have a drinking problem. (3) Possible Problem Drinker: A person who you believe or were told might have (had) a drinking problem but whom you are not certain actually has (had) a drinking problem. (4) Definite Problem Drinker: Only include here persons who either are known to have received treatment of a drinking problem (including being a regular member of Alcoholics Anonymous), or who are known to have experienced several negative consequences of their drinking. (5) No Relative: Only applicable for brothers

and sisters. Or (6) Don't Know/Don't Remember. Grandparents that were categorized as definite problem drinkers were coded as 1 and parents categorized as definite problem drinkers were coded as 2 (all other categories coded as 0). A weighted mean for definite problem drinkers was created from those values. Participants' scores were added and then divided by the number of relatives reported on.

Comprehensive Adolescent Drinking History Form (CEDHF). The CEDHF gathers information about age of onset and age of first intoxication, along with quantity/frequency for both typical and heavy drinking periods for each year from age of first regular use (Hartman, Corbin, Chassin, & Doane, 2019). A sample question for typical drinking includes, "When you were (age of first regular use) how often did you typically consume alcohol (i.e., beer, wine, wine cooler, or liquor)?" In addition, the CEDHF includes a question about aggregate drinking experiences from age of onset to when an individual first started drinking regularly. The CEDHF has been shown to be significantly correlated with other alcohol use assessments and predictive of concurrent and future alcohol-related problems over and above commonly used measures (e.g. TLFB, age of first use, age of first intoxication). This measure was administered during session 1, the 12-month follow-up, and the 24-month follow-up. In order to maximize our sample size, we chose to include the measure that was administered at the 12-month follow-up and excluded the current year of drinking to allow for prospective prediction across the 2-year follow-up.

Alcohol Response. The following measures were completed during the lab session at baseline, on the ascending limb, at peak BrAC, and again on the descending limb. At baseline, questions asked, "On a scale of 0-10 please rate the extent to which

you are CURRENTLY experiencing each of these feelings." All other assessments asked, "On a scale of 0-10 please rate the extent to which drinking alcohol has produced these feelings in you AT THE PRESENT TIME."

The Biphasic Alcohol Effects Scale (BAES). The BAES assesses both stimulant (7 items) and sedative (7 items) alcohol effects and has demonstrated reliability and validity for use in alcohol administration studies (Martin et al., 1993). Participants rated the extent to which they experienced each effect on an 11-point Likert scale ranging from 0 = *not at all* to 10 = *extremely*. Sample items on the stimulant subscale include "excited" and "talkative." Sample items on the sedative subscale include "sluggish" and "down." Internal consistency reliabilities of the two BAES subscales ranged from .80 to .92 across timepoints.

The Subjective Effects of Alcohol Scale (SEAS). The 14-item SEAS covers the full valence by arousal affective space including high arousal positive, low arousal positive, high arousal negative, and low arousal negative effects (Morean, Corbin, & Treat, 2013). Participants rated the extent to which they experienced each effect on an 11-point Likert scale ranging from 0 = *not at all* to 10 = *extremely*. The current study will only utilize the high arousal positive and low arousal negative subscales as they correspond to the BAES and the SHAS and are the most widely assessed aspects of alcohol response. Sample items for these subscales respectively include "lively" and "wobbly." The SEAS has demonstrated incremental validity in the prediction of alcohol-related outcomes relative to the BAES and SHAS. Internal consistency reliabilities of the two SEAS subscales ranged from .85 to .95 across timepoints.

Timeline Follow-Back Interview (TLFB). The 30-day TLFB was collected at all time-points (Sobell & Sobell, 1992). Participants filled out a calendar of their drinking behavior over the past month including how many drinks they had on each occasion and the time over which they drank them. To enhance memory recall, participants were given a drink conversion chart, told to think about important events that happened within the past 30 days, and were allowed to check their personal calendars. Previous studies have shown the TLFB to be a reliable and valid retrospective alcohol use measure.

Young Adult Alcohol Consequences Questionnaire (YAACQ). The YAACQ is a 48-item measure that assesses eight categories of consequences resulting from alcohol use in the past 30-days and was administered at all time-points (Read, Kahler, Strong, & Colder, 2006). Sample items include, "I have passed out from drinking," and "I have neglected my obligations to family, work, or school because of drinking." Responses are in a dichotomous yes/no format. Internal consistency reliabilities of the YAACQ across timepoints ranged from .92 to .96 across timepoints.

CHAPTER 3

DATA ANALYTIC PLAN

The proposed analyses were carried out in Mplus version 7.4 (Muthen & Muthen, 2012) using robust maximum likelihood estimation (robust to non-normal data) as well as full information maximum likelihood estimation to handle missing data. Prior to conducting the main analyses, descriptive statistics were examined to properly characterize the sample. Further, distributions of all variables were examined for non-normality and outliers and appropriate transformation techniques (e.g., logarithmic) were employed as needed.

First, confirmatory factor analysis (CFA) was applied to the alcohol response measures including the SEAS and BAES. We conducted a CFA that included both baseline and peak AR. Given that our proposed factors only included two indicators, we constrained the communalities to be equal within each factor. Model fit was evaluated using the Chi-Square Test of Model Fit, Comparative Fit Index (CFI), Root Mean Square Error of Approximation (RMSEA), and Standardized Root Mean Square Residual (SRMR). Good model fit is indicated by CFI > .95, RMSEA < .06, and SRMR < .08 (Hu & Bentler, 1999). We expected a 2-factor structure for each timepoint. We hypothesized that the high arousal positive subscale of the SEAS and the stimulant subscale of the BAES would load together creating a high arousal positive factor (HAP). The low arousal negative subscale of the SEAS and the sedation subscale of the BAES were expected to load together creating a low arousal negative factor (LAN).

Next, growth mixture modeling (GMM) was used to identify alcohol use trajectory classes using data from the CEDHF. This method was utilized to identify

latent classes of individuals with relatively homogeneous growth patterns (Nagin, 1999; Bauer 2007). Ideally analyses would have used negative binomial distributions to account for positive skew, however, given that the variables were not comprised entirely of integers, this was not possible. Thus, the GMM used maximum likelihood with robust standard errors (Reinecke & Seddig, 2011). The models were to include 10 time points across the ages of 16 to 25 and both linear and quadratic models were tested. We hypothesized that these models would be quadratic as drinking tends to increase and then decrease across this time period. Classes that comprised less than 10% of the total sample were not to be included. The Akaike's Information Criterion (AIC), Bayesian Information Criterion (BIC), Entropy, and the Bootstrap Likelihood Ratio Test (BLRT) were used to determine the optimal number of classes (Nylund, Asparouhov, & Muthen 2007). Lower AIC and BIC values indicate better model fit. The BLRT provides *p*-values that are used to determine whether there is a significant increase in model fit from adding one more class. It was hypothesized that 4 trajectory classes would emerge: High stable drinkers (HH), individuals who drink heavily initially and decrease over time (HL), Low/social stable drinkers (LL), and those who are light drinkers initially but escalate to heavier drinking over time (LH). The trajectory classes were saved as a separate categorical variable to be used in additional analyses.

First, we assessed whether drinking history significantly predicted the two AR latent factors (the A-path). Three dummy codes were to be created for the drinking history data, (1) HH coded against LL, (2) HL coded against LL, and (3) LH coded against LL. Next, drinking history was included as a predictor of both the intercept and slope of alcohol use or alcohol-related problems across the follow-up assessments (C-

path; Bauer, 2007). Follow-ups (TLFB and YAACQ) were collected every 6-months. Separate models were tested for alcohol use and problems. Both linear and quadratic latent growth curve models were tested, though models were expected to be linear given that drinking levels tend to either be stable or decreasing in the mid-twenties. We then examined whether the two AR latent factors predicted the longitudinal alcohol outcomes (B-path). Finally, we used the *model indirect* command in Mplus to test for indirect effects of drinking history on the intercepts and slopes of the drinking outcomes through the mediating mechanism of AR. Bias corrected bootstrap confidence intervals were used to test indirect effects given the asymmetric nature of confidence intervals (MacKinnon, Lockwood, & Williams, 2004). Current age, sex, age of onset, lag between age of onset and both age of first intoxication and age of first regular use, physical context, social context, and family history were included as covariates in all models.

CHAPTER 4

RESULTS

We first examined the distributions of all variables for non-normality and outliers. Given positive skew in the CEDHF and clear outliers, these variables were winsorized such that values outside of 3 standard deviations from the grand mean were replaced with the next highest value. Further, the sedative subscale of the BAES and the low arousal negative subscale of the SEAS were log transformed to address skewness.

The overall sample was 55% male with an average age of 22.69 at baseline. The average age of onset was 16.54, the average age of first intoxication was 17.53, and the average age of first regular use was 18.97. With regard to family history, 17.1% of the sample identified at least one biological grandparent as a definite problem drinker, 10.4% identified at least one biological parent as a definite problem drinker, and 21.8% of the sample reported they had at least one biological parent or grandparent that was a definite problem drinker. Concerning drinking behavior prior to baseline assessments, participants on average consumed approximately 5.24 drinks per week at age 17 and peaked in their alcohol consumption at age 21 with approximately 10.40 drinks per week. After baseline assessments, participants peaked in their alcohol consumption and related problems at the 6-month follow-up with approximately 9.28 drinks per week and 9.35 alcohol-related problems in the past month. Alcohol use and problems then decreased over time. These rates of drinking were expected given only moderate to heavy drinkers were included in the current sample, and average weekly use was consistent with prior studies using these criteria (Corbin et al., 2015). Although individuals with current AUDs were excluded, levels of alcohol use were considerably higher than national

norms. According the National Survey on Drug Use and Health (NSDUH, 2019) only 52.5% of college students ages 18-22 and 44% of non-college students ages 18-22 reported any alcohol use in the past month. Moreover, rates dropped to 33% of college students and 27.7% of non-college students for endorsement of binge drinking in the last month. Further, according to the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), young adults ages 18-20 endorsed consuming on average 3.06 drinks per week and 21-24-year old's endorsed drinking 4.88 drinks per week (2004). Thus, the current sample reflects a higher risk subset of the population. Means and standard deviations of all study variables are presented in Table 1.

We then applied a CFA to the alcohol response measures including the BAES and SEAS. We proposed a two-factor structure at each timepoint characterized by a high arousal positive factor (HAP) and a low arousal negative factor (LAN) for both baseline and peak BAC. This model provided less than adequate fit to the data (χ^2= 129.301, CFI = 0.847, RMSEA = 0.170, SRMR, 0.071). HAP comprised the high arousal positive subscale of the SEAS and the stimulant subscale of the BAES, whereas LAN comprised the low arousal negative subscale of the SEAS and the sedative subscale of the BAES. The standardized factor loadings for baseline and peak LAN were 0.480 and 0.670, respectively. The standardized factor loadings for baseline and peak HAP were 0.881 and 0.904, respectively. Though the model fit was poor, we chose to retain the latent factors as they were presumed to be more reliable than the measured variables alone. The factor scores for baseline HAP, baseline LAN, peak HAP, and peak LAN were saved as separate variables and used in subsequent analyses.

We then examined a series of quadratic GMM models with 1 to 4 classes to identify drinking trajectories across adolescence and young adulthood. We proposed using 10 timepoints (ages 16-25), however, given the low endorsement rates of drinking at early ages and the smaller sample size at later ages (46 participants with valid data at age 16 and 53 participants with valid data at age 25), we included only 8 timepoints (ages 17-24) in the analyses. The sample consisted of 211 participants. Initially, models failed to converge given a non-positive definite covariance matrix. This appeared to be driven by a negative variance at age 17. Therefore, we constrained the variances at all ages to be equal in each model which allowed the models to converge.

We first compared the linear and quadratic models to ensure that we were properly modeling growth. As hypothesized, the 1-, 2-, 3-, and 4-class quadratic models each fit the data better than their linear model counterparts with lower BIC values for all models. Therefore, we proceeded with the quadratic models. The 1-class model provided a loglikelihood value of -6765.267, an AIC of 13550.53, and a BIC of 13584.05. The 2-class model showed better fit to the data than the 1-class model based on a BLRT of 83.122, $p < .001$. This model was characterized by a stably low/social drinking group (86% of the sample) and an increasing group (14% of the sample). The 3-class model also showed significantly better fit to the data relative to the 2-factor model based on a BLRT of 63.761, $p < .001$. This model represented a stably low/social drinking class (76.9% of the sample), an increasing class (7.1% of the sample), and a developmentally limited drinking class such that drinking increased and then decreased over time (16.1% of the sample). The 4-class model also showed significantly better fit to the data than the 3-factor model based on a BLRT of 42.507, $p < .001$. This model

showed a stably low/social drinking group (74.8% of the sample), an increasing group (7% of the sample), an early developmentally limited group (10.5% of the sample), and a late developmentally limited group (7.7% of the sample).

Although they provided better fit to the data than the one and two-factor models, the three and four-factor models did not meet our original criteria given that at least one group in each model was comprised of less than 10% of the sample. Therefore, we had to adjust criteria for model selection. The gain in model fit was larger for the 3-class model than the 4-class model. Moreover, 2 classes for the 4-factor model were small, and entropy was highest for 3-factor model. Additionally, the classes in the 3-factor model were conceptually meaningful and distinct. Thus, we chose to use the 3-class model as this was the most interpretable, provided adequate fit to the data, and included classes that approached the 10% threshold. AIC, BIC, and entropy values are provided in Table 3 and the final drinking trajectories are depicted in Figure 1. The trajectory classes were saved as categorical variables and two sets of dummy codes were created: 1) the stably low class as the reference group and 2) the developmentally limited class as the reference group. These were used in two separate sets of analyses to allow for all comparisons between classes.

Next, we examined whether drinking history trajectories predicted peak AR including high arousal positive effects and low arousal negative effects. We controlled for social and physical context, current age, sex, age of onset, and lag between age of onset with both age of first intoxication and age of first regular use in this and all subsequent analyses. Further, family history was included as a covariate to account for possible heritable effects. We initially allowed all covariates to correlate freely. This

resulted in a non-positive definite first-order derivative product matrix. Therefore, we only included significant correlations between covariates in all subsequent models which allowed the models to converge normally.

There were no significant effects and only one marginally significant effect of trajectory classes on AR. Results showed that those categorized in the developmentally limited class experienced marginally less LAN effects than those in the low/social class (Unstandardized coefficient = -0.125, SE = 0.073, p = 0.088; Standardized coefficient = -0.055). Correlations among covariates and AR variables are presented in Table 3 and unstandardized coefficients of covariates and drinking trajectory classes are presented in Table 4.

Next, we examined whether trajectory class membership predicted drinking and alcohol-related problems across the two-year follow-up. Results showed that those categorized in both the increasing class and the developmentally limited class had a significantly higher intercepts for drinking than those in the low/social class (Increasing: Unstandardized coefficient = 0.834, SE = 0.139, p < .001; Standardized coefficient = 0.299; Dev Lim: Unstandardized coefficient = 0.442, SE = 0.168, p = .009; Standardized coefficient = 0.240). The increasers also had a significantly higher intercept when compared to those in the developmentally limited class (Unstandardized coefficient = 0.391, SE = 0.198, p = .048; Standardized coefficient = 0.140). This suggests that increasers drank significantly more than both stably low/social drinkers and developmentally limited drinkers at the 6-month follow-up and the low/social drinkers drank significantly less than the developmentally limited drinkers at this timepoint.

There were no significant effects of drinking class on slope. Unstandardized coefficients of covariates and drinking trajectory classes are presented in Table 5.

With regard to alcohol-related problems, results showed that both increasers and those in the developmentally limited class had a significantly higher intercept than stably low/social drinkers (Increasers: Unstandardized coefficient = 0.984, SE = 0.286, p = .001; Standardized coefficient = 0.275; Dev Lim: Unstandardized coefficient = 0.715, SE = 0.194, p < .001; Standardized coefficient = 0.302). Participants in the increasing and developmentally limited groups experienced more alcohol-related problems at the 6-month follow up than those in either of the other two groups. Again, there were no significant effects of drinking class on slope. Unstandardized coefficients of covariates and drinking trajectory classes are presented in Table 6.

In order to plot the trajectories for each class, we first attempted to run a known class model with the full sample to generate those estimates. The model would not converge, even when covariates were excluded. Therefore, we ran models for each class separately. Again, these models failed to converge. Thus, we excluded the covariates which allowed for convergence. Sample means for each class, not accounting for covariates, in relation to drinking and problems are presented in Figures 2 and 3, respectively.

We then sought to determine if AR predicted longitudinal drinking outcomes. In regard to alcohol use, results showed that, when controlling for baseline AR and the other covariates, greater LAN significantly predicted a lower intercept (Unstandardized coefficient = -0.805, SE = 0.247, p = 0.001; Standardized coefficient = -0.922). In contrast, greater HAP significantly predicted a higher intercept (Unstandardized

coefficient = 0.347, SE = 0.113, p = 0.002; Standardized coefficient = 0.454) and a smaller slope (Unstandardized coefficient = -0.127, SE = 0.050, p = 0.011; Standardized coefficient = -0.841). Thus, those with a stronger LAN response to alcohol drank significantly less at the 6-month follow-up. Conversely, those with a greater HAP response tended to drink significantly more at the 6-month follow-up but then decreased in their alcohol use over time. Unstandardized coefficients for the covariates and AR variables are presented in Table 7.

When examining effects for alcohol-related problems, stronger HAP effects significantly predicted a higher intercept (Unstandardized coefficient = 0.310, SE = 0.151, p = 0.040; Standardized coefficient = 0.329) and marginally predicted a smaller slope (Unstandardized coefficient = -0.115, SE = 0.065, p = 0.079; Standardized coefficient = -0.863). Thus, those with a higher HAP response to alcohol showed potentially meaningful differences in alcohol-related problems across the two-year follow-up. There were no significant or marginally significant effects of LAN on alcohol-related problems. Unstandardized coefficients of covariates and AR variables are presented in Table 8.

Finally, given that there were no significant paths from drinking history to AR, there was no evidence to support mediated effects of drinking history on alcohol outcomes through AR. Therefore, we did not conduct formal tests of indirect effects.

CHAPTER 5

DISCUSSION

The current study examined how alcohol use trajectories across late adolescence and early adulthood impacted relations between AR after an alcohol challenge and future drinking outcomes. More specifically, we assessed whether drinking history worked through AR to confer risk for greater alcohol consumption and problems across a 2-year follow-up. Broadly, we hypothesized that those categorized in a high-risk drinking trajectory class would also show a risky AR profile and therefore would drink more/experience more alcohol-related problems over time. Further, given prior research on the heritability of sedative AR, we expected that drinking history would have a greater impact on stimulant relative to sedative alcohol response. To our knowledge, this is the first longitudinal alcohol-challenge study that has examined relations between early drinking history and AR and the extent to which AR serves as a mediator of the effects of early drinking history on later drinking outcomes. Thus, the current study serves to fill an important gap in the literature.

With regard to drinking history, we found 3 distinct drinking trajectory classes. As hypothesized, we found both a stably light/social drinking class and an increasing class. This supports prior literature examining drinking trajectories across this time period (Brunborg et al., 2018, Danielsson et al., 2010). We also identified a developmentally limited class, similar to Su et al. (2019), which was characterized by increases in adolescence followed by decreases in emerging adulthood, with a peak around the ages of 20-21. Of note, the vast majority of our sample were categorized into

the low/social drinking trajectory class and the smallest class was comprised of those that increased their use over time.

Contrary to hypotheses, these drinking history trajectory classes did not significantly predict either high arousal positive (HAP) or low arousal negative (LAN) response at peak blood alcohol concentration (BAC). However, consistent with the low level of response (LLR) model, those categorized in the developmentally limited class reported marginally weaker LAN effects of alcohol when compared to low/social drinkers. We expected even stronger effects of drinking history on stimulant response to alcohol, given evidence for substantial heritability of sedative alcohol response and limited evidence for genetic effects on stimulant response. However, the drinking history classes did not differ with respect to reported stimulant alcohol effects. Although this finding is surprising given evidence for differences in stimulant response between light and heavy drinkers, it is not particularly surprising that drinking history impacted sedative alcohol response. Heavier drinkers may develop tolerance to alcohol effects, and tolerance seems to be more evident for sedative relative to stimulant response (Enoch, 2014; Quinn & Fromme, 2011).

In addition to predicting AR, we expected drinking history to predict future patterns of consumption and related problems. Thus, we examined drinking history as a predictor of the intercept and slope of alcohol outcomes across a 2-year follow-up. Results partially supported our hypotheses, as both of the higher risk trajectory classes (increasers and developmentally limited drinkers) consumed significantly more alcohol and experienced significantly more alcohol-related problems at the 6-month follow-up relative to those in the low/social drinking class. Further, those classified as increasers

also consumed significantly more alcohol at the six-month follow-up than did those in the developmentally limited class. However, contrary to hypotheses, the drinking classes did not differ with respect to growth in alcohol use or problems over time. In other words, drinking history predicted intercepts but not slopes of later drinking outcomes. Given that drinking history is a robust predictor of later drinking behavior, the lack of continued influence of drinking history on growth in drinking outcomes was surprising. This may be attributable to the fact that there was less room for growth among the higher risk drinking classes which started out at higher levels of consumption and further increased relative to lighter drinking class at 6-month follow-up. Comparisons between the two higher risk groups provide support for this as both of the heavier drinking groups reported higher risk at the 6-month follow-up, despite differences in the overall patterns of consumption for these two trajectory classes. Further, those who sustained heavy drinking in the post-college years were at greater risk than those who peaked in their alcohol use at around the age of 21. It is important to acknowledge that though all three trajectory classes tended to decrease in their consumption and related problems at similar rates over time, the two high-risk classes remained at higher risk at the time of the last follow-up, suggesting sustained impact of drinking history.

Consistent with a growing literature, we expected both stimulant and sedative AR to predict patterns of heavy drinking and alcohol-problems across the two-year follow-up. In support of the Differentiator Model (DM), stronger peak HAP and weaker peak LAN predicted significantly greater drinking at the 6-month follow-up. Further, greater peak HAP was associated with significantly higher levels of alcohol-related problems at the 6-month follow-up. Contrary to predictions, stronger HAP response was associated with a

significant decrease in alcohol consumption and a marginal decrease in problems from 6-months after the lab session through the end of the two-year follow-up. It is possible that these decreases were a result of regression to the mean given the relatively high levels of drinking and problems at the 6-month follow-up among those with strong stimulant AR. There was also no support for the hypothesis that stronger LAN response would be associated with greater increases in alcohol use and problems over time. Thus, although our results at the 6-month follow-up largely supported our hypotheses and prior studies, our findings that LAN effects were unrelated to changes in drinking outcomes and that HAP effects were associated with decreases in heavy drinking over time conflict with prior research. Previous research has demonstrated heavier drinking among those with low sedative and strong stimulant effects across periods as long as 30 years.

There are several possible explanations for these findings. First, it is possible that the drinking contexts and dosing protocol in the current study contributed to the lack of significant effects of AR on drinking outcomes over time. Compared to other studies examining AR, the current study's drinking contexts and dosing protocols were much more ecologically valid. For example, 3 out of our 4 contexts were in a simulated bar and/or in a group, and alcohol administration lasted 20 minutes (1-part alcohol to 3 parts mixer, 3 drinks with resting periods in between) with a beverage that most participants enjoyed. Further, alcohol administration occurred after 5pm. This is in stark contrast to previous studies. For example, Schuckit and colleagues (2004, 2006, 2014) began alcohol administration at 9am in a lab environment. Further, participants consumed 20% alcohol solution (90-proof ethanol) in a decaffeinated sugar-free carbonated mixer in a single beverage in only 8-minutes. Although King and colleagues (2002, 2014, 2016,

2017) dosed their participants in a living room like lab setting, they started drinking as early as noon with only a 15-minute dosing period and a beverage containing 16% alcohol (180-proof ethanol) mixed with water, Nutrasweet, and sugar-free grape flavoring in two servings (5 minute per drink with a resting period in between). Though this is more similar to the protocol used in the current study, it is possible that these drinking environments and dosing methods led to differences in AR. These quick bolus doses of high-content alcohol in more sterile and living room like environments would likely elicit more sedative/negative effects of alcohol rather than stimulant/rewarding effects. Because our solitary non-bar context is most similar to those used in prior studies, it is possible that results in this context would have been more similar to results of prior studies. We may have found greater LAN effects in this context which could have led to sustained prediction in outcomes over time. However, we were underpowered to examine contexts specific relations in this current study. Though the differences in context may have led to discrepancies between the findings of the current study and prior work, the use of more ecologically valid environments may better generalize to real-life drinking experiences. Future studies using similarly ecologically valid contexts, and comparing these contexts to more traditional lab contexts, are needed to better understand the long-term impact of AR on drinking outcomes.

It may also be the case that we captured AR too late in participants' drinking histories. It is possible the impact of drinking history on AR occurs quickly after drinking initiation and therefore needs to be assessed closer to the onset of drinking. Given that alcohol administration studies cannot be conducted with those under the age of 21, ecological momentary assessment (EMA) studies may be a useful alternative. Future

EMA studies targeting 18-19 year old's that allow participants to complete measures of AR during real world drinking occasions may be better able to capture relations between drinking history and AR.

Aspects of the study sample may have also contributed to the unique pattern of findings in the current study. Because this was an alcohol-challenge study that involved dosing participants to a target BAC of .08 g%, only moderate to heavy drinkers were included to ensure the safety of all participants. In addition, individuals with AUDIT scores above 15 or who met past month-criteria for an AUD were excluded to avoid administering alcohol to individuals with significant alcohol-related problems. Thus, the lightest and heaviest drinkers were excluded from the sample, which lead to decreased variability in current drinking, and possibly to differences in drinking history and future drinking outcomes. For instance, the majority of our sample were classified as low/social drinkers, and they averaged about 3.5-5.5 drinks per week, which in a normative sample, might not be considered light drinkers. Further, the two higher-risk trajectory classes had quite small sample sizes, suggesting considerable homogeneity in drinking histories across the full sample. This may also help explain why we did not find support for a decreasing drinking class as originally hypothesized. It may be that in order to capture those that decrease across this developmental period, we would need to include true current light drinkers along with past problematic drinkers that may have engaged in early heavy drinking and/or engaged in some sort of prevention or intervention efforts during this time that may result in decreases in consumption.

Further, although the range of reported alcohol problems was substantial, it is possible that our truncated range made it more difficult to detect differences between

classes for both AR and drinking outcomes. If we had the full range of drinker status from abstainers to those with current AUD, we likely would have had larger class sizes, which would have strengthened our ability to detect relations between AR and future drinking outcomes. Further, our sample tended to decrease in use and problems over time. If we had the highest and lowest risk participants in the study, we may have had greater variability in the outcome trajectories, which again could have increased our ability to find sustained effects over time. Given our ability to detect differences in initial drinking outcomes at the 6-month follow-up even with the limited range of drinking at initiation into the study, future studies are needed to further examine relations between drinking history and later AR and drinking outcomes.

The restricted range of drinking behavior is also important when interpreting the findings regarding AR. It is possible, and perhaps likely that, if true light drinkers and problematic drinkers were included in the sample, the findings would have been quite different. A study by King et al., (2016), who included light drinkers, heavy drinkers with few AUD symptoms, and heavy drinkers with several AUD symptoms in a within-subjects design demonstrated the potential of this approach. King et al. found that only those in the high AUD heavy drinking group continued to show a risky AR profile several years later, whereas the low AUD heavy drinking group showed a decrease in stimulation over time. Further, those in the high AUD group continued to exhibit risky drinking at follow-up 5-6 years later. The fact that the current study excluded those who would have met criteria for the high AUD group in the aforementioned study could help explain why we did not find evidence for sustained risk associated with heavier early drinking history and AR. Perhaps AR is only predictive of future drinking outcomes and

predicted by previous drinking behavior for the heaviest drinkers who were not included in the current study. Future studies hoping to further understand relations of drinking history with AR and future alcohol-related outcomes may benefit from a more heterogenous sample that includes the full range of drinking status to better capture true differences and sustained risk between groups. However, there may be ethical concerns about administering alcohol to either very light drinkers or those with alcohol-related problems. Thus, the relative costs and benefits of this approach must be carefully considered.

It is also important to note the developmental stage in which the follow-ups were conducted. We assessed participants in their mid-twenties which has been shown to be a time where young adults begin maturing out of heaving drinking as they transition into adulthood (Jochman & Fromme, 2010). This maturing out process appears to be supported by the current study given that all of the classes in our sample tended to decrease in their use and problems at similar rates across the follow-ups. However, studies examining patterns of alcohol outcomes over the life course have shown that drinking tends to begin increasing once again later into adulthood (Chan, Neighbors, Gilson, Larimer, & Marlatt, 2007; Verges et al., 2012). This could help explain why prior studies that have assessed participants into their thirties and beyond have found stronger evidence for sustained impact of AR on future alcohol outcomes (Schuckit, 1994; Schuckit et al., 2006, 2011; Trim et al., 2008). It is possible that our sample with a truncated range of drinker status in young adulthood could have shown greater variability in alcohol outcomes later in life. Future studies may benefit from follow-up assessments that extend further into adulthood to capture these possible meaningful differences.

Although the current study addressed an important gap in the literature, there are some limitations that must be considered. First, the AR latent factors included only two indicators, the SEAS and the BAES. Preferably, each of the latent factors would have included at least three indicators, as originally suggested by Anderson & Rubin (1956). This meant that we had to impose certain constraints on the latent factor model for it to converge, and the model provided less than adequate fit to the data. Despite the less than adequate fit, latent factor scores were deemed preferable to a single measured variable for stimulation and sedation, and items comprising each latent factor showed strong correlations. Nonetheless, future studies with more indicators of stimulation and sedation would improve upon the approach used in the current study.

The current study also examined the lag between age of onset and both age of first intoxication and age of first regular use, rather than using the ages of first intoxication and regular use. Both approaches have benefits and drawbacks. Including ages for each milestone as simultaneous predictors does not acknowledge the codependence of age of first intoxication and age of first regular use on age of onset, and using the delay variables also reduces collinearity between these milestones. However, using the delay variables assumes that these delays operate similarly across time. This is problematic as a 2-year delay between the ages of 13-15 may have quite different meaning than a 2-year delay from ages 19-21. We proceeded with the delay variables to reduce collinearity in these complex analyses and because previous research demonstrates that the lag between first use and first intoxication is predictive of future drinking outcomes over and above age of first use (Morean et al., 2014; Morean, L'Insalata, Butler, McKee, & Krishnan-Sarin, 2018; Patrick, Evans, Terry-McElrath, 2019). The analyses were also replicated

with the raw ages and the results were comparable. Future studies are needed to better understand the implications of using difference scores versus individual ages at which drinking milestones occur.

The self-report nature of the retrospective drinking history measure used in the current study should also be noted. The CEDHF asked participants to retrospectively report on their drinking behavior across many years. Although numerous studies have shown that participants can reliably report on past drinking behavior (Burleson & Kaminer, 2006; Chu et al., 2010; Donohue, Hill, Azrin, Cross, & Strada, 2007; Hagman, Cohn, Noel, & Clifford, 2010; Harris, Wilsnack, & Klassen, 1994; McGillicuddy & Eliseo-Arras, 2012), there are also studies that call the accuracy of these types of retrospective self-report measures into question (Fendrich & Rosenbaum, 2003; Hoeppner et al., 2010; Percy, McAlister, Higgins, McCrystal, & Thornton, 2005; Searles, Helzer, & Walter, 2002). Given the lack of other measures that gather this type of detailed drinking information across this length of time, it is not possible to make direct comparisons regarding the reliability of this measure. However, similar measures that gather less detailed information over much larger stretches of time have repeatedly been shown to have high reliability (Jacob, Seilhamer, Bargeil, & Howell, 2006; Russell et al., 1998). This suggests that it is possible for individuals to reliably report on their behaviors over long periods of time, though this does not speak to the validity of these reports. Future studies are needed to further assess the validity of the CEDHF against prospective longitudinal measurements of alcohol consumption across adolescence and young adulthood. However, given that so few studies have this kind of prospective longitudinal data, the CEDHF offers a valuable alternative in the absence of such data.

Thus, although the retrospective self-report nature of our alcohol use trajectories is a limitation, and longitudinal prospective measures of consumption would be preferable, the CEDHF allowed us to address an important empirical question that has not been studied previously.

Despite these limitations, results of the current study have important implications for the development and timing of future prevention and intervention efforts. Greater HAP and lesser LAN effects of alcohol were risk factors for heavier drinking 6-months later. Greater HAP also predicted greater alcohol-related problems at the 6-month follow-up. Because AR was a risk factor for later drinking outcomes, it may be beneficial to incorporate information on the risks associated with AR into intervention and prevention programs. Schuckit and colleagues (2011) developed an intervention that included specific information on the various negative impacts of a low level of response to alcohol. Further, they found this to be related to significant decreases in drinking a year later, particularly for those who demonstrated this pattern of response (Schuckit et al., (2016). Given the success of this program along with the results of the current study, it may be beneficial to develop a similar prevention/intervention program that also includes information on the impact of sensitization to HAP effects. This could be particularly important during adolescence and early adulthood as drinking during these developmental periods often involves drinking in more stimulating and less sedating social environments (e.g. parties, bars, etc.; Clapp et al., 2007; Wechsler & Nelson, 2008).

Further, given the lack of significant effects of drinking history on AR, results did not refute the idea that individual differences in AR are innate rather than a consequence

of drinking experience. If this is the case, results speak to the importance of the early identification of high-risk AR profiles in order to prevent the development of heavy drinking during late adolescence and early adulthood. Future efforts may consider developing and implementing prevention programs for younger adolescents targeting those with a family history of AUD who may have inherited risk and/or those who show an early risky AR response pattern. Currently, the SRE is often used to assess early AR, however, as discussed previously, the SRE mainly captures negative and/or sedating effects of alcohol (Schuckit, Smith, & Tipp, 1997). It may be beneficial to create a measure of early AR that includes both HAP and LAN effects in order to thoroughly screen adolescents and young adults for risky AR profiles. Further, ongoing longitudinal studies that examine rates of use over time may consider including such a measure in future surveys. This could allow for a better understanding of the prevalence of heightened stimulant response and blunted sedative response to alcohol across this developmental period and may serve to inform the timing of prevention/intervention efforts.

Overall, the findings of the current study did not support significant indirect effects of drinking history on later drinking outcomes operating through individual differences in alcohol response. Rather, both drinking history and AR were independently predictive of alcohol outcomes at the 6-month follow-up such that a more extensive drinking history, greater HAP effects, and lesser LAN effects predicted greater drinking and alcohol-related problems 6-months later. However, given that drinking history marginally predicted less LAN effects, it is possible that in a less restrictive sample with greater power to detect effects, a significant mediational relationship

between drinking history and AR would emerge. Although we did not find support for several key study hypotheses, this is the first study, to our knowledge, to address relations among drinking history, AR, and later drinking outcomes using a longitudinal alcohol challenge design with a full account of early drinking history. We hope this work will generate questions for future study. Future research would benefit from inclusion of a broad range of drinkers and longer follow-up assessments to better understand the complex pathways of risk from early drinking history and AR to future drinking outcomes. Ultimately, such efforts may allow us to determine who is at greatest risk and/or would benefit most from specific intervention programs.

REFERENCES

Anderson, T. W., & Rubin, H. (1956). Statistical inference in factor analysis. In Proceedings of the Third Berkeley Symposium (Vol. 5). Berkeley, CA: University of California Press.

Bauer (2007) Observations on the Use of Growth Mixture Models in Psychological Research, MULTIVARIATE BEHAVIORAL RESEARCH, 42:4, 757-786.

Bell, S., Britton, A., Kubinova, R., Malyutina, S., Pajak, A., Nikitin, Y., & Bobak, M. (2014). Drinking pattern, abstention and problem drinking as risk factors for depressive symptoms: evidence from three urban Eastern European populations. *PLoS One*, *9*(8), e104384.

Berridge, K. C., & Robinson, T. E. (1995). The mind of an addicted brain: Neural sensitization of wanting versus liking. *Current Directions in Psychological Science, 4*(3), 71-76.

Berridge, K. C., & Robinson, T. E. (1998). What is the role of dopamine in reward: Hedonic impact, reward learning, or incentive salience? *Brain Research Reviews, 28*(3), 309-369.

Brunborg, G. S., Norström, T., & Storvoll, E. E. (2018). Latent developmental trajectories of episodic heavy drinking from adolescence to early adulthood: Predictors of trajectory groups and alcohol problems in early adulthood as outcome. *Drug and alcohol review*, *37*(3), 389-395.

Burleson, J. A., & Kaminer, Y. (2006). Adolescent alcohol and marijuana use: Concordance among objective-, self-, and collateral-reports. *Journal of Child & Adolescent Substance Abuse, 16*(1), 53-68.

Center for Behavioral Health Statistics and Quality. (2018). 2015 National Survey on Drug Use and Health, Substance Abuse and Mental Health Services Administration, Rockville, MD.

Chan, K. K., Neighbors, C., Gilson, M., Larimer, M. E., & Marlatt, G. A. (2007). Epidemiological trends in drinking by age and gender: Providing normative feedback to adults. *Addictive Behaviors, 32*(5), 967-976.

Chartier, K. G., Hesselbrock, M. N., & Hesselbrock, V. M. (2010). Development and vulnerability factors in adolescent alcohol use. *Child and Adolescent Psychiatric Clinics of North America, 19*(3), 493-504.

Chen, C. M., Dufour, M. C., & Yi, H. Y. (2004). Alcohol consumption among young adults ages 18–24 in the United States: Results from the 2001–2002 NESARC survey. *Alcohol Research & Health*, *28*(4), 269.

Chou, K., Liang, K., & Mackenzie, C. S. (2011). Binge drinking and axis I psychiatric disorders in community-dwelling middle-aged and older: Results from the national epidemiology survey on alcohol and related conditions (NESARC). *The Journal of Clinical Psychiatry*, *72*(5), 640-647.

Chu, A. Y., Meoni, L. A., Wang, N. Y., Liang, K., Ford, D. E., & Klag, M. J. (2010). Reliability of alcohol recall after 15 years and 23 years of follow-up in the johns hopkins precursors study. *Journal of Studies on Alcohol and Drugs*, *71*(1), 143-149.

Clapp, J. D., Holmes, M. R., Reed, M. B., Shillington, A. M., Freisthler, B., & Lange, J. E. (2007). Measuring college students' alcohol consumption in natural drinking environments: field methodologies for bars and parties. *Evaluation review*, *31*(5), 469-489.

Colder, C. R., Campbell, R. T., Ruel, E., Richardson, J. L., & Flay, B. R. (2002). A finite mixture model of growth trajectories of adolescent alcohol use: Predictors and consequences. *Journal of consulting and clinical psychology*, *70*(4), 976.

Corbin, W. R., Gearhardt, A., & Fromme, K. (2008). Stimulant alcohol effects prime within session drinking behavior. *Psychopharmacology*, *197*(2), 327-337.

Corbin, W. R., Scott, C., Leeman, R. F., Fucito, L. M., Toll, B. A., & O'Malley, S. S. (2013). Early subjective response and acquired tolerance as predictors of alcohol use and related problems in a clinical sample. *Alcoholism: Clinical and Experimental Research*, *37*(3), 490-497.

Cranford, J. A., McCabe, S. E., & Boyd, C. J. (2006). A new measure of binge drinking: Prevalence and correlates in a probability sample of undergraduates. *Alcoholism: Clinical and Experimental Research*, *30*(11), 1896-1905.

Danielsson, A., Wennberg, P., Tengström, A., & Romelsjö, A. (2010). Adolescent alcohol use trajectories: Predictors and subsequent problems. *Addictive Behaviors*, *35*(9), 848-852.

Dawson, D. A., Goldstein, R. B., Patricia Chou, S., June Ruan, W., & Grant, B. F. (2008). Age at first drink and the first incidence of adult-onset DSM-IV alcohol use disorders. *Alcoholism: Clinical and Experimental Research*,*32*(12), 2149-2160.

DeWit, D. J., Adlaf, E. M., Offord, D. R., & Ogborne, A. C. (2000). Age at first alcohol use: a risk factor for the development of alcohol disorders.*American Journal of Psychiatry*, *157*(5), 745-750.

Donohue, B., Hill, H. H., Azrin, N. H., Cross, C., & Strada, M. J. (2007). Psychometric support for contemporaneous and retrospective youth and parent reports of adolescent marijuana use frequency in an adolescent outpatient treatment population. *Addictive Behaviors*, *32*(9), 1787-1797.

Eng, M. Y., Schuckit, M. A., & Smith, T. L. (2005). The level of response to alcohol in daughters of alcoholics and controls. *Drug and Alcohol Dependence, 79*(1), 83-93.

Enoch, M. (2014). Genetic influences on response to alcohol and response to pharmacotherapies for alcoholism. *Pharmacology, Biochemistry and Behavior, 123*, 17-24.

Enoch, M. (2008). The role of $GABA_A$ receptors in the development of alcoholism. *Pharmacology, Biochemistry and Behavior, 90*(1), 95-104.

Fendrich, M., & Rosenbaum, D. (2003). Recanting of substance use reports in a longitudinal prevention study. *Drug and Alcohol Dependence, 70*(3), 241-253.

Fillmore, M. T., & Jude, R. (2011). Defining "binge" drinking as five drinks per occasion or drinking to a .08% BAC: Which is more sensitive to risk? *The American Journal on Addictions, 20*(5), 468-475.

Foulds, J. A., Adamson, S. J., Boden, J. M., Williman, J. A., & Mulder, R. T. (2015). Depression in patients with alcohol use disorders: Systematic review and meta-analysis of outcomes for independent and substance-induced disorders. *Journal of Affective Disorders, 185*, 47-59.

Gilman, J. M., Ramchandani, V. A., Crouss, T., & Hommer, D. W. (2012). Subjective and neural responses to intravenous alcohol in young adults with light and heavy drinking patterns. *Neuropsychopharmacology, 37*(2), 467-477.

Grant, B., Stinson, F., & Harford, T. (2001). Age at onset of alcohol use and DSM-IV alcohol abuse and dependence: A 12-year follow-up. *Journal of Substance Abuse, 13*(4), 493-504.

Hagman, B. T., Cohn, A. M., Noel, N. E., & Clifford, P. R. (2010). Collateral informant assessment in alcohol use research involving college students. *Journal of American College Health, 59*(2), 82-90.

Harrington, M., Velicer, W. F., & Ramsey, S. (2014). Typology of alcohol users based on longitudinal patterns of drinking. *Addictive Behaviors, 39*(3), 607-621.

Hartman, J. D., Corbin, W. R., Chassin, L., & Doane, L. D. (2019). The comprehensive early drinking history form: a novel measure of early alcohol exposure. *Alcoholism: clinical and experimental research, 43*(3), 453-464.

Hartman, J. D., Corbin, W. R., Curlee, A. S., & Fromme, K. (2019). Indirect and moderated effects of parent-child communication on drinking outcomes in the transition to college. *Addictive Behaviors, 90*, 1-9.

Harris, T. R., Wilsnack, R. W., & Klassen, A. D. (1994). Reliability of retrospective self-reports of alcohol consumption among women: Data from a U.S. national sample.

Journal of Studies on Alcohol, 55(3), 309-314.

Heath, A. C., Madden, P. A. F., Bucholz, K. K., Dinwiddie, S. H., Slutske, W. S., Bierut, L. J., . . Martin, N. G. (1999). Genetic differences in alcohol sensitivity and the inheritance of alcoholism risk. *Psychological Medicine, 29*(5), 1069-1081.

Hinckers, A. S., Laucht, M., Schmidt, M. H., Mann, K. F., Schumann, G., Schuckit, M. A., & Heinz, A. (2006). Low level of response to alcohol as associated with serotonin transporter genotype and high alcohol intake in adolescents. *Biological Psychiatry, 60*(3), 282-287.

Hingson, R., Heeren, T., Levenson, S., Jamanka, A., & Voas, R. (2002). Age of drinking onset, driving after drinking, and involvement in alcohol related motor-vehicle crashes. *Accident Analysis & Prevention, 34*(1), 85-92.

Hingson, R. W., Heeren, T., & Winter, M. R. (2006). Age at drinking onset and alcohol dependence: age at onset, duration, and severity. *Archives of pediatrics & adolescent medicine, 160*(7), 739-746.

Hoeppner, Stout, Jackson, & Barnett. (2010). How good is fine-grained Timeline Follow-back data? Comparing 30-day TLFB and repeated 7-day TLFB alcohol consumption reports on the person and daily level. *Addictive Behaviors, 35*(12), 1138-1143.

Holdstock, L., King, A. C., & de Wit, H. (2000). Subjective and objective responses to ethanol in moderate/heavy and light social drinkers. *Alcoholism: Clinical and Experimental Research, 24*(6), 789-794.

Hu, L., & Bentler, P. M. (1999). Cutoff criteria for fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling, 6*(1), 1-55.

Jacob, T., Seilhamer, R. A., Bargeil, K., & Howell, D. N. (2006). Reliability of lifetime drinking history among alcohol dependent men. *Psychology of Addictive Behaviors, 20*(3), 333-337.

Jochman, K. A., & Fromme, K. (2010). Maturing out of substance use: The other side of etiology. In L. Scheier (Ed.), *Handbook of drug use etiology: Theory, methods, and empirical findings; handbook of drug use etiology: Theory, methods, and empirical findings* (pp. 565-578, Chapter xxvi, 689 Pages) American Psychological Association, Washington, DC.

Johnston, L. D., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E. & Miech, R. A. (2016). Monitoring the Future national survey results on drug use, 1975– 2015: Volume 2, College students and adults ages 19–55. Ann Arbor: Institute for Social Research, The University of Michigan.

Kalu, N., Ramchandani, V. A., Marshall, V., Scott, D., Ferguson, C., Cain, G., & Taylor,

R. (2012). Heritability of level of response and association with recent drinking history in nonalcohol-dependent drinkers. *Alcoholism: Clinical and Experimental Research, 36*(6), 1034-1041.

Kann, L., McManus, T., Harris, W. A., Shanklin, S. L., Flint, K. H., Queen, B., ... & Lim, C. (2018). Youth risk behavior surveillance—United States, 2017. *MMWR Surveillance Summaries, 67*(8), 1-114.

King, A. C., de Wit, H., McNamara, P. J., & Cao, D. (2011). Rewarding, stimulant, and sedative alcohol responses and relationship to future binge drinking. *Archives of General Psychiatry, 68*(4), 389-399.

King, A. C., Hasin, D., O'Connor, S. J., McNamara, P. J., & Cao, D. (2016). A prospective 5-year re-examination of alcohol response in heavy drinkers progressing in alcohol use disorder. *Biological Psychiatry, 79*(6), 489-498.

King, A. C., Houle, T., de Wit, H., Holdstock, L., & Schuster, A. (2002). Biphasic alcohol response differs in heavy versus light drinkers. *Alcoholism: Clinical and Experimental Research, 26*(6), 827-835.

King, A. C., McNamara, P. J., Hasin, D. S., & Cao, D. (2014). Alcohol challenge responses predict future alcohol use disorder symptoms: A 6-year prospective study. *Biological Psychiatry, 75*(10), 798-806.

Liang, W., & Chikritzhs, T. (2015). Age at first use of alcohol predicts the risk of heavy alcohol use in early adulthood: A longitudinal study in the United States. *International Journal of Drug Policy, 26*(2), 131-134.

Loree, A. M., Lundahl, L. H., & Ledgerwood, D. M. (2015). Impulsivity as a predictor of treatment outcome in substance use disorders: Review and synthesis. *Drug and Alcohol Review, 34*(2), 119-134.

MacKinnon, D. P., Lockwood, C. M., & Williams, J. (2004). Confidence limits for the indirect effect: Distribution of the product and resampling methods. *Multivariate behavioral research, 39*(1), 99-128.

Mann, R.E., Sobell, L.C., Sobell, M.B. & Sobell, D.P. (1985). Reliability of a family tree questionnaire for assessing family history of alcohol problems. *Drug and Alcohol Dependence,* 15, 61-67.

Martin, C. S., Earleywine, M., Musty, R. E., Perrine, M. W., & Swift, R. M. (1993). Development and validation of the biphasic alcohol effects scale. *Alcoholism: Clinical and Experimental Research, 17*(1), 140-146.

Martineau, K. M., & Cook, E. C. (2017). Trajectories of adolescent alcohol use: The effect of individual and social risk factors by race. *Journal of Child & Adolescent Substance Abuse, 26*(5), 387-400.

McGillicuddy, N. B., & Eliseo-Arras, R. (2012). Parent–adolescent report correspondence on adolescent substance abuse among teens in residential rehabilitation. *Addictive Behaviors, 37*(4), 456-462.

Mokdad, A. H., Marks, J. S., Stroup, D. F., & Gerberding, J. L. (2004). Actual causes of death in the United States, 2000. *Jama, 291*(10), 1238-1245.

Morean, M. E., & Corbin, W. R. (2008). Subjective alcohol effects and drinking behavior: The relative influence of early response and acquired tolerance.*Addictive Behaviors, 33*(10), 1306-1313.

Morean, M. E., Corbin, W. R., & Fromme, K. (2012). Age of first use and delay to first intoxication in relation to trajectories of heavy drinking and alcohol-related problems during emerging adulthood. *Alcoholism: Clinical and Experimental Research, 36*(11), 1991-1999.

Morean, M. E., Corbin, W. R., & Treat, T. A. (2013). The subjective effects of alcohol scale: Development and psychometric evaluation of a novel assessment tool for measuring subjective response to alcohol. *Psychological Assessment, 25*(3), 780-795.

Morean, M. E., Kong, G., Camenga, D. R., Cavallo, D. A., Connell, C., & Krishnan-Sarin, S. (2014). First drink to first drunk: Age of onset and delay to intoxication are associated with adolescent alcohol use and binge drinking. *Alcoholism: Clinical and Experimental Research, 38*(10), 2615-2621.

Morean, M. E., L'Insalata, A., Butler, E. R., McKee, A., & Krishnan-Sarin, S. (2018). Age at drinking onset, age at first intoxication, and delay to first intoxication: Assessing the concurrent validity of measures of drinking initiation with alcohol use and related problems. *Addictive Behaviors, 79*, 195-200.

Muthen L. K., Muthen B. O. *Mplus User's Guide*. Los Angeles, CA: Author; 2012.

Nagin D. Analyzing developmental trajectories: a semiparametric group-based approach. *Psychol Methods* 1999; 4: 139–57.

National Institute on Alcohol Abuse and Alcoholism (2006). Young adult drinking. Alcohol Research & Health, Volume 28, Number 4

Newlin, D. B., & Thomson, J. B. (1990). Alcohol challenge with sons of alcoholics: A critical review and analysis. *Psychological Bulletin, 108*(3), 383-402.

Newlin, D. B., & Thomson, J. B. (1991). Chronic tolerance and sensitization to alcohol in sons of alcoholics. *Alcoholism: Clinical and Experimental Research, 15*(3), 399-405.

Newlin, D. B., & Thomson, J. B. (1999). Chronic tolerance and sensitization to alcohol in sons of alcoholics: II. replication and reanalysis. *Experimental and Clinical*

Psychopharmacology, 7(3), 234-243.

Nylund K., Asparouhov T., Muthen B. Deciding on the number of classes in latent class analysis and growth mixture modeling: a Monte Carlo simulation study. *Struct Equat Model* 2007; 14: 535–68.

Patrick, M. E., Evans-Polce, R., & Terry-McElrath, Y. (2019). Faster escalation from first drink to first intoxication as a risk factor for binge and high-intensity drinking among adolescents. *Addictive Behaviors, 92*, 199-202.

Percy, A., McAlister, S., Higgins, K., McCrystal, P., & Thornton, M. (2005). Response consistency in young adolescents' drug use self-reports: A recanting rate analysis. *Addiction, 100*(2), 189-196.

Quinn, P. D., & Fromme, K. (2011). Subjective response to alcohol challenge: A quantitative review. *Alcoholism: Clinical and Experimental Research, 35*(10), 1759-1770.

Read, J. P., Kahler, C. W., Strong, D. R., & Colder, C. R. (2006). Development and preliminary validation of the young adult alcohol consequences questionnaire.*Journal of Studies on Alcohol, 67*(1), 169-177.

Reinecke, J., & Seddig, D. (2011). Growth mixture models in longitudinal research. *AStA Advances in Statistical Analysis*, *95*(4), 415-434.

Robinson, T. E., & Berridge, K. C. (2000). The psychology and neurobiology of addiction: An incentive-sensitization view. *Addiction, 95*, S91-S117.

Robinson, T. E., & Berridge, K. C. (1993). The neural basis of drug craving: An incentive-sensitization theory of addiction. *Brain Research Reviews, 18*(3), 247-291.

Russell, M., Peirce, R. S., Vana, J. E., Nochajski, T. H., CAROSELLA, A., Muti, P., & Trevisan, M. (1998). Relations among alcohol consumption measures derived from the Cognitive Lifetime Drinking History. *Drug and alcohol review*, *17*(4), 377-387.

Sacks, J. J., Gonzales, K. R., Bouchery, E. E., Tomedi, L. E., & Brewer, R. D. (2015). 2010 national and state costs of excessive alcohol consumption. *American journal of preventive medicine*, *49*(5), e73-e79.

SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2015 and 2016.

Schuckit, M. A. (1980). Alcoholism and genetics: Possible biological mediators. *Biological Psychiatry, 15*(3), 437-447.

Schuckit, M. A. (1985). Ethanol-induced changes in body sway in men at high alcoholism risk. *Archives of General Psychiatry, 42*(4), 375-379.

Schuckit, M. A. (1994). Low level of response to alcohol as a predictor of future alcoholism. *The American Journal of Psychiatry, 151*(2), 184-189.

Schuckit, M. A. (1984). Subjective responses to alcohol in sons of alcoholics and control subjects. *Archives of General Psychiatry, 41*(9), 879-884.

Schuckit, M. A., Smith, T. L., Clausen, P., Fromme, K., Skidmore, J., Shafir, A., & Kalmijn, J. (2016). The low level of response to alcohol-based heavy drinking prevention program: One-year follow-up. *Journal of Studies on Alcohol and Drugs, 77*(1), 25-37.

Schuckit, M. A., Smith, T. L., Danko, G., Kramer, J., Bucholz, K. K., McCutcheon, V., . . . Mendoza, L. A. (2018). A 22-year follow-up (range 16 to 23) of original subjects with baseline alcohol use disorders from the collaborative study on genetics of alcoholism. *Alcoholism: Clinical and Experimental Research, 42*(9), 1704-1714.

Schuckit, M. A., Smith, T. L., Danko, G., Kuperman, S., Bierut, L. J., & Hesselbrock, V. (2005). Correlations among first-degree relatives for responses on the self-rating of the effects of alcohol questionnaire in teenagers. *Journal of Studies on Alcohol, 66*(1), 62-65.

Schuckit, M. A., Smith, T. L., Hesselbrock, V., Bucholz, K. K., Bierut, L., Edenberg, H., ... & Danko, G. P. (2008). Clinical implications of tolerance to alcohol in nondependent young drinkers. *The American journal of drug and alcohol abuse*, *34*(2), 133-149.

Schuckit, M. A., Smith, T. L., Heron, J., Hickman, M., Macleod, J., Lewis, G., . . . Davey-Smith, G. (2011). Testing a level of response to alcohol-based model of heavy drinking and alcohol problems in 1,905 17-yearolds. *Alcoholism: Clinical and Experimental Research, 35*, 1897–1904.

Schuckit, M. A., Smith, T. L., & Kalmijn, J. (2004). Findings across subgroups regarding the level of response to alcohol as a risk factor for alcohol use disorders: A college population of women and latinos. *Alcoholism: Clinical and Experimental Research, 28*(10), 1499-1508.

Schuckit, M. A., Smith, T. L., Kalmijn, J., Tsuang, J., Hesselbrock, V., & Bucholz, K. (2000). Response to alcohol in daughters of alcoholics: A pilot study and a comparison with sons of alcoholics. *Alcohol and Alcoholism, 35*(3), 242-248.

Schuckit, M. A., Smith, T. L., Pierson, J., Danko, G. P., & Beltran, I. A. (2006). Relationships among the level of response to alcohol and the number of alcoholic relatives in predicting alcohol-related outcomes. *Alcoholism: Clinical and Experimental Research, 30*(8), 1308-1314.

Schuckit, M. A., Smith, T. L., & Tipp, J. E. (1997). The self-rating of the effects of alcohol (SRE) form as a retrospective measure of the risk for alcoholism. *Addiction,*

92(8), 979-988.

Schuckit, M. A., Smith, T. L., Trim, R. S., Allen, R. C., Fukukura, T., Knight, E. E., . . . Kreikebaum, S. A. (2011). A prospective evaluation of how a low level of response to alcohol predicts later heavy drinking and alcohol problems. *The American Journal of Drug and Alcohol Abuse, 37*(6), 479-486.

Schuckit, M. A., Smith, T. L., Trim, R. S., Kuperman, S., Kramer, J., Hesselbrock, V., . . . Saunders, G. (2012a). Sex differences in how a low sensitivity to alcohol relates to later heavy drinking. *Drug and Alcohol Review, 31*(7), 871-880.

Schuckit, M. A., Smith, T. L., Kalmijn, J., Trim, R. S., Cesario, E., Saunders, G., . . . Campbell, N. (2012b). Comparison across two generations of prospective models of how the low level of responses to alcohol affects alcohol outcomes. *Journal of Studies on Alcohol and Drugs, 73*(2), 195-204.

Searles, J., Helzer, J., Rose, G., & Badger, G. (2002). Concurrent and retrospective reports of alcohol consumption across 30, 90 and 366 days: Interactive voice response compared with the timeline follow back. *Journal of Studies on Alcohol, 63*(3), 352-62.

Shamblen, S. R., Ringwalt, C. L., Clark, H. K., & Hanley, S. M. (2014). Alcohol use growth trajectories in young adolescence: Pathways and predictors. *Journal of Child & Adolescent Substance Abuse, 23*(1), 9-18.

Sobell, L. C., & Sobell, M. B. (1992). Timeline follow-back. In *Measuring alcohol consumption* (pp. 41-72). Humana Press.

Spear, L. (2013). The teenage brain: Adolescents and alcohol. *Current Directions in Psychological Science, 22*(2), 152-157.

Stice, E., Myers, M. G., & Brown, S. A. (1998). A longitudinal grouping analysis of adolescent substance use escalation and de-escalation.*Psychology of Addictive Behaviors, 12*(1), 14.

Su, J., Supple, A. J., Leerkes, E. M., Sally, I., & Kuo, C. (2019). Latent trajectories of alcohol use from early adolescence to young adulthood: Interaction effects between 5-HTTLPR & parenting quality & gender differences. *Development and psychopathology, 31*(2), 457-469.

Substance Abuse and Mental Health Services Administration (SAMHSA). 2015 National Survey on Drug Use and Health (NSDUH). Table 6.84B—Tobacco Product and Alcohol Use in Past Month among Persons Aged 18 to 22, by College Enrollment Status: Percentages, 2014 and 2015.

Thomas, S. E., Drobes, D. J., Voronin, K., & Anton, R. F. (2004). Following alcohol consumption, nontreatment-seeking alcoholics report greater stimulation but similar

sedation compared with social drinkers. *Journal of Studies on Alcohol, 65*(3), 330-335.

Townshend, J. M., & Duka, T. (2005). Binge drinking, cognitive performance and mood in a population of young social drinkers. *Alcoholism: Clinical and Experimental Research, 29*(3), 317-325.

Trim, R. S., Schuckit, M. A., & Smith, T. L. (2008). Level of response to alcohol within the context of alcohol-related domains: An examination of longitudinal approaches assessing changes over time. *Alcoholism: Clinical and Experimental Research, 32*(3), 472-480.

Vergés, A., Jackson, K. M., Bucholz, K. K., Grant, J. D., Trull, T. J., Wood, P. K., & Sher, K. J. (2012). Deconstructing the age-prevalence curve of alcohol dependence: Why "maturing out" is only a small piece of the puzzle. *Journal of Abnormal Psychology, 121*(2), 511-523.

Viken, R. J., Rose, R. J., Morzorati, S. L., Christian, J. C., & Li, T. (2003). Subjective intoxication in response to alcohol challenge: Heritability and covariation with personality, breath alcohol level, and drinking history. *Alcoholism: Clinical and Experimental Research, 27*(5), 795-803.

Warner, L. A., & White, H. R. (2003). Longitudinal effects of age at onset and first drinking situations on problem drinking. *Substance use & misuse,38*(14), 1983-2016.

Warner, . A., White, H. R., & Johnson, V. (2007). Alcohol initiation experiences and family history of alcoholism as predictors of problem-drinking trajectories. *Journal of studies on alcohol and drugs, 68*(1), 56-65.

Wetherill, L., Morzorati, S. L., Foroud, T., Windisch, K., Darlington, T., Zimmerman, U. S., . . . O'Connor, S. J. (2012). Subjective perceptions associated with the ascending and descending slopes of breath alcohol exposure vary with recent drinking history. *Alcoholism: Clinical and Experimental Research, 36*(6), 1050-1057.

Wilhelmsen, K. C., Schuckit, M., Smith, T. L., Lee, J. V., Segall, S. K., Feiler, H. S., & Kalmijn, J. (2003). The search for genes related to a low-level response to alcohol determined by alcohol challenges. *Alcoholism: Clinical and Experimental Research, 27*(7), 1041-1047.

Wills, T. A., McNamara, G., Vaccaro, D., & Hirky, A. E. (1996). Escalated substance use: a longitudinal grouping analysis from early to middle adolescence. *Journal of abnormal psychology, 105*(2), 166.

Witt, E. D. (2010). Research on alcohol and adolescent brain development: Opportunities and future directions. *Alcohol, 44*(1), 119-124.

World Health Organization (WHO). *Global Status Report on Alcohol and Health*. p. XIII. 2014 ed.

Table 1. Raw Descriptive Statistics of Main Study Variables

	N	Mean	SD	Range	Min	Max	Skewness	Kurtosis
Gender	211	55% Male	-------	----------	------	--------	----------	----------
Age at Baseline	211	22.69	1.38	5	21	25	0.51	-0.60
Age of Onset	211	16.54	2.12	12	10	22	0.06	0.15
Age of First Intoxication	211	17.53	2.30	13	10	23	-0.09	-0.11
Age of First Regular Use	211	18.97	2.03	11	13	24	-0.26	-0.27
Family History (Weighted Mean)	211	0.09	0.21	1.25	0.00	1.25	2.95	9.43
Baseline HAP	211	.0012	0.75	4.20	-1.36	2.84	0.69	0.38
Baseline LAN	211	.0047	0.82	3.65	-1.31	2.33	0.29	-0.73
Peak HAP	211	.0007	0.93	4.84	-2.18	2.66	0.17	0.12
Peak LAN	211	-.0011	0.95	4.20	-2.17	2.03	-0.19	-0.32
Alcohol Use Age 17	44	272.41	273.62	1653.60	37.92	1691.52	3.57	16.71
Alcohol Use Age 18	94	403.38	383.83	1691.52	0.00	1691.52	1.61	2.47
Alcohol Use Age 19	125	476.51	455.87	1691.52	0.00	1691.52	1.32	.86
Alcohol Use Age 20	146	482.34	479.78	1691.52	0.00	1691.52	1.26	.61

Alcohol Use Age 21	196	540.71	497.29	1691.52	0.00	1691.52	1.14	.20
Alcohol Use Age 22	156	435.71	457.85	1691.52	0.00	1691.52	1.52	1.47
Alcohol Use Age 23	104	348.08	403.38	1691.52	0.00	1691.52	2.21	4.65
Alcohol Use Age 24	57	391.66	400.94	1685.52	6.00	1691.52	1.72	2.66
TLFB Baseline	210	32.63	32.63	184.00	0	184	1.92	7.00
TLFB 6-Month Follow-Up	202	37.10	37.10	207	0	207	1.65	4.07
TLFB 12-Month Follow-Up	204	35.42	35.42	205	0	205	2.01	5.55
TLFB 18 -Month Follow-Up	196	33.70	33.70	291	0	291	3.28	18.09
TLFB 24-Month Follow-Up	190	30.97	30.97	201	0	201	2.17	7.91
YAACQ Baseline	206	7.60	6.74	32	0	32	1.23	1.54
YAACQ 6-Month Follow-Up	204	9.35	9.36	48.00	0	48	1.54	2.59
YAACQ 12-Month Follow-Up	204	6.57	8.10	48	0	48	1.85	4.27
YAACQ 18-Month Follow-Up	198	7.75	9.71	48	0	48	2.02	4.47
YAACQ 24-Month Follow-Up	192	5.62	6.46	33	0	33	1.39	1.62

Table 2. Trajectory Class Comparisons

Models	AIC	BIC	Entropy
Quadratic 1-Class	13550.53	13584.05	-------
Quadratic 2-Class	13475.41	13522.34	0.886
Quadratic 3-Class	13430.80	13491.13	0.908
Quadratic 4-Class	13396.29	13470.03	0.892

Table 3. Correlations between covariates and AR by gender

	1	2	4	5	6	7	8	9	10	11	12
1. Physical Context	1.000	*.020*	*.058*	*.004*	*-.100*	*-.060*	*-.019*	*.064*	*.025*	*.048*	*-.047*
2. Social Context	**-.029**	1.000	*.022*	*.099*	*-.045*	*-.061*	*-.026*	*.070*	*.110*	*.049*	*.065*
4. Age	**-.163**	**.084**	1.000	*.177*	*.050*	*-.027*	*-.021*	*.109*	*.076*	*.107*	*.164*
5. Age of Onset	**-.053**	**.099**	**-.145**	1.000	*-.229**	*-.469****	*-.195**	*.165*	*.171*	*.141*	*.158*
6. Intoxication Lag	**-.341****	**.088**	**-.162**	**-.067**	1.000	*.522****	*.169*	*.045*	*.087*	*.071*	*.160*
7. Regular Lag	**-.122**	**-.159**	**.015**	**-.398*****	**.486*****	1.000	*.014*	*.041*	*.067*	*-.092*	*-.036*
8. Family History	**.015**	**.001**	**.068**	**.056**	**.030**	**-.030**	1.000	*-.045*	*.002*	*.024*	*.055*
9. Baseline HAP	**-.070**	**-.008**	**.111**	**-.078**	**-.011**	**-.089**	**.122**	1.000	*.914****	*.245***	*.200**
10. Baseline LAN	**-.110**	**.043**	**.154**	**.010**	**.043**	**-.101**	**.210***	**.919*****	1.000	*.097*	*.288***
11. Peak HAP	**.107**	**.053**	**-.062**	**-.041**	**.016**	**.081**	**-.182**	**-.141**	**-.293****	1.000	*.697****
12. Peak LAN	**.006**	**.091**	**.046**	**.022**	**.070**	**.092**	**-.091**	**-.129**	**-.098**	**.756*****	1.000

Note: Female in bold, male in italics. * p <.05, ** p <.01, *** p <.001.

Table 4. Unstandardized Regression Coefficients of Drinking Trajectory Classes Predicting AR.

	Peak HAP			Peak LAN		
Variable	*β*	SE	*p*-value	*β*	SE	*p*-value
Physical Context	-0.136	0.091	0.134	-0.055	0.047	0.237
Social Context	0.040	0.090	0.656	0.070	0.044	0.117
Gender	0.273	0.092	0.003	0.060	0.043	0.159
Age	0.056	0.033	0.095	0.004	0.018	0.823
Age of Onset	0.022	0.025	0.384	0.014	0.011	0.186
Onset to Intoxication Lag	0.042	0.044	0.334	0.025	0.026	0.334
Onset to Regular Lag	0.008	0.033	0.808	-0.001	0.018	0.935
Family History	0.248	0.208	0.233	0.303	0.099	0.002
Baseline AR	0.894	0.039	< .001	1.003	0.025	< .001
Increasers vs. Low/Social	0.081	0.135	0.547	0.007	0.076	0.931
Dev Lim vs. Low/Social	-0.133	0.128	0.301	-0.125	0.073	0.088
Increasers vs. Dev Lim	0.214	0.170	0.208	0.131	0.099	0.185

Note: Significant paths are highlighted in grey

Table 5. Unstandardized Regression Coefficients of drinking trajectories predicting drinking (TLFB) across the two-year follow-up.

	Intercept			Slope		
Variable	*β*	SE	*p*-value	*β*	SE	*p*-value
Physical Context	0.002	0.108	0.984	-0.052	0.044	0.241
Social Context	-0.049	0.110	0.658	-0.052	0.047	0.272
Gender	0.243	0.111	0.028	-0.021	0.044	0.641
Age	-0.061	0.039	0.119	0.040	0.017	0.018
Age of Onset	-0.088	0.031	0.005	-0.008	0.012	0.516
Onset to Intoxication Lag	-0.059	0.055	0.287	-0.021	0.024	0.381
Onset to Regular Lag	-0.070	0.050	0.160	0.007	0.017	0.660
Family History	0.134	0.229	0.559	0.063	0.086	0.465
Increasers vs. Low/Social	0.834	0.139	<0.001	-0.095	0.084	0.260
Dev Lim vs. Low/Social	0.442	0.168	0.009	0.028	0.057	0.621
Increasers vs. Dev Lim	0.391	0.198	0.048	-0.123	0.094	0.191

Note: Significant paths are highlighted in grey

Table 6. Unstandardized Regression Coefficients of drinking trajectories predicting alcohol-related problems (YAACQ) across the two-year follow-up.

	Intercept			**Slope**		
Variable	*β*	SE	*p*-value	*β*	SE	*p*-value
Physical Context	0.145	0.149	0.329	-0.009	0.064	0.887
Social Context	-0.180	0.160	0.259	0.051	0.061	0.406
Gender	-0.013	0.149	0.933	-0.044	0.059	0.456
Age	-0.055	0.051	0.284	0.009	0.023	0.684
Age of Onset	-0.034	0.043	0.431	-0.018	0.017	0.286
Onset to Intoxication Lag	0.017	0.073	0.811	-0.043	0.027	0.119
Onset to Regular Lag	-0.018	0.067	0.794	-0.003	0.023	0.883
Family History	0.333	0.323	0.303	0.031	0.137	0.819
Increasers vs. Low/Social	0.984	0.286	0.001	-0.088	0.095	0.356
Dev Lim vs. Low/Social	0.715	0.194	<0.001	0.089	0.078	0.252
Increasers vs. Dev Lim	0.269	0.304	0.376	-0.177	0.108	0.101

Note: Significant paths are highlighted in grey

Table 7. Unstandardized Regression Coefficients of AR predicting drinking (TLFB) across the two-year follow-up.

	Intercept			Slope		
Variable	*β*	SE	*p*-value	*β*	SE	*p*-value
Physical Context	0.019	0.107	0.857	-0.076	0.042	0.071
Social Context	0.042	0.115	0.717	-0.063	0.046	0.170
Gender	0.228	0.116	0.050	0.003	0.049	0.950
Age	-0.079	0.039	0.046	0.046	0.016	0.004
Age of Onset	-0.112	0.032	0.001	-0.008	0.012	0.494
Onset to Intoxication Lag	-0.062	0.053	0.246	-0.018	0.025	0.460
Onset to Regular Lag	-0.099	0.049	0.043	0.008	0.016	0.609
Family History	0.458	0.249	0.065	0.064	0.085	0.446
Baseline HAP	-0.336	0.126	0.007	0.122	0.052	0.019
Baseline LAN	0.739	0.258	0.004	-0.041	0.108	0.704
Peak HAP	0.347	0.113	0.002	-0.127	0.050	0.011
Peak LAN	-0.805	0.247	0.001	0.113	0.107	0.292

Note: Significant paths are highlighted in grey

Table 8. Unstandardized Regression Coefficients of AR predicting alcohol-related problems (YAACQ) across the two-year follow-up.

	Intercept			**Slope**		
Variable	*β*	SE	*p*-value	*β*	SE	*p*-value
Physical Context	0.174	0.152	0.252	-0.034	0.060	0.571
Social Context	-0.158	0.154	0.305	0.047	0.060	0.440
Gender	-0.048	0.158	0.760	<0.001	0.062	0.994
Age	-0.085	0.052	0.101	0.022	0.022	0.331
Age of Onset	-0.098	0.040	0.016	-0.018	0.015	0.238
Onset to Intoxication Lag	-0.001	0.071	0.984	-0.033	0.027	0.214
Onset to Regular Lag	-0.073	0.060	0.220	-0.009	0.021	0.655
Family History	0.490	0.282	0.082	0.045	0.126	0.723
Baseline HAP	-0.321	0.157	0.041	0.075	0.070	0.288
Baseline LAN	0.269	0.348	0.440	-0.036	0.128	0.778
Peak HAP	0.310	0.151	0.040	-0.115	0.065	0.079
Peak LAN	0.020	0.313	0.950	0.051	0.126	0.689

Note: Significant paths are highlighted in grey

Figure 1. Sample Means of CEDHF Trajectory Classes

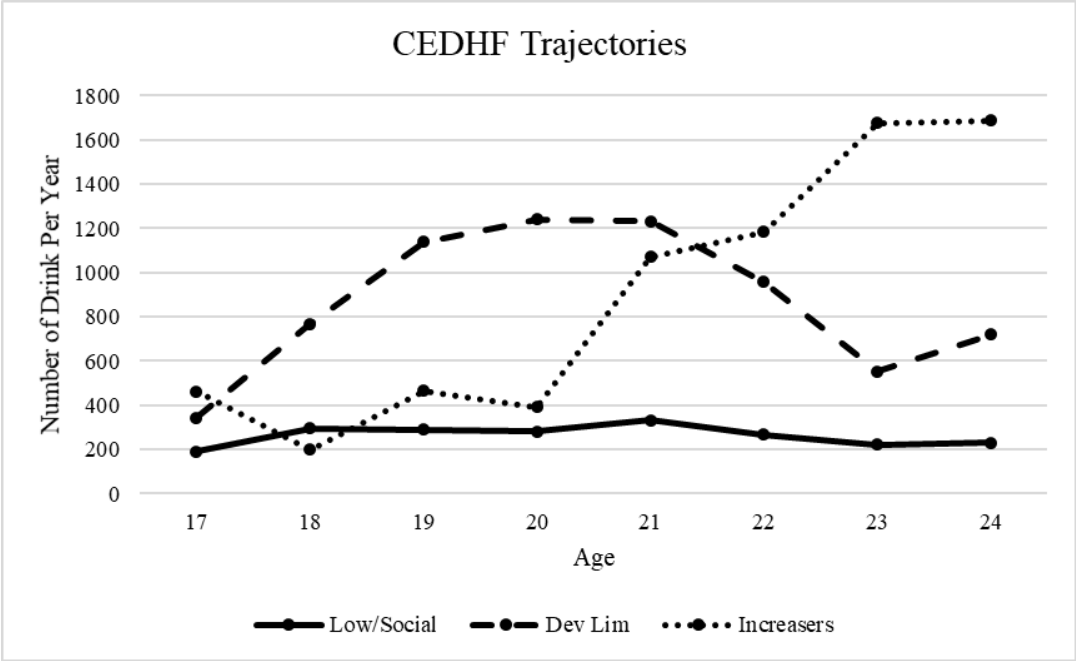

Figure 2. TLFB Total Drinks at each time-point by CEDHF Trajectory Class

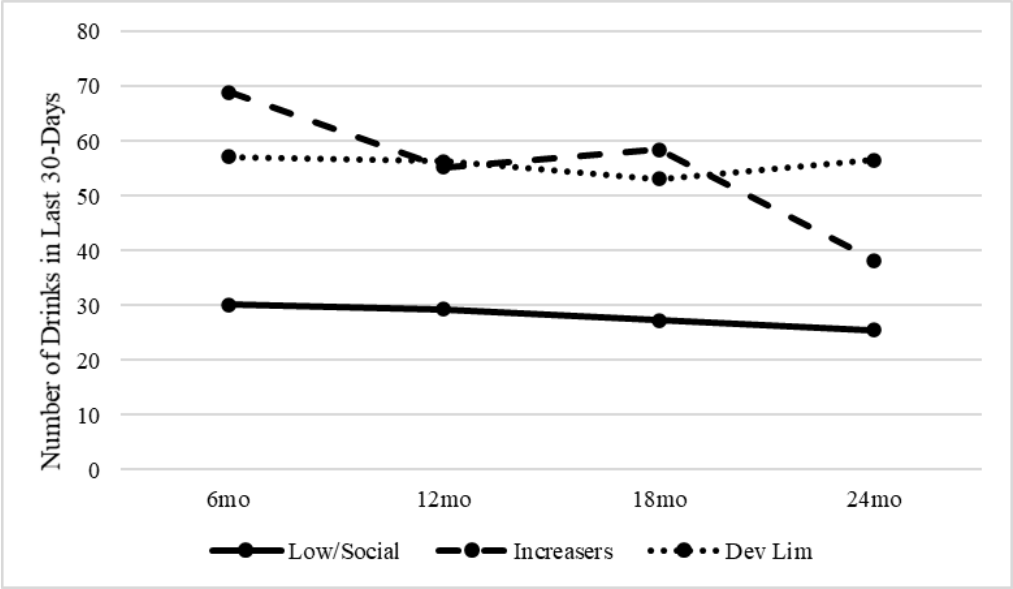

Figure 3. YAACQ Scores at each time-point by CEDHF Trajectory Class