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Binge Drinking: Predictors, Patterns, and Consequences

DEPARTMENT OF HEALTH AND HUMAN SERVICES • USA

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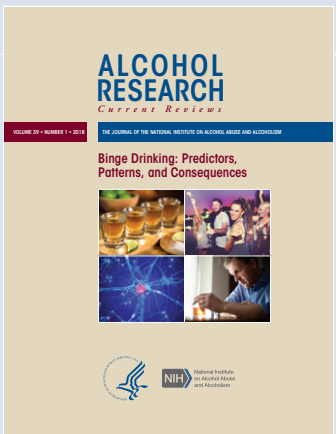

About the Cover

Binge drinking, broadly defined as consuming a large amount of alcohol in a short period of time, is a dangerous—and sometimes fatal—practice. Despite the adverse consequences associated with it, far too many people, particularly young adults, binge drink. This issue of *Alcohol Research: Current Reviews* examines the predictors, prevalence, and patterns of binge alcohol consumption and its effects on health and well-being.

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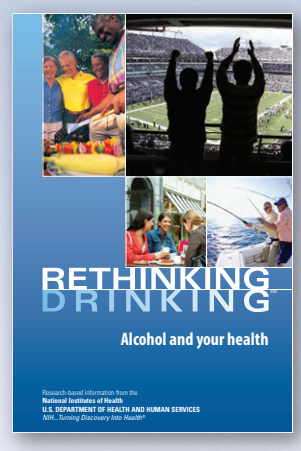

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Binge Drinking

Predictors, Patterns, and Consequences

Aaron M. White, Susan Tapert, and Shivendra D. Shukla

The National Institute on Alcohol Abuse and Alcoholism defines binge drinking as a pattern of consumption that causes blood alcohol concentration to rise to .08%—the legal limit for adults ages 21 or older operating a motor vehicle—or more. This level typically occurs after a woman consumes four drinks or a man consumes five drinks—in about 2 hours. Research suggests that three out of four adolescents who drink, and half of adults who drink, engage in binge drinking each month. Because of the impairments it produces, binge drinking increases the likelihood of a host of acute consequences, including injuries and deaths from falls, burns, drownings, car crashes, and alcohol overdoses. Of the roughly 88,000 deaths that result from alcohol use in the United States each year, more than half stem from binge drinking,[1] and binge drinking accounts for 77% ($191.1 billion) of the annual economic cost of alcohol misuse.[2]

Several important questions related to binge drinking warrant further exploration. For instance, how have patterns of binge drinking changed in recent years in the United States? What is known about drinking at levels far beyond the standard binge thresholds? How does the peak number of drinks a person consumes relate to risks for experiencing alcohol-related harm? Are there unique risks of binge drinking for women? How does binge alcohol consumption affect brain development and function? What is the effect of binge drinking on organs other than the brain? The articles in this volume explore what is known about these and other topics related to binge drinking.

In **Adolescent Binge Drinking: Developmental Context and Opportunities for Prevention**, Chung and colleagues examine binge drinking among adolescents. National surveys suggest that drinking, including binge drinking, is declining among teens. The declines have been greater for young males than females, leading to a significant narrowing of differences in alcohol misuse between the genders. For instance, in the 1975 Monitoring the Future study, 49% of male high school seniors reported binge drinking, compared to only 26% of female seniors.[3] By 2014, binge drinking declined in both genders, but more so for males, with 22% of males and 17% of females crossing the binge threshold. The authors examine the consequences of binge drinking for teens and discuss the developmental context in which adolescent drinking occurs.

Considerable research has focused on alcohol use, particularly binge drinking, among college students. Young adults in college are more likely to binge drink than their noncollege peers, though the differences are narrowing. Krieger and colleagues, in **The Epidemiology of Binge Drinking Among College-Age Individuals in the United States**, explore current knowledge of binge drinking and its consequences among college students and other young adults. As with binge drinking among high school students, binge drinking has declined among college students, but less so among college women. In contrast to the declines in binge drinking at colleges, binge drinking increased among young adults in the military and among young women in the general population. The authors examine the characteristics (i.e., race and ethnicity, Greek affiliation, and drinking motives) of young adults who engage in binge drinking relative to those who do not.

Traditionally, binge drinking has been studied using a single threshold, typically four or more drinks for females and five or more drinks for males, or just

five or more drinks for both males and females. However, knowing that someone binge drank does not reveal how much alcohol he or she actually consumed. Using a single binge threshold has the unintended consequence of assigning the same level of potential risk to all binge drinkers, regardless of how much they drank. Recent studies have examined the prevalence and correlates of drinking at levels two and three times the standard binge thresholds, also known as high-intensity or extreme binge drinking. In **High-Intensity Drinking**, Patrick and Azar assess current knowledge of the prevalence of high-intensity drinking, the contexts in which it tends to occur (e.g., sporting events and 21st birthday celebrations), and the consequences of drinking at these high peak levels.

Recent studies suggest that long-standing differences between men and women in alcohol use are narrowing. This is concerning, given evidence that women might experience certain health effects of alcohol, such as cirrhosis of the liver and cardiovascular disease, at lower levels of consumption than men.[4] In **Gender Differences in Binge Drinking: Prevalence, Predictors, and Consequences**, Wilsnack and colleagues examine changes in binge drinking and related outcomes in males and females, and they explore potential explanations for the convergence of alcohol misuse between the genders.

Over the past few decades, a paradigm shift has occurred in our understanding of brain development. It is now clear that brain development, once thought to taper off with the end of childhood, enters a unique phase during the adolescent years. Changes in the brain during adolescence lead to improvements in the ability to engage in complex social behaviors and to make forward-thinking decisions.[5] Hiller-Sturmhöfel and Spear, in **Binge Drinking's Effects on the Developing Brain—Animal Models**, explore animal research findings demonstrating that repeated binge exposure during adolescence causes structural and functional damage in the brain that leads to social and cognitive deficits during adulthood. In **Effects of Binge Drinking on the Developing Brain: Studies in Humans**, Jones and colleagues discuss evidence from human research on the effects of repeated binge drinking on adolescent brain development and brain function, including lingering deficits in attention and memory.

The chronic health effects of alcohol misuse are well-documented. Alcohol consumption is associated with roughly half the liver cirrhosis deaths in the United States and increases the risk of cancers of the mouth, throat, liver, and breast. Yet the health effects of binge drinking are less well-known. In **Binge Drinking's Effects on the Body**, Molina and Nelson review what is known about the effects of binge drinking on organ systems, including the heart, gastrointestinal tract, and brain.

The research explored in this volume indicates that crossing the binge threshold increases the risk of acute harm, such as injuries, memory blackouts, and overdoses, and that the risk of negative outcomes increases further at higher peak levels of consumption. Repeated binge drinking during the teen years can alter the trajectory of adolescent brain development and cause lingering deficits in attention, memory, and other cognitive functions. Binge drinking can damage organs other than the brain, including the gastrointestinal tract, liver, and heart. While binge drinking declined in recent years for men in some age groups, women exhibited either smaller declines or increases, leading to gender convergence in alcohol use and related harms. Hopefully, insight into the prevalence and consequences of binge drinking, and the social and developmental contexts within which it occurs, will lead to improvements in prevention strategies aimed at minimizing binge drinking and the associated harms.

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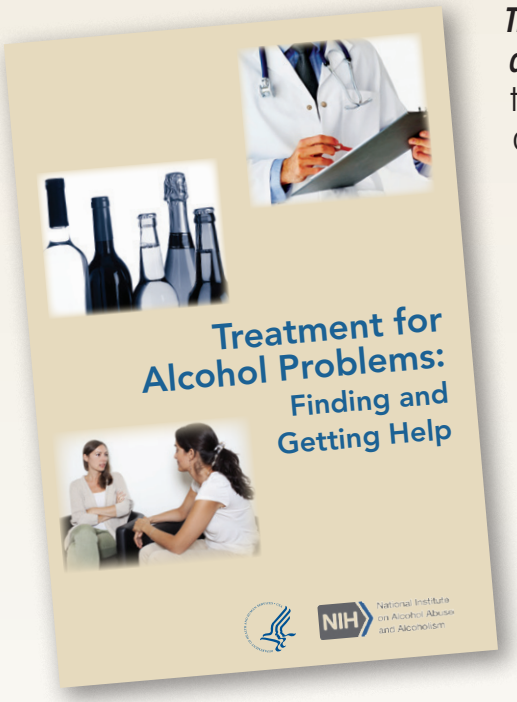
Treatment for Alcohol Problems: Finding and Getting Help



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Adolescent Binge Drinking

Developmental Context and Opportunities for Prevention

Tammy Chung, Kasey G. Creswell, Rachel Bachrach, Duncan B. Clark, and Christopher S. Martin

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Binge drinking, commonly defined as consuming five or more standard drinks per occasion for men and four or more drinks for women, typically begins in adolescence. Adolescents, although they may drink less often, tend to consume higher quantities of alcohol per occasion compared with adults. This developmental difference in pattern of alcohol consumption may result, in part, from maturational changes that involve an adolescent-specific sensitivity to certain alcohol effects and greater propensity for risk-taking behaviors, such as binge drinking. Adolescent binge drinking is associated with a range of acute alcohol-related harms, some of which may persist into adulthood. The prevalence of binge drinking, including high-intensity drinking (i.e., 10 or more and 15 or more drinks per occasion), has declined among adolescents in recent years. Overall, however, the proportion of youth who engage in binge drinking remains high. This article reviews the definition and prevalence of binge drinking in adolescence, trajectories of binge drinking and their correlates, and implications for prevention.

Key words: Alcohol consumption; binge drinking; brain development; college students; high-intensity drinking; underage drinking

Compared with adults, adolescent drinkers tend to consume higher quantities of alcohol per occasion but drink less frequently.[1] Thus, underage drinkers ages 12 to 20 typically consume 4 to 5 drinks per drinking episode, which is nearly double the average of the 2 to 3 drinks usually consumed by adults (older than age 25).[1] Most of the alcohol consumption of underage drinkers occurs during "binge" episodes characterized by drinking high quantities.[2,3] This binge pattern of consumption has been linked to serious alcohol-related harm, such as alcohol poisoning, as well as to sometimes fatal injuries and accidents resulting from acute intoxication.[4] The adverse consequences of adolescent binge drinking affect not only the adolescents but also their families, peers, and community.[5]

This article reviews various definitions of binge drinking, the acute adverse consequences associated with binge drinking, the prevalence of adolescent binge drinking, and demographic factors (e.g., gender and race/ethnicity) associated with adolescent binge drinking. It then discusses the developmental context of adolescent binge drinking, including adolescent-specific sensitivity to certain alcohol effects that may contribute to episodes of high-volume alcohol consumption in adolescence. After a summary of trajectories of binge drinking in adolescence, trajectory correlates representing risk factors and young-adult outcomes, and possible neurocognitive consequences of adolescent binge drinking, the implications of research on adolescent binge drinking for prevention efforts are briefly reviewed.

Definitions of Binge Drinking for Youth

Binge drinking, or an episode of high-volume alcohol consumption, has been defined in various ways.[6,7] (For more information, see **Drinking Patterns and Their Definitions** in this issue.) According to the National Institute on Alcohol Abuse and Alcoholism (NIAAA),[8] "binge drinking" refers to alcohol consumption that brings the blood alcohol concentration (BAC) to .08 g/dL, which is commonly associated with acute impairment in motor coordination and cognitive functioning.[9] BACs of more than .08 g/dL typically occur in men after consuming five or more drinks in about 2 hours, and in women after consuming four or more drinks. This is known as the "5+/4+" binge definition. This definition is consistent with

epidemiological data indicating an association at the population level between greater frequency of 5+/4+ binge episodes and more adverse drinking-related consequences.[10]

When applied to adolescents, binge-drinking definitions based on adult levels of alcohol intake (e.g., 5+/4+ drinks per occasion) often are too high. Children and adolescents are likely to reach BACs of more than .08 g/dL at lower levels of consumption due, in part, to factors such as smaller body size. Donovan used an updated Widmark equation and population data on average body weight in boys and girls to estimate the levels of drinking that would produce BACs of more than .08 g/dL in youth ages 9 to 17.[11] For those ages 9 to 13, a binge episode was estimated to occur with intake of 3 or more drinks within a 2-hour period; for those ages 14 to 15, with 4 or more drinks for boys and 3 or more drinks for girls; and for those ages 16 to 17, with 5 or more drinks for boys and 3 or more drinks for girls. These proposed binge-drinking thresholds for youth are theoretical and based on estimated, rather than observed, BACs. Nevertheless, the identification of lower drinking-quantity thresholds to define binge drinking for younger drinkers suggests that the use of standard adult-based binge definitions may underestimate the prevalence of drinking behavior that leads to BACs of more than .08 g/dL, particularly among females and youth.

Extreme binge, or high-intensity, drinking involves the intake of dangerously high quantities of alcohol per occasion. (For more information, see **High-Intensity Drinking** in this issue.) Thresholds of 10 or more drinks (i.e., double the usual definition of binge drinking of 5 or more drinks) and 15 or more drinks per occasion (i.e., triple the usual definition of binge drinking of 5 or more drinks), as well as gender-specific cutoffs of 8 or more drinks for females and 10 or more drinks for males, respectively, have been used to define high-intensity drinking.[12-14] These definitions specify thresholds that are two to three times higher than the 5+/4+ binge definition and have been examined in part because of limitations in the reliability of the 5+/4+ binge definition for identifying drinkers with BACs of more than .08 g/dL.[15] As a point of reference, among adolescent drinkers, alcohol-related blackouts, or acute alcohol-related memory loss, may occur after consuming nine or more drinks per occasion for males and five or more drinks for females.[16]

Acute Adverse Consequences of Binge Drinking

Acute negative alcohol-related consequences generally show a dose-response relationship with binge drinking,[17] such that greater risk for many adverse consequences has been associated with higher drinking quantities and more frequent binge episodes.[18-20] A significant literature has examined the diverse acute health harms associated with binge drinking, such as alcohol poisoning, alcohol-related blackouts and injury, involvement in car crashes and fatalities, alcohol-related physical and sexual assault, increased risk for sexually transmitted infection, and problems at school or work.[4,21] Risk behaviors associated with binge drinking may include, for example, simultaneous use of other substances (e.g., marijuana) and greater likelihood of riding with an intoxicated driver.[22] Although many of the acute adverse consequences of binge drinking are not unique to adolescents, young drinkers may be at higher risk than adult drinkers for certain acute alcohol-related harms (e.g., alcohol poisoning) because of their relative inexperience with alcohol's effects. Importantly, although some adolescent heavy drinkers meet the criteria for an alcohol use disorder (2.7% of those ages 12 to 17), many more youth report binge alcohol use (6.1%)[23] and may experience acute adverse effects from binge drinking that are not covered by diagnostic criteria.

Prevalence of Adolescent Binge Drinking

Numerous studies have assessed the prevalence of adolescent binge drinking in the United States, as well as in other countries. These studies also have assessed the association between binge-drinking rates and demographic characteristics.

Trends in the Prevalence of Adolescent Binge Drinking in the United States

Three national surveys in the United States provide data on the prevalence of adolescent binge drinking, including the National Survey on Drug Use and Health (NSDUH), which until 2015 defined binge drinking as consumption of five or more drinks on the same occasion;* the Monitoring the Future (MTF) survey, which defines it as five or more drinks in a row; and the Youth Risk Behavior Survey (YRBS), which defines it as five or more drinks of alcohol in a row—that is, within a couple of hours. (For more information on these surveys, see **Surveys That Include Information Relevant to Binge Drinking** in this issue.) Thus, until 2015, these surveys all used the same threshold to define binge drinking in males and females, albeit with slightly different wording and with differences in the time frame used to assess binge drinking (i.e., within the past month for the NSDUH and YRBS, and within the past 2 weeks for the MTF). The NSDUH has collected annual data since 1991 on individuals ages 12 and older using interviews conducted in the home.[5] In contrast, both MTF and YRBS are school-based

*Since 2015, the NSDUH defines binge drinking as consumption of 4 or more drinks for women or 5 or more drinks for men on the same occasion on at least 1 day in the past 30 days.

surveys. MTF has collected annual data since 1975 from 12th graders, and since 1991 from 8th, 10th, and 12th graders.[24] YRBS has collected data biennially since 1991 from 9th to 12th graders.[25]

All three surveys show similar time trends in adolescent binge drinking.[26] The MTF data indicate a peak in the prevalence of youth binge drinking in the late 1970s to early 1980s, followed by a decrease from 41% in 1983 to 28% in 1992.[24] In the 2015 MTF survey, binge drinking in the past 2 weeks was reported by 4.6% of 8th graders, 10.9% of 10th graders, and 17.2% of 12th graders.[24] This reduction in youth binge-drinking prevalence over time may reflect factors such as enactment of a minimum legal drinking age of 21 and other alcohol regulatory policies.[4,27] Time-trend data from the YRBS (from 1999 to 2013) and NSDUH (from 2002 to 2014) indicate a similar decrease in youth binge drinking in recent years.[5,25]

The prevalence of high-intensity drinking (10 or more or 15 or more drinks in a row in the past 2 weeks) was relatively stable among high school seniors in the MTF from 2006 to 2012, but, like binge drinking, has shown a decline in recent years. Thus, the prevalence of consuming 10 or more drinks in a row declined from 10.4% in 2012 to 6.1% in 2015, and the prevalence of consuming 15 or more drinks in a row declined from 5.5% in 2012 to 3.5% in 2015.[24]

In all three national surveys, binge-drinking prevalence increases with age during adolescence. For example, in 2015, the most recent year in which all three national surveys collected data on binge drinking, NSDUH indicated that 9.6% of youth ages 12 to 17 reported alcohol use in the past month, with roughly half (i.e., 5.8%) of these drinkers reporting binge drinking in the past month.[28] Among respondents ages 12 to 17 in the 2015 NSDUH, past-month binge-drinking prevalence increased from 0.5% at ages 12 to 13 to 15.3% at age 17. In the 2015 YRBS, 17.7% of all high school students reported binge drinking in the past month, increasing from 10.4% in 9th graders to 24.6% in 12th graders.[29] According to the 2015 MTF survey, 4.6% of 8th graders, 10.9% of 10th graders, and 17.2% of 12th graders reported binge drinking in the 2 weeks prior to the survey.[24]

The results from these three national surveys are broadly consistent in a given year, although YRBS data generally indicate somewhat higher binge prevalences compared with NSDUH and MTF, and MTF tends to report higher prevalences compared with NSDUH.[26] The differences in binge-drinking prevalence across the surveys may result from methodological differences, such as sampling strategy used, survey location (e.g., school or home), type of data collection (e.g., paper survey or self-administered computer assessment), item wording, and time frames for querying binge drinking.[26] Interpretation of results from these national surveys also needs to consider that use of the "5+" binge definition in these surveys may underestimate the prevalence of binge drinking in younger adolescents and females, because, as mentioned earlier, lower drinking-quantity thresholds to define binge drinking are indicated in this age group.[11]

International Surveys of Adolescent Binge-Drinking Prevalence

International data on the prevalence of adolescent binge drinking are available from sources such as the European School Survey Project on Alcohol and Other Drugs (ESPAD) and the Australian School Students Alcohol and Drug (ASSAD) survey. In 2011, the ESPAD report on 15- to 16-year-old students in 36 European countries indicated that the average prevalence of consuming 5 or more drinks on at least 1 occasion in the past 30 days was 39% across countries.[30] However, ESPAD countries differed in the average alcohol quantity that students reported consuming on their most recent drinking day. Thus, students in Nordic countries and the British Isles generally reported consuming a higher average quantity than did students in southeastern Europe (e.g., Greece or Italy).[30] By comparison, the 2011 ASSAD survey found that among students ages 12 to 17 who reported drinking in the week prior to the survey (17.5% of all students queried), more than one-third (36.2%) drank 5 or more drinks in a day.[31]

In general, countries with lower legal drinking ages have a higher prevalence of adolescent binge drinking compared with countries with higher legal drinking ages.[32] Also, rates of adolescent binge drinking generally are higher in many European countries[4] and Australia[31] than in the United States. However, such variations in binge-drinking prevalence across studies need to be interpreted with caution because methodological differences (e.g., in sampling method, ages covered, item wording, time frames, and the definition of a standard drink) exist across surveys.

Adolescent Binge-Drinking Prevalence by Demographic Characteristics

In general, males tend to report higher rates of binge drinking in adolescence than do females (see Figure 1).[13,14,23,24] These gender differences typically increase with age during adolescence.[22,30,33] However, time-trend data from MTF have indicated a narrowing of the gender gap starting in the mid-1970s, particularly among high school seniors. Thus, in the 1975 MTF, 49% of male high school seniors, but only 26% of females, reported binge drinking, corresponding to a 23-percentage-point difference. By 2014, in contrast, a mere 5-percentage-point difference existed between male (22%) and female (17%) high school seniors who reported binge drinking.[33] Conversely, NSDUH time-trend data from 2002 to 2012 for youth ages 12 to 17 indicate that although binge drinking

decreased for both males (from 11.3% in 2002 to 7.4% in 2012) and females (from 10.2% in 2002 to 6.8% in 2012), with more males than females reporting binge drinking at both time points, there was little support for a narrowing of the gender gap over these years.[34] The time-trend results for gender differences from the MTF and NSDUH surveys are not directly comparable because of differences in the ages covered, as well as in item wording and time frames assessed (i.e., the MTF asked about 5 or more drinks in a row in the past 2 weeks, whereas the NSDUH asked about 5 or more drinks on an occasion in the past month). Nevertheless, both surveys indicate greater binge-drinking prevalence among male than among female adolescents.[22]

The prevalence of adolescent binge drinking in the United States also differs by race/ethnicity (see Figure 1). Among adolescents ages 12 to 17 in the 2014 NSDUH, the prevalence of past-month binge drinking was higher among Whites (7.1%) and Hispanics/Latinos (6.3%) compared with Blacks (3.6%) and Asians (1.5%).[23] MTF time-trend data from 1975 to 2014 suggest that these race/ethnic differences may differ by year in high school.[33] For example, among 8th-grade students, more Hispanics tended to report binge drinking compared with Whites and Blacks. Among 10th- and 12th-grade students, however, Hispanics and Whites were more likely to report binge drinking than were Blacks.

In the United States, binge-drinking prevalence also varies by region, with differences observed between and within states (see Figure 2).[33] For example, based on recent NSDUH data, past-month binge-drinking prevalence among underage drinkers ages 12 to 20 at the state level was highest in four states in the Northeast, four states in the Midwest, the District of Columbia, and one state in the West.[35] Even within a region, such as the District of Columbia, subregions differed in the prevalence of past-month binge drinking, ranging from 10.8% to 42.4% in the District of Columbia, with an overall estimate of 18.0%.[35] High-intensity or extreme binge-drinking prevalence was especially high among high school seniors in the Midwest.[13] Binge-drinking prevalence also differed by urban versus rural setting, with high school students living in rural areas tending to report the highest rates of binge drinking.[33] These regional differences suggest that factors such as local and regional norms regarding alcohol use, as well as local alcohol regulatory policies and enforcement, have an important influence on prevalence of binge drinking.

Developmental Context of Adolescent Binge Drinking

During adolescence, ongoing brain development and rapid changes in physical maturation occur in the context of a shift from parents and family to peers as a primary source of support and guidance.[36,37] These normative, adolescent-specific changes in

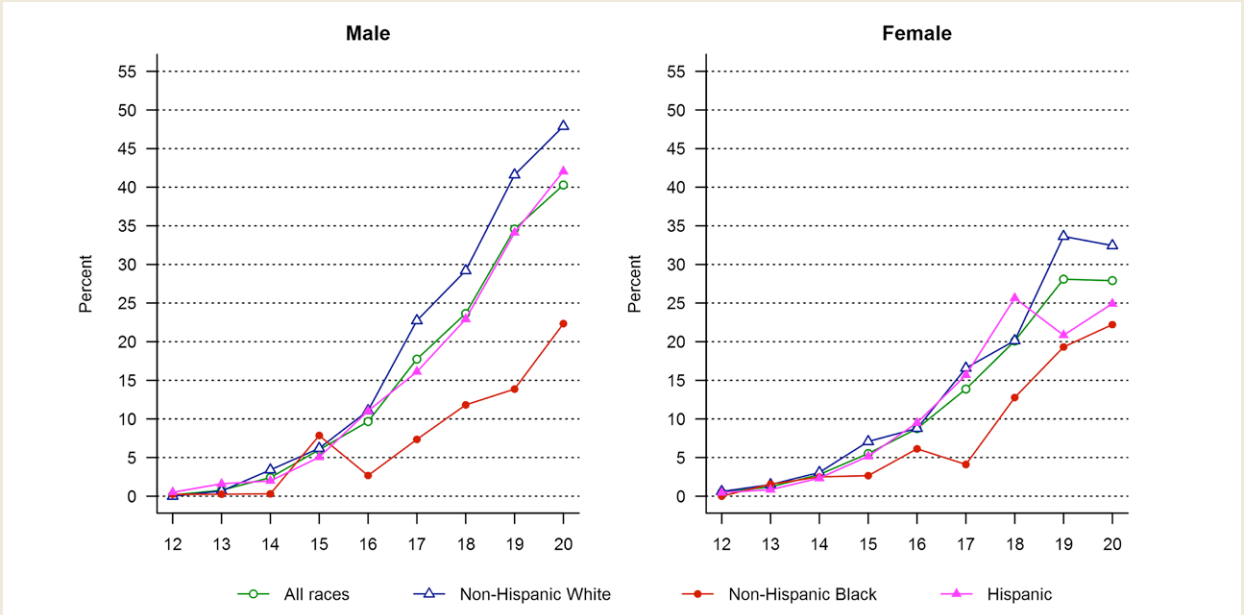

Figure 1 Prevalence of binge drinking in the past 30 days among 12- to 20-year-olds, by age, sex, and race/Hispanic origin, as reported in the 2013 NSDUH.

physical maturation and social context can contribute to the risk for binge drinking. In particular, the fine tuning of the neural circuitry that occurs during this developmental period is associated with an adolescent-specific elevation in the ability to consume alcohol, which appears to be conserved across species.[38] Animal (e.g., rodent) models indicate that neural changes occurring in adolescence may temporarily increase sensitivity to certain alcohol effects (e.g., rewarding effects) that promote consumption within a drinking episode, while reducing sensitivity to other effects (e.g., sedative effects) that may help to limit drinking during an episode.[38] Evidence for such an adolescent-specific sensitivity to alcohol effects in humans is sparse but aligns with animal models to suggest that compared with their adult counterparts, human adolescents may be more sensitive to alcohol's rewarding and stimulant effects[39] and less sensitive to its sedative effects.[40] Related research has found that, among college students, high-intensity binge drinking (i.e., 8 or more/10 or more drinks for females/males) is experienced as more rewarding than non–high-intensity drinking (i.e., less than 8/10 drinks for females/males).[41] Furthermore, many college students reported willingness to tolerate adverse alcohol effects in order to experience the positive effects associated with high-intensity drinking.[41]

The adolescent-specific shift from family to peers as important sources of influence on youth attitudes and behavior also can contribute to risk-taking behaviors, such as binge drinking.[42,43] Higher levels of sensation seeking and impulsivity, which are associated with risk-taking behaviors and binge drinking, tend to be endorsed more often by adolescent males than by females, which may help explain the generally greater prevalence of binge drinking among males.[44] Risk-taking behavior may be facilitated by the presence of peers.[43] Consistent with this observation, adolescent binge drinking tends to occur in social contexts with peers.[45,46] This may encourage episodes of high-volume consumption through mechanisms such as peers providing access to alcohol, peer norms that are favorable to binge-drinking behavior, and positive feelings generated by social activities that involve alcohol use.[37,47]

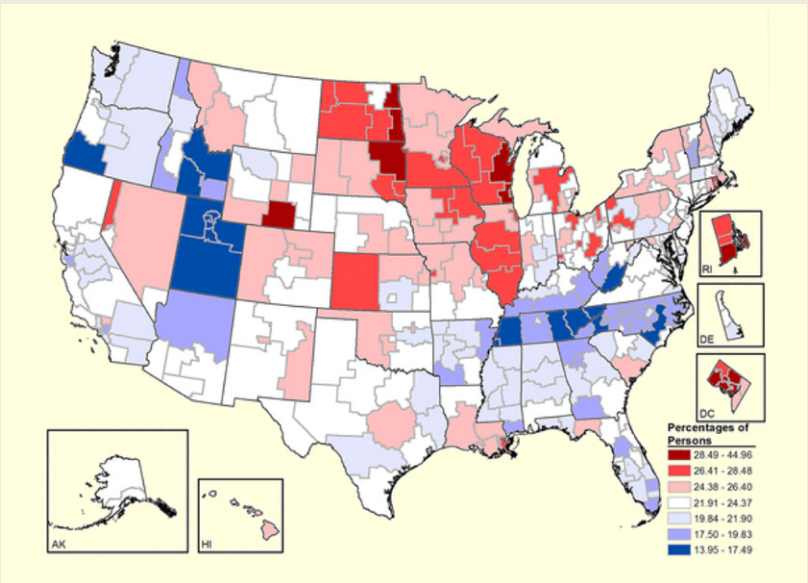

Figure 2 Binge alcohol use in the past month among individuals ages 12 to 20, by substate region in the United States. *Note:* For substate region definitions, see the 2012–2014 NSDUH, substate region definitions at www.samhsa.gov/data. *Source:* SAMHSA, Center for Behavioral Health Statistics and Quality, 2012, 2013, and 2014 NSDUH.

Binge drinking among underage drinkers in the United States often involves distilled spirits, with consumption of beer reported in less than one-third of binge episodes.[48] For some youth, consumption of liquor may reflect the intent to drink to get drunk as quickly as possible. The preferential consumption of liquor by adolescents during binge episodes is particularly concerning because it has been linked with increased risk for alcohol-related consequences, such as blackouts or injury.[49]

Young drinkers also often lack knowledge regarding standard drink servings, particularly for spirits, which can result in overpouring—that is, pouring greater volumes than used for standard drink servings.[50] Overpouring can increase the likelihood of high-volume consumption, rapid intoxication, and risk for certain alcohol-related harms, such as blackouts.[50]

Other contextual factors relevant to adolescent binge drinking include the places where drinking occurs and the temporal patterning (e.g., weekend or seasonal) of drinking. For example, certain places where adolescent binge drinking occurs, such as at someone else's home without parental supervision or at a bar or nightclub, have been associated with greater risk for alcohol-related violence.[51] With regard to temporal patterning, the timing of adolescent binge drinking shows some predictability: Binge drinking may be more likely to occur during weekends, summer and spring breaks, holidays (e.g., New Year's Eve), and occasions such as prom and sports events.[52] These contextual factors, in combination with an adolescent-specific sensitivity pattern to alcohol effects and the peer social context of drinking, may interact with individual difference

factors, such as heritable risk and exposure to trauma, in contributing to increased risk for binge drinking and related harm in adolescence.[38]

Binge-Drinking Trajectories in Adolescence

The onset of alcohol use peaks during grades 7 to 11.[24] By 8th grade, 11% of students report having been drunk (a self-report proxy for high-quantity consumption) at least once in their lifetime, with an increase to 29% among 10th graders and 47% among high school seniors.[24] Reports of the onset of consuming 3 or more drinks per occasion begin to increase between ages 13.5 and 15.5, and reports of an episode of binge drinking (5 or more drinks per occasion) start to rise around age 16.[53] Although rates of binge drinking peak between ages 18 and 25,[54] the onset of binge drinking (i.e., 3 or more or 5 or more drinks per occasion) and episodes of being drunk typically occur in early to mid-adolescence (i.e., ages 12 to 16). Early age of first intoxication (younger than 15 years old) and rapid progression from first drink to first intoxication both are early warning signs of heavy, particularly binge, drinking.[55,56]

Longitudinal studies that span adolescence through emerging adulthood (i.e., ages 12 to 25) have identified three to five prototypical trajectories of binge drinking (see Figure 3).[57-63] The trajectories derived in these studies provide useful heuristics for understanding different patterns of change in binge drinking across adolescence. They highlight heterogeneity in course, and differ with respect to age at onset of binge drinking; timing, rate, and direction of change in binge drinking (e.g., escalation and desistance); and frequency of binge drinking.

Most youth in community samples fall into the low-frequency binge-drinking and nonbinge-drinking trajectories. In some studies, nonbinge trajectories may include youth who drink but do not report binge episodes, as well as abstainers.[59,60] Trajectories indicating persistence of binge drinking from adolescence into young adulthood, which typically represent a minority of youth in community samples, tend to show onset of binge drinking in early adolescence (i.e., at ages 12 to 13) and an increase to weekly or more frequent binges by late adolescence (i.e., at ages 17 to 18).[7] Other binge-drinking trajectories are characterized by earlier (e.g., age 16 and younger) versus later (e.g., age 17 and older) onset of binge drinking or by a pattern of adolescent-limited binge drinking, in which binge drinking peaks in adolescence, then declines in early adulthood.[7] One study that followed a high-risk sample of youth into young adulthood identified four types of binge-drinking† trajectories, including nonbinger (39.5%), infrequent (9.6%), late-onset moderate (30.0%), and early-onset heavy drinking (20.9%).[57] Studies vary in the relative proportions of youth in each trajectory type because of methodological factors, such as differences in sampling (e.g., community vs. high-risk sample), age range, binge-drinking definition, and whether nonbinge trajectories include both abstainers and drinkers who do not report binge episodes.

Correlates of Adolescent Binge-Drinking Trajectories: Risk Factors and Young-Adult Outcomes

Distinct trajectories of binge drinking are thought to reflect different etiologic mechanisms.[64] According to an ecological systems model,[36,65] these etiologic mechanisms represent multiple systems (e.g., family, peer group, and community) that interact across development to influence binge-drinking trajectories.

Developmental factors associated with an increase in binge drinking during adolescence include, for example, reduced parental monitoring as youth mature[37,66] and greater independence (e.g., obtaining a driver's license) in daily activities.[36] In addition, for some youth, onset of binge drinking may be associated with important school transitions (e.g., junior high to high school or high school to college), which can involve restructuring of peer groups and increased opportunities to engage in alcohol use.[36] Importantly, processes of peer selection and peer influence have been associated with changes in binge drinking in adolescence.[67-69] In particular, selection of peers who engage in binge drinking has been associated with an adolescent's initiation and frequency of binge drinking.[69]

Several studies analyzed factors associated with binge trajectories, relative to nonbinge trajectories, at the individual level. Nonbinge trajectories in these studies included youth who abstained and youth who reported alcohol use below a given binge threshold. Risk factors identified in these studies included, for example, engaging in delinquent behavior, exposure to more stressful life events, and lower task persistence.[61-63] Some of these risk factors may be associated with gender; for example, females may be more likely to experience certain stressful life events (e.g., sexual trauma), whereas males may be more likely to be involved in delinquent behavior or to show lower levels of impulse control.[44,70] Moreover, in contrast to youth in binge-drinking trajectories, youth in nonbinge trajectories were more likely to report greater self-efficacy to resist social pressure to engage in substance use,[62] as well as greater religiosity.[63]

With regard to the social context in which youth are nested, parental alcoholism and disrupted family relations (e.g., parental separation or divorce) each were associated with binge-drink-

†The study defined binge drinking as "5+ drinks in a row."

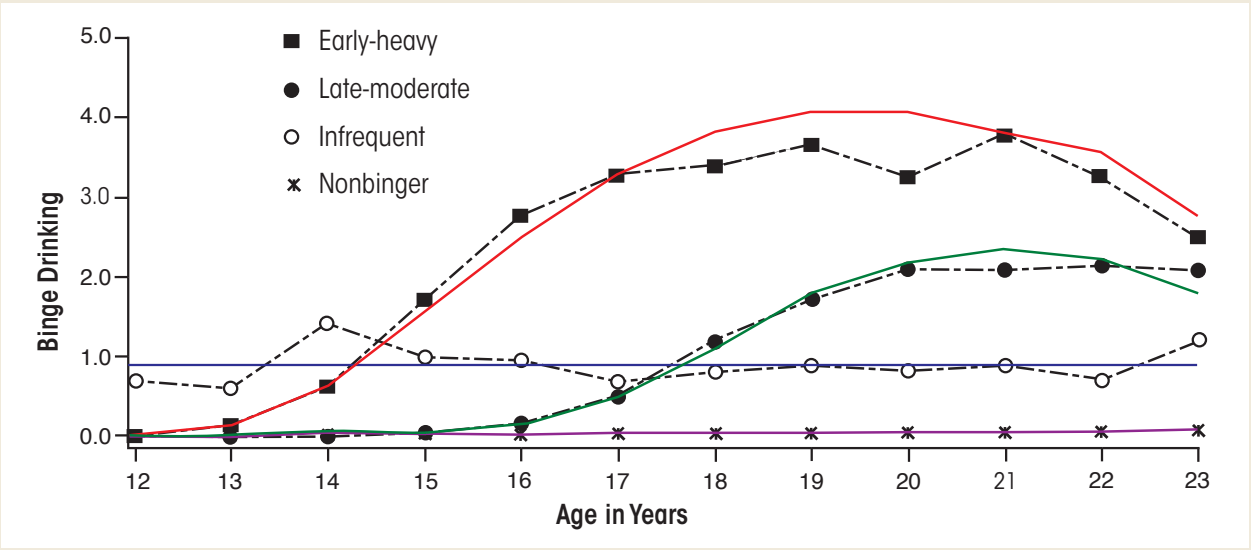

Figure 3 Trajectories of binge drinking from adolescence through emerging adulthood. Estimated growth trajectories for the three groups are indicated by solid lines. Dashed black lines represent observed means of binge drinking at each age for each group. Observed frequencies of binge drinking (past year) ranged from 0 (none) to 5 (one to two times a week). *Note:* Early-heavy group, $n = 99$, 20.9% of the sample. Late-moderate group, $n = 134$, 30.0% of the sample. Infrequent group, $n = 43$, 9.6% of the sample. Nonbinger group, $n = 176$, 39.5% of the sample. *Source:* Chassin L, Pitts SC, Prost J. Binge drinking trajectories from adolescence to emerging adulthood in a high-risk sample: Predictors and substance abuse outcomes. *J Consult Clin Psychol.* 2002;70(1):67-78. Copyright © 2002 by the American Psychological Association. Reprinted with permission.

ing trajectories.[57,62] Conversely, an adolescent's perception of high parental disapproval of substance use was prospectively associated with a nonbinge trajectory.[60] Peer relations also had an impact, because changes in binge drinking tended to occur in parallel with changes in affiliation with drinking peers.[60] However, despite the robust influence of peers on drinking behavior, an adolescent's report of high parental disapproval of substance use weakened the effect of peers on binge drinking,[60,69] indicating the important role that parents play in providing clear messages to their children regarding disapproval of underage drinking. It is important to note, however, that many individual and social risk factors associated with adolescent alcohol and other substance use have a more general influence and are not necessarily specific to binge drinking.

Community-level influences on adolescent binge-drinking trajectories include factors such as neighborhood and school environments, as well as local alcohol regulatory policies and enforcement. For example, one study found that youth living in neighborhoods with higher densities of on-premise alcohol outlets (e.g., bars and nightclubs) were more likely to report binge drinking, controlling for neighborhood-level socioeconomic status.[71] However, neighborhood risks may be buffered by protective factors. In particular, a recent study found that a supportive school environment (e.g., alcohol prevention incorporated into the curriculum) was associated with reduced adolescent binge drinking over and above individual, family, and peer risk factors.[72] Further, comprehensive and stringent local alcohol control policies and enforcement have been associated with lower levels of youth binge drinking, highlighting the importance of these community-level factors.[73] The unique and cumulative effects of family, peer, and community influences on youth binge drinking emphasize the need for coordinated, developmentally tailored prevention programs that address each of these multiple interacting social systems to reduce risk.

Compared with nonbinge trajectories, binge-drinking trajectories in adolescence, particularly frequent and chronic binge drinking, have been associated with poorer functioning in young adulthood. For example, youth in binge trajectories were more likely to have an alcohol or other drug use disorder in young adulthood than those in nonbinge trajectories (which may include abstainers and youth who drink, but do not report binge episodes, depending on the study).[57,62,74,75] In contrast, youth in nonbinge trajectories had better young-adult outcomes across domains such as educational attainment and employment, family and peer relations, and mental and physical health than did those in

binge trajectories, particularly those who engaged in frequent, chronic binge drinking.[57,59,62,76]

Other analyses have compared different binge-drinking trajectories (e.g., chronic vs. adolescent-limited). Such studies found that compared with adolescent-limited trajectories, chronic binge-drinking trajectories exhibited stronger associations with other substance use[75] and with stressful life events.[63] Further, compared with alcohol use that did not meet definitions of binge drinking (i.e., less than five drinks per occasion), adolescent binge drinking (five or more drinks per occasion) was associated with adverse outcomes, such as lower academic performance, greater likelihood of reporting drunk driving in the past month, and other substance use.[58] In sum, a pattern of relatively frequent and chronic binge drinking during adolescence, compared to nonbinge trajectories, was associated with worse young-adult outcomes across multiple domains, including risk for substance use disorder.

Neurocognitive Consequences of Adolescent Binge Drinking

In the context of the ongoing brain maturation that occurs in adolescence and young adulthood,[77,78] binge drinking could result in potentially long-lasting neural alterations. For example, in rodent models, a binge pattern of alcohol exposure in adolescence has been associated with disrupted hippocampal functioning.[79] Further, animal models indicate that binge alcohol exposure during adolescence can have downstream effects on cognition and behavior through epigenetic mechanisms.[80,81] The specific effects of binge drinking during adolescence on the brain and neurocognition may depend on the timing, dose, and chronicity of alcohol exposure.[38,82]

Similar to animal research, in studies of human adolescents, heavy drinking has been associated with deficits in neuropsychological functioning[83,84] and aberrations in brain structure and functioning.[85-88] Some research suggests possible gender-specific adverse consequences of binge alcohol consumption on neurocognition.[89] However, other research has found no difference between adolescent heavy drinkers (defined as 5+/6+ glasses, 10 g alcohol per glass, per occasion for females/males at least weekly) and light/nondrinkers in the maturation of basic executive functions (e.g., working memory).[90] Overall, binge drinking in human adolescents may have relatively subtle effects on neuropsychological measures at the level of behavioral performance; given relatively short drinking histories among youth, differences between young binge drinkers and their healthy counterparts more readily are observed at the level of brain structure and functioning.[86] Importantly, research suggests that after controlling for overall quantity of alcohol consumed, a binge pattern (i.e., consuming five or more drinks per occasion vs. consuming fewer than five drinks per occasion), in particular, was associated with adverse effects on brain functioning in young adults.[91]

Because most of the existing studies on binge drinking and neurocognition in human adolescents have been cross-sectional, the extent to which the findings reflect preexisting characteristics or persistent (vs. possibly transient) consequences of heavy or binge alcohol use are unclear. However, emerging research suggests that aberrations in the brain circuitry underlying decision-making may not only signal risk for binge drinking in adolescence prior to heavy drinking[92] but also may be adversely affected by binge drinking in adolescence and young adulthood.[93] The reversibility of the effects of adolescent binge drinking on brain structure and functioning with sustained abstinence warrants study, particularly because brain maturation continues into young adulthood.[78] Large ongoing multisite studies, such as the National Consortium on Alcohol and Neurodevelopment in Adolescence,[94] the IMAGEN study in Europe,[95] and the Adolescent Brain and Cognitive Development Study (https://abcdstudy.org), which are examining the effects of alcohol and other substance use on the developing brain in adolescence, are poised to address these gaps in knowledge.

Implications for Prevention and Intervention

To reduce binge drinking, coordinated prevention and intervention efforts that operate across multiple levels (e.g., individual, family, community, and national policy), as well as continue across the life span, are needed.[1,21] Such prevention efforts should be timed to begin by late childhood and should be tailored to address risks most salient to specific developmental periods and individual circumstances. For example, gender differences in risk factors for underage drinking[44,70] suggest the potential utility of gender-specific interventions. Increasingly, developmental neuroscience provides the basis for novel prevention and intervention approaches that strengthen the social-emotional and decision-making skills needed to refrain from binge drinking, such as emotion regulation or resisting peer pressure to engage in risky behavior.[95,96] Additional interventions for youth are needed that address alcohol's strongly perceived positive effects. One approach may be to support alternative socially based rewarding and healthy activities, because experiencing adverse alcohol-related consequences may not reduce binge drinking in young populations.[12]

Ideally, prevention should include routine alcohol screening and brief intervention for all youth, as well as supportive guidance for parents and caregivers.[97,98] Community-based prevention and intervention programs have shown effects in reducing underage drinking.[99] School-based programs[100] and easy access to a continuum of services[4] are other examples

of community-level supports for youth and families. At the level of public policy, strong alcohol policy environments[101] and enhanced enforcement of local alcohol regulatory policies,[102] such as the minimum legal drinking age and social-hosting laws, have deterred underage drinking.[4]

Conclusions

Adolescence is a critical period of risk for binge drinking. An adolescent-specific sensitivity to alcohol's effects may interact with a normative propensity for greater risk-taking behavior and peer social environment in contributing to risk for binge drinking during this developmental period. Although there is debate regarding the definition of a binge-drinking episode, a dose-response relationship between episodic high-quantity alcohol consumption and increased risk for adverse consequences generally has been observed.[18-20] Binge drinking in adolescence has been associated with multiple acute harms to health,[4] including possible effects of heavy drinking on neuropsychological functioning[83,84,87] and potential longer term adverse young-adult outcomes.[57] Of particular concern is emerging research with young adults, which suggests that certain negative consequences of alcohol use on neurocognition may be specific to a binge pattern of alcohol consumption.[91] Although the prevalence of adolescent binge drinking has declined since the 1970s, rates are still high. Moreover, binge-drinking prevalence likely is underestimated by surveys that use a binge definition of five or more drinks per occasion, because lower drinking-quantity thresholds to define binge drinking may be indicated, particularly for youth. Strategically coordinated prevention programs that operate across the life span and at multiple levels, ranging from individuals and families to public policy, are essential to reducing adolescent binge drinking.

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Drinking Patterns and Their Definitions

Alcohol Research: Current Reviews Editorial Staff

The number of drinks a person consumes and the rate at which he or she consumes them influence how much alcohol enters the brain and how impaired that person becomes. Many people are surprised to learn what counts as a drink. The amount of liquid in one's glass, can, or bottle does not necessarily match up to how much alcohol is in the drink. To facilitate research and clinical care and to help individuals make informed choices about how much alcohol they are consuming, public health agencies in the United States have established a definition of a standard drink, as well as definitions of various alcohol consumption patterns. These definitions facilitate objective assessments of how much a person is drinking, enable comparisons of alcohol consumption within and across studies, and help consumers follow low-risk drinking guidelines.

What Is a Standard Drink?

In the United States, a standard drink is defined as a drink with 14 grams (0.6 fluid ounces) of pure alcohol. This is found in:

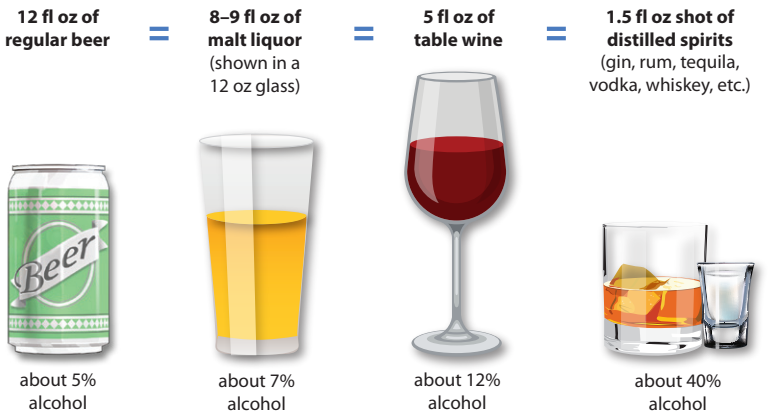
- 12 ounces of regular beer, which is usually about 5% alcohol
- 5 ounces of wine, which is typically about 12% alcohol
- 1.5 ounces of distilled spirits, which is about 40% alcohol

Although the standard drink amounts are helpful for following health guidelines, they may not reflect customary serving sizes. In addition, while the alcohol concentrations listed above are typical, there is considerable variability in alcohol content within and across beverage type (e.g., beer, wine, and distilled spirits). For example, some light beers contain half as much alcohol as a regular beer, while some craft and specialty beers contain twice as much. Similarly, the alcohol content in wines can vary from 5% to 15%.[1]

Moderate Alcohol Consumption

According to the Dietary Guidelines for Americans, which are intended to help individuals improve and maintain overall health and reduce chronic disease risk, moderate drinking is defined as up to 1 drink per day for women and up to 2 drinks per day for men.[2]

What Is a Standard Drink?



Each beverage portrayed above represents one standard drink of "pure" alcohol, defined in the United States as 0.6 fl oz or 14 grams. The percentage of pure alcohol, expressed here as alcohol by volume (alc/vol), varies within and across beverage types. Although the standard drink amounts are helpful for following health guidelines, they may not reflect customary serving sizes.

Drinking Patterns and Their Definitions *(continued)*

Low-Risk Drinking and Alcohol Use Disorder (AUD)

As defined by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), for women, low-risk drinking is no more than 3 drinks on any single day and no more than 7 drinks per week. For men, it is defined as no more than 4 drinks on any single day and no more than 14 drinks per week. NIAAA research shows that only about 2 in 100 people who drink within these limits meet the criteria for AUD. Even within these limits, people can have problems if they drink too quickly or if they have other health issues.[3]

Binge Drinking

NIAAA defines binge drinking as a pattern of drinking that brings blood alcohol concentration to 0.08 grams per deciliter (0.08%) or higher. This typically occurs after a woman consumes 4 drinks or a man consumes 5 drinks in a 2-hour time frame.[3]

The Substance Abuse and Mental Health Services Administration (SAMHSA), which conducts the annual National Survey on Drug Use and Health (NSDUH), defines binge drinking as 4 or more drinks for a woman or 5 or more drinks for a man on the same occasion on at least 1 day in the past 30 days.[4]

Extreme Binge Drinking

Extreme binge drinking, also known as high-intensity drinking, refers to drinking at levels far beyond the binge threshold, resulting in high peak blood alcohol concentrations. Though definitions vary, some studies define extreme binge drinking as 2 or more times the gender-specific binge drinking thresholds (i.e., 10 or more standard drinks for men, and 8 or more for women).[5] Other studies use a higher threshold that may[6] or may not[7] be gender specific.

Heavy Drinking

SAMHSA defines heavy drinking as binge drinking on each of 5 or more days in the past 30 days.[4]

International Drink Definitions

Standard-drink definitions vary widely across countries, from 8 grams of alcohol in Iceland and the United Kingdom to 20 grams in Austria. To assess the prevalence of high-risk drinking globally, the World Health Organization uses a measure called heavy episodic drinking, defined as consuming 60 grams of alcohol or more on at least one occasion in the past 30 days. In the United States, where a standard drink equals 14 grams, that would be 4.25 standard drinks. In China, France, Ireland, and Spain, where a standard drink equals 10 grams, 6 drinks on a single occasion would constitute heavy episodic drinking.

Because of the risks of drinking, certain people should avoid alcohol completely:

- Individuals under the minimum legal drinking age of 21
- Women who are pregnant or trying to become pregnant
- People who have a medical condition that alcohol can aggravate
- Individuals taking medications that interact with alcohol
- People driving vehicles or operating machinery (or who plan to do so shortly after drinking)

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Surveys That Include Information Relevant to Binge Drinking

Alcohol Research: Current Reviews Editorial Staff

This table provides a brief overview of selected surveys administered in the United States and internationally that collect information that can be used to study binge drinking. This list reflects relevant surveys referenced in this issue of *Alcohol Research: Current Reviews*. It is not a comprehensive compilation of all of the surveys relevant to this topic.

Select U.S. Surveys

Survey Name and Frequency	Population Surveyed	Binge Drinking Measure* and Definition of a Drink	Notes
• Behavioral Risk Factor Surveillance System (BRFSS) • Every year since 1984	Civilian noninstitutionalized adults ages 18 and older	• Binge drinking is measured as 5+ drinks for males or 4+ drinks for females on an occasion in the past 30 days. • One drink is equivalent to a 12-ounce beer, a 5-ounce glass of wine, or a drink with one shot of liquor.	The survey was first administered in 15 states. It became a nationwide surveillance system in 1993 and is now administered in all 50 states, the District of Columbia, and 5 U.S. territories. Since 2011, this survey has included adult students living in college housing. https://www.cdc.gov/brfss
• Core Alcohol and Drug Survey • Every year from 2006 to 2013	College students	• Binge drinking is measured for males and females as 5+ drinks in one sitting in the past 2 weeks. • A drink is defined as a bottle of beer, a glass of wine, a wine cooler, a shot glass of liquor, or a mixed drink.	http://core.siu.edu/results/index.php
• Harvard School of Public Health College Alcohol Study • Conducted four times (1993, 1997, 1999, and 2001)	4-year college students	• Binge drinking is measured as 5+ drinks for males or 4+ drinks for females once in the past 2 weeks. • A drink is defined as a 12-ounce beer, a 4-ounce glass of wine, a 12-ounce wine cooler, or a shot of liquor taken straight or in a mixed drink.	http://archive.sph.harvard.edu/cas/About
• Health Related Behaviors Survey of Active Duty Military Personnel • About every 3 years since 1980	Active-duty service and U.S. Coast Guard members	• Binge drinking is measured as 5+ drinks for males or 4+ drinks for females on the same occasion in the past 30 days. • A drink is defined as a can or bottle of beer, a glass of wine or a wine cooler, a shot of liquor, or a mixed drink with liquor in it.	Most recent report available: https://www.documentcloud.org/documents/694942-2011-final-department-of-defense-survey-of.html

*Surveys may not explicitly use the term binge drinking.

Surveys That Include Information Relevant to Binge Drinking *(continued)*

Select U.S. Surveys

Survey Name and Frequency	Population Surveyed	Binge Drinking Measure* and Definition of a Drink	Notes
• Monitoring the Future (MTF) study • Every year since 1975	8th, 10th, and 12th graders in public and private schools, college students, and young adults	• Binge drinking is measured for males and females as 5+ drinks in a row in the past 2 weeks. • The definition of a drink varies slightly among survey forms, although a drink is generally defined as a bottle of beer, a glass of wine, a wine cooler, a shot glass of liquor, a mixed drink, etc.	This survey began with 12th graders in 1975. Since 1991, surveys of 8th and 10th graders have been conducted annually. Beginning with the class of 1976, a randomly selected sample from each senior class has received biennial follow-up surveys. http://www.monitoringthefuture.org
• National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) • Three surveys conducted since 2001 to 2002	Civilian noninstitutionalized adults ages 18 and older	• NESARC does not explicitly measure binge drinking, although respondents are asked about drinking at or above levels commonly used to assess binge drinking. For males ages 65 and younger, the level is 5+ drinks in a single day or in 2 hours or less. For males ages 65 and older and women, the levels are 4+ drinks in 2 hours or less, 4+ drinks in a single day, and 5+ drinks in a single day. • One standard drink is defined as 0.6 ounces of ethanol.	Three NESARC waves have been conducted. Wave 1 was from 2001 to 2002, Wave 2 was from 2004 to 2005, and NESARC-III was from 2012 to 2013. https://www.niaaa.nih.gov/research/nesarc-iii
• National Survey on Drug Use and Health (NSDUH) • 1979, 1982, 1985, 1988, 1990, and every year thereafter	Civilian noninstitutionalized population ages 12 and older	• Binge drinking is measured as 5+ drinks for males or 4+ drinks for females on the same occasion on at least 1 day in the past 30 days. NSDUH defined binge drinking as 5+ drinks for males and females until 2015. • A drink is defined as a can or bottle of beer, a glass of wine or a wine cooler, a shot of liquor, or a mixed drink with liquor in it.	Called the National Household Survey on Drug Abuse (NHSDA) from 1979 to 2001, called NSDUH since 2002. https://www.samhsa.gov/data/population-data-nsduh
• Youth Risk Behavior Surveillance System (YRBSS) • Every 2 years since 1993	9th through 12th graders in public and private schools in the United States	• Binge drinking is measured as 5+ drinks for males or 4+ drinks for females on a single occasion in the past 30 days. Before 2017, YRBSS surveys defined binge drinking for males and females as 5+ drinks. • A drink includes beer, wine, wine coolers, and liquor such as rum, gin, vodka, or whiskey.	The YRBSS includes national surveys conducted by the Centers for Disease Control and Prevention. It also includes state, territorial, tribal government, and local surveys conducted by departments of health and education, which provide data representative of mostly public high school students in each jurisdiction. https://www.cdc.gov/healthyYouth/data/yrbs/index.htm

Surveys That Include Information Relevant to Binge Drinking *(continued)*

Select International Surveys†

Survey Name and Frequency	Population Surveyed	Binge Drinking Measure* and Definition of a Drink	Notes
• Australian School Students Alcohol and Drug (ASSAD) survey • Every 3 years since 1984	Students ages 12 to 17 who are in school years 7 to 12 and are from government, Catholic, and independent schools in the state of Western Australia	• Risky drinking is defined as drinking 4+ standard drinks on any 1 day, if alcohol was consumed in the previous week. • A standard drink is defined as any drink containing 10 grams of alcohol.	https://www.mhc.wa.gov.au/reports-and-resources/reports/australian-school-students-national-alcohol-and-drug-survey
• European School Survey Project on Alcohol and Other Drugs (ESPAD) • Every 4 years since 1995	European students ages 15 to 16	• Heavy episodic drinking is defined as drinking 5+ alcoholic beverages on one occasion at least once in the past 30 days. • Nationally relevant examples of a drink are included in the surveys.	The ESPAD survey notes that its measure of heavy episodic drinking corresponds to a cutoff of approximately 9 centiliters of pure alcohol. http://www.espad.org
• Healthy Ireland • 1998, 2002, and 2007	Adults ages 18 and older from private households in the Republic of Ireland	• Binge drinking is defined as 6+ standard drinks on one occasion in the past 12 months. • A standard drink is defined as a half pint or a glass of beer, lager, or cider; a single measure of spirits; a single glass of wine, sherry, or port; or a bottle of alcopop (long neck).	Healthy Ireland is the successor to the Survey of Lifestyle, Attitudes and Nutrition in Ireland. http://www.healthyireland.ie/accessibility/healthy-ireland-survey

†For a list of additional international surveys relevant to binge drinking, see **Gender Differences in Binge Drinking: Prevalence, Predictors, and Consequences** in this issue.

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The Epidemiology of Binge Drinking Among College-Age Individuals in the United States

Heather Krieger, Chelsie M. Young, Amber M. Anthenien, and Clayton Neighbors

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Rates of alcohol consumption continue to be a concern, particularly for individuals who are college age. Drinking patterns have changed over time, with the frequency of binge drinking (consuming four/five or more drinks for women/men) remaining high (30% to 40%). Young adults in the college age range are developmentally and socially at higher risk for drinking at binge levels. Changes in autonomy, parental control, norms, and attitudes affect binge drinking behaviors. This article reviews those changes, as well as the individual and environmental factors that increase or decrease the risk of participating in binge drinking behaviors. Risk factors include risky drinking events (e.g., 21st birthdays), other substance use, and drinking to cope, while protective factors include religious beliefs, low normative perceptions of drinking, and use of protective behavioral strategies. Additionally, this article discusses the physical, social, emotional, and cognitive consequences of consuming alcohol at binge levels. Alcohol policies and prevention and intervention techniques need to incorporate these factors to reduce experiences of alcohol-related problems. Targeting policy changes and prevention and intervention efforts toward young adults may increase effectiveness and prevent both short- and long-term consequences of binge drinking.

Key words: Alcohol consumption; binge drinking; consequences; risk and protective factors; young adults

Binge drinking, particularly among college-age individuals, has been a significant topic of research for more than 20 years because of associations between greater quantity and frequency of alcohol consumption and alcohol-related consequences. To identify factors associated with binge drinking over time, several large-scale studies have assessed trends in binge drinking among young adults. This article aims to summarize those trends and the developmental and social factors that impact the likelihood of, the risk and protective factors related to, and the negative alcohol-related consequences of binge drinking behaviors. Some studies examined young adults who are not in college, but the majority of the literature regarding binge drinking focuses specifically on college students. Further, there is variability in the definition of college students. Some studies sampled only full-time students from four-year institutions, whereas other studies included part-time and community college students.

The term "binge drinking" has a somewhat controversial history. The term was originally defined by Wechsler and colleagues as five or more drinks for men, or four or more drinks for women (5/4+), on a single occasion.[1] Criticisms of this conceptualization of binge drinking were based largely on the substantial variability in blood alcohol concentrations (BACs) due to differences in weight and duration of consumption. When individuals who met these binge drinking criteria had consumed the alcohol over a long period of time, they did not reach BACs higher than .08%.[2,3]

In 2004, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) provided a revised definition of binge drinking, acknowledging that consuming 5/4+ drinks in a 2-hour time period would result in a BAC of at least .08% for most individuals. Although subsequent questions continue to be raised regarding the validity of defining binge drinking at 5+ or 5/4+ on one occasion, these are still the most commonly used definitions in the literature. Research covered in this review includes studies on binge

drinking that use the 5/4+ criteria or a BAC of at least .08%.

Trends in Young Adult Binge Drinking Rates

Binge drinking among young adults has concerned researchers and educators for decades, prompting multiple national initiatives to track patterns in binge drinking. The longest continuous running national survey of drug and alcohol use among adolescents and young adults is the Monitoring the Future (MTF) study, which is funded by the National Institute on Drug Abuse and conducted by the University of Michigan's Institute for Social Research.[4] Approximately 15,000 high school seniors in 133 schools are surveyed each year, and, since 1976, a subset of about 2,400 have been followed biennially by mail. Survey results indicate that the rate of self-reported college student binge drinking in the previous 2 weeks dropped from 1980 (44%) to 1993 (40%) and continued to decrease through 2014 (35%). Estimates for college student engagement in extreme binge drinking, defined as consuming 10 or more drinks on one occasion in the previous 2 weeks, varied from 14% in 2005 to 20% in 2014.

Another national survey assessing college student binge drinking is the Substance Abuse and Mental Health Services Administration's (SAMHSA) National Survey on Drug Use and Health (NSDUH), which includes yearly assessments of 60,000 to 70,000 individuals ages 12 and older. Results indicate that for young adults ages 18 to 25, rates of binge drinking in the previous 30 days decreased slightly from 44.6% in 1988 to 37.7% in 2014.[5]

The Core Alcohol and Drug Survey sampled more than 140,000 students and found a slight decline in the percentage of students who binge drank in the previous 2 weeks, from 45.9% in 2006 to 43.9% in 2013.[6,7] The College Alcohol Survey (CAS) also attempted to assess student drinking rates. At 120 colleges, the CAS measured alcohol use among college students at four time points between 1993 and 2001.[8] The survey included more than 14,000 students and provided the first gender-specific measure of binge drinking (i.e., 5/4+ drinks for males/females). Contrary to findings from the MTF study and the Core Alcohol and Drug Survey, the CAS found little change between 1993 (43.2%) and 2001 (44.5%) in the number of students reporting binge drinking in the previous 2 weeks.[9]

The most recently initiated nationwide survey of college student alcohol use is the National Epidemiologic Survey on Alcohol and Related Conditions. This survey began the first of three waves of data collection in 2001, which included data from approximately 43,000 individuals.[10] Prevalence rates, only reported for 2001, indicate that 57% of 18- to 24-year-olds binge drank in the previous year, and 40% binge drank 12 or more times in the previous year.

College attendance, gender, and ethnic variations in binge drinking have been identified. A number of studies have examined differences in alcohol use between college and same-age noncollege peers, consistently finding higher rates of heavy drinking and alcohol-related problems among college students than among noncollege peers.[11] The annual prevalence of alcohol use reported in the MTF study suggested small differences between male and female drinking rates and modest decreases over time.[4] However, a declining gender gap exists for binge drinking rates, with female binge drinking (i.e., 4+) decreasing from 31% in 1988 to 26% in 2014, and male binge drinking (i.e., 5+) decreasing more substantially, from 52% to 43%.

Currently, the MTF study does not report racial or ethnic differences in binge drinking among college students. However, the U.S. Centers for Disease Control and Prevention reported that more White college students engaged in binge drinking in the previous 30 days (31.6% of females and 49.4% of males) than Hispanic students (22.6% of females and 39.9% of males).[12] Also, African American students (6.1% of males) were less likely to report binge drinking than White students (22.8% of males), although this difference was less pronounced among females.

Rates of binge drinking have also been assessed in military samples. Starting in 1980, the U.S. Department of Defense issued several large-scale, anonymous health surveys (most recently called the Health Related Behaviors Survey) to active-duty military personnel, with the first assessment of binge drinking appearing in 1998. Rates of binge drinking for military personnel overall increased from 35% in 1998 to 47% in 2008.[13] The 2008 survey sampled more than 28,000 service members and found that young adult military personnel (ages 18 to 25) had the highest rates of frequent binge drinking (once a week or more) at 26%.[14] This is significantly higher than the rate for same-age civilians (16%), as reported in the 2007 NSDUH.[15] Rates of binge drinking also differ by military branch.[14]

Developmental and Social Factors

Developmental and social factors are important contributors to binge drinking among college-age adults. The college-age years (approximately ages 18 to 24) correspond with the developmental stage widely referred to as "emerging adulthood."[16,17] Dramatic cultural changes in the United States and other countries with similar socioeconomic structures have occurred over time. Arnett notes that post–high school education rose from 14% in 1940 to more than 60% in the mid-1990s.[16] College attendance has resulted in the delay of traditional adult responsibilities. Consequently, in recent decades this developmental period has become a time when individuals

explore new freedoms and experiment with behaviors that were previously less accessible, including alcohol consumption.[18,19]

In their seminal paper, "Getting Drunk and Growing Up: Trajectories of Frequent Binge Drinking During the Transition to Young Adulthood," Schulenberg and colleagues identified five distinct trajectories of binge drinking that occur in young adults ages 18 to 24.[20] This analysis was one of the first to use a national sample to identify distinct patterns of changes in binge drinking over time. The national sample included four consecutive waves of data from the MTF study. More than 90% of the sample was categorized as engaging in no binge drinking during any wave (35.9%). Or, they were categorized as one of five binge drinking trajectories:

1. Rare (16.7%): binge drinking during at least one wave but no frequent binge drinking, defined as two or more binge episodes in the past 2 weeks.
2. Decreasing (11.7%): frequent binge drinking during Wave 1 and decreasing or no frequent binge drinking by Wave 4.
3. Fling (9.9%): frequent binge drinking during Wave 2 or Wave 3 but no binge drinking in Wave 1 or Wave 4.
4. Increasing (9.5%): no frequent binge drinking during Wave 1 increasing to frequent binge drinking by Wave 4.
5. Chronic (6.7%): frequent binge drinking throughout Waves 1, 2, 3, and 4.

Most young adults reported binge drinking during at least one of the four assessment waves, but less than half of the sample drank at rates that could be considered problematic.[20] Young adults in the Increasing and Chronic categories were identified as having the most difficulty navigating the transition to adulthood. Identified trajectories were associated with stability and changes in alcohol problems, attitudes regarding heavy drinking, and heavy drinking or drug-using peers.

Interrelated factors associated with increased heavy drinking and alcohol-related problems include moving out of the parent home, going to college, and decreased parental involvement, each of which has a unique contribution. Moving out of the parent home contributed to the risk of increased drinking, but additional risk was found for students who lived on campus.[21] White and colleagues found that living in a college environment contributed to increases in heavy drinking more than all the other developmental factors they examined.[22] Further, although peer influences are paramount among college students, one study found that parental involvement played a protective role in reducing the likelihood of problem drinking.[23]

For young adults ages 18 to 24, many of the factors attributed to high rates of binge drinking are social in nature. Perceptions and overestimations of the prevalence and approval of heavy drinking among one's peers have been consistently documented and associated with heavier drinking. Reducing normative misperceptions has been the most consistently supported brief intervention strategy for reducing heavy drinking among young adults. Most studies that successfully used such interventions to reduce perceived norms also demonstrated reductions in drinking.[24-28]

The vast majority of research on the influence of social norms on heavy drinking has been done using college samples. Similar results have been found in the general adult population, with heavy drinkers more likely to view heavy drinking as normative and to overestimate drinking norms.[29] In a large general population study of adults who drank alcohol at least monthly (N = 14,009), age was negatively associated with normative misperceptions of drinking.[30] However, the magnitude of the correlation was only .07, suggesting that age is not a strong predictor of normative perceptions of drinking.

The MTF study collected data (for ages 18 to 30) on perceived close-friend disapproval of respondents' binge drinking once or twice per weekend. Respondents ages 19 to 22 and 23 to 26 reported less disapproval from their friends (54.5% and 52.3%, respectively) relative to respondents ages 18 (65.6%) and ages 27 to 30 (57.1%).[4] Few studies have directly examined perceived norms and their influence on college versus noncollege young adult binge drinking, but the available evidence suggests perceived norms have less influence on noncollege young adults.[31]

Related to social norms, membership in specific groups has been associated with higher rates of binge drinking. Foremost among these are college fraternity or sorority affiliation,[32-34] participation in collegiate athletics,[35,36] and being in the military, especially the U.S. Army or U.S. Marines.[14,37,38]

Risk and Protective Factors

Person-level risk factors. Demographic factors such as age, sex, and race have been linked to binge drinking rates among college students. Individuals who began drinking before age 16 were found to be more likely to binge drink in college.[39] An examination of MTF data found that, among recent cohorts, individuals entering the 18 to 26 age range reported less binge drinking than previous cohorts, and individuals leaving the 18 to 26 age range reported more binge drinking than previous cohorts.[40] Several longitudinal studies found that male college students were more likely than female students to binge drink.[41,42] Also, studies have shown that White college students were more likely to engage in binge drinking than non-White students.[39,43]

Personality traits and individual difference variables have also been identified as risk factors for binge drinking. A longitudinal investigation

using MTF data from 18- to 24-year-olds found that individuals lower in self-efficacy had a greater likelihood of engaging in binge drinking over time.[42] Similarly, another longitudinal study among adults ages 18 to 31 found that, across time points, problem drinkers scored higher on disinhibition.[41]

Binge drinking also has been positively correlated with neuroticism-anxiety and impulsive sensation-seeking. In particular, one study found that women who engaged in binge drinking tended to score higher on neuroticism-anxiety, and men who engaged in binge drinking were more likely to score highly on impulsivity and sensation-seeking.[44] Another study found that binge drinkers tended to be less conscientious and more thrill-seeking than those who did not engage in binge drinking.[45] Also, individuals who scored higher on measures of antisocial personality disorder were more likely to engage in binge drinking.[46]

Other studies report that motivations for drinking and attitudes toward drinking can influence the likelihood of binge drinking. Drinking to cope with negative affect and drinking to fit in with peers have both been associated with binge drinking.[45] Sex-seeking as a motivation for drinking has been associated with binge drinking among college men.[45] Individuals who reported drinking alcohol for the purpose of getting drunk were also more likely to engage in binge drinking.[42] Positive attitudes toward drinking have also been associated with an increased likelihood of binge drinking among college students.[39]

Problem behaviors and other substance use also have been associated with binge drinking. For example, one longitudinal study found that, across ages 18 to 31, heavy drinkers were more likely to exhibit problem behavior.[41] A longitudinal examination of trajectories of binge drinking found that adolescents who reported using drugs and scored low on measures of depression were more likely to engage in binge drinking at an earlier age during young adulthood.[46]

In conclusion, several consistent risk factors for binge drinking have been identified, including early onset of alcohol use, being male, identifying as White, having low self-efficacy, scoring high on disinhibition, scoring high on neuroticism-anxiety (for women), being impulsive and sensation-seeking (especially for men), having higher scores on antisocial personality disorder measures, using alcohol to cope or fit in with others, using alcohol for sex-seeking purposes, drinking to get drunk, exhibiting problem behavior, scoring low on depression, and engaging in other substance use.

Risky contexts and events. Specific events and contexts that promote heavy drinking are additional factors that contribute to high rates of binge drinking. Such events include New Year's Eve, St. Patrick's Day, and Halloween.[47,48] Some high-risk drinking events tend to be more prevalent in young adulthood. For example, homecoming, athletic events, weddings, and graduations are all relatively common events for people in this age range and have been associated with heavy drinking.[49,50] In addition, 21st birthdays,[51] spring break,[48] football tailgating,[52] pregame partying,[53-55] and drinking games[56,57] have all been associated with excessive drinking among college students. For undergraduates, weekends and the beginning of a semester have been associated with higher levels of drinking.[47,49]

Social influences, often from close relationships, can contribute to increased risk of binge drinking among college students. For example, having parents who are alcoholics, having friends who drink, and participating in Greek life have all been associated with a greater likelihood of binge drinking.[46,58-60] Also, peer drinking and use of cigarettes and marijuana have been associated with an increased likelihood of binge drinking.[61]

Person-level protective factors. Several protective factors associated with a lower likelihood of engaging in binge drinking have been identified. Gender is one of these factors. Females tend to drink less than males.[62] Also, females and individuals with higher grade point averages tend to use more protective behavioral strategies, such as alternating drinking alcohol and water.[63] Protective behavioral strategies have been shown to reduce the likelihood of experiencing negative alcohol-related consequences.[62,64]

Protective contexts and events. Certain cultural climates that promote a normative perception of disapproval toward excessive drinking can protect their adherents against binge drinking. For example, parental disapproval of alcohol use protects against binge drinking.[39,61] Many religions disapprove of drinking heavily and promote drinking only in moderation or ban drinking among members altogether. As such, religion can exert a protective influence on college student binge drinking.[61,65] Neighborhood norms against heavy drinking have also been found to protect against binge drinking.[66]

College environments tend to encourage heavy drinking; however, some contextual factors surrounding students can protect against binge drinking and negative alcohol-related consequences. Drinking in college is often a social activity among friends. Close friends who encourage safe drinking can help protect against the negative consequences of excessive drinking.[67] College drinking that occurs in locations that provide food and water or that accompanies a meal has been shown to reduce negative alcohol consequences.[68] Additionally, drinking that occurs in bars is somewhat regulated, because bartenders can stop serving individuals who appear drunk.[69] These specific college drinking contexts allow for use of protective behavioral strategies, such as eating food, drinking water, limiting the number of drinks consumed, and drinking with close friends.[62]

Other factors specific to certain colleges have been associated with lower rates of binge drinking. For instance,

college students who attended schools with higher social capital (defined as the average time students spent volunteering) were less likely to engage in binge drinking.[70] Furthermore, research has suggested that attending commuter schools, all-female colleges, and Protestant religious colleges is associated with lower rates of binge drinking.[39]

Certain social roles and their inherent responsibilities can lead to lower likelihood of binge drinking. For example, studies have found that cohabitation, getting married, and having children all protect against heavy drinking.[71-75]

Alcohol-related laws and policies and their connections to the likelihood of binge drinking have been examined. Plunk, Cavazos-Rehg, Bierut, and Grucza found that more permissive laws regarding the minimum legal drinking age were associated with more binge drinking.[76] Using MTF data collected from 1976 to 2011 from high school seniors who were followed up to age 26, Jager, Keyes, and Schulenberg found that laws dictating the minimum legal drinking age were associated with decreases in binge drinking for 18-year-olds, but those laws were associated with increases in binge drinking rates across all male participants ages 18 to 22.[40] Another study found that lower age requirements for purchasing and consuming alcohol were associated with more hazardous and problematic drinking. These findings have clear implications for alcohol policy.[76]

Another study investigated whether personal endorsement of alcohol policies was associated with college student drinking. The authors found that college students who personally endorsed the alcohol laws and policies were significantly less likely to binge drink.[77] Thus, laws that set a minimum drinking age or a low BAC level for drivers, and personal endorsements of college alcohol policies, can serve as protective contextual factors against college student binge drinking.

Consequences of Binge Drinking

Overall, binge drinking and frequent binge drinking have been consistently, significantly, and positively associated with alcohol-related problems.[78,79] These problems impact multiple aspects of life for young adults and the people around them and include physical, legal, emotional, social, and cognitive consequences, as well as an increased likelihood of having an alcohol use disorder.

Physical and legal outcomes. Binge drinking is associated with significant increased risk for experiencing consequences, including physical harm, legal problems, and failure to meet role obligations (e.g., work responsibilities). Active-duty military personnel who binge drink are about five times as likely to report drinking and driving or riding with someone who has been drinking.[38] College students who binge drank in the previous year were more than twice as likely to be taken advantage of sexually or have unplanned sex, and they were four times as likely to be physically injured.[80] Additionally, individuals who engaged in frequent binge drinking reported experiencing more sick days and having poorer overall physical and mental health than non–binge drinkers.[81] Binge drinkers also reported having greater sleep problems, including having more trouble falling asleep and staying asleep than those who did not binge drink.[82] Binge drinking also increases an individual's likelihood of driving after drinking.[80,83]

Emotional and social outcomes. Binge drinking has been associated with a variety of negative emotional and social outcomes. For example, binge drinkers tended to score higher on measures of depression and anxiety[84-86] and reported lower positive mood than nondrinkers.[86,87] Furthermore, students who binge drank in the previous year were more than twice as likely to report having serious thoughts of suicide.[80] Another study reported that feelings of remorse after drinking were more common following a binge drinking episode than a nonbinge episode.[1] Few longitudinal studies have examined associations between emotions and binge drinking; however, frequent binge drinking in young adulthood has been found to increase risk for depression 5 years later.[88]

Social outcomes related to binge drinking often involve negative interpersonal interactions and failure to meet relational obligations. When compared to infrequent and non–binge drinkers, frequent binge drinkers are twice as likely to experience interpersonal consequences, including arguing with friends,[1] experiencing strain on relationships,[89] and getting into physical fights.[38] Binge drinkers in college were two to three times as likely to miss class and twice as likely to perform poorly or get behind on schoolwork.[1,80] Among active-duty military personnel, frequent binge drinking was associated with failure to be promoted and substandard work performance.[38]

Cognitive outcomes. Binge drinking results in high concentrations of alcohol entering the bloodstream quickly, which can affect cognitive processing. One of the most prevalent cognitive effects of binge drinking is blacking out, a failure to encode memories. Frequent binge drinkers are twice as likely as infrequent binge drinkers to experience blackouts.[1] Several studies reported that the consumption of alcohol at binge levels was associated with poor performance on cognitive tasks, such as recall, spatial recognition, search, and planning tasks.[86,90-92] Also, gender differences in cognitive function have been noted, with women being more susceptible to the negative cognitive effects of binge drinking.[87,93]

Research suggests that binge drinking affects the amygdala and prefrontal cortex, and that repeated binge drinking can damage these brain structures.[94] One study reported that extreme binge drinkers (those who consumed 10 or more drinks per occasion) displayed electroencephalography

(EEG) spectral patterns similar to the patterns displayed in individuals with alcohol use disorder, suggesting that extreme binge drinking can alter the brain negatively and permanently.[95] Examination of the effects of binge drinking on cognitive structures and on performance in young adults continues to expand as more psychological research incorporates cognitive and neurological testing.

Alcohol use and abuse disorders. In addition to the negative consequences of binge drinking, frequent binge drinking is associated with increased likelihood of consuming alcohol at twice (8+/10+ drinks for women/men) or even three (12+/15+ drinks for women/men) times binge drinking levels.[96] These high-intensity levels of drinking likely intensify the risk of experiencing negative alcohol-related consequences.

Young adults who binge drink have alcohol use disorder scores that are double the scores of those who do not meet binge drinking criteria.[97] Also, binge drinkers report consuming twice the alcohol per week and spending a third more time drinking than non–binge drinkers.[97] Both occasional and frequent binge drinking are associated with a significantly greater risk of abusing alcohol and becoming dependent than non–binge drinkers or abstainers.[80,85,98] Rates of alcohol abuse and dependence in college student binge drinkers have been reported to be between 14% and 24%.[99] Furthermore, alcohol withdrawal symptoms have been reported by 15% to 29% of students.[99]

Conclusion

Research on binge drinking in college-age samples suggests that binge drinking rates have decreased over time. Despite this trend, rates still remain high, with 30% to 40% of young adults reporting binge drinking at least once in the previous month. Developmentally and socially, this age range is at higher risk for consuming alcohol at binge levels. This review summarized individual and environmental factors associated with increased or decreased risk for binge drinking. Understanding these factors is important in guiding future prevention and intervention efforts and in shaping alcohol policies. Targeting prevention and intervention efforts toward young adults during their college years may increase the effectiveness of those efforts, reducing the negative consequences of alcohol use and averting problematic trajectories.

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"Maturing Out" of Binge and Problem Drinking

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This article reviews literature aiming to explain the widespread reductions in binge and problem drinking that begin around the transition to young adulthood (i.e., "maturing out"). Whereas most existing literature on maturing out emphasizes contextual effects of transitions into adult roles and responsibilities, this article also reviews recent work demonstrating further effects of young adult personality maturation. As possible mechanisms of naturally occurring desistance, these processes could inform both public health and clinical interventions aimed at spurring similar types of drinking-related behavior change. This article also draws attention to evidence that the normative trend of age-related reductions in problem drinking extends well beyond young adulthood. Specific factors that may be particularly relevant to problem drinking desistance in these later periods are considered within a broader life span developmental framework.

Binge drinking is strikingly prevalent in the United States. An estimated 66.7 million (24.9%) of Americans age 12 or older report binge drinking in the past month, according to the National Survey on Drug Use and Health (NSDUH).[1] This estimate is based on a binge drinking definition of 4 or more drinks on the same occasion for women, and 5 or more drinks on the same occasion for men, on at least 1 day in the past 30 days (see **Drinking Patterns and Their Definitions** in this issue for a review of binge drinking definitions). In addition to high binge drinking rates, alcohol use disorder (AUD) is among the most prevalent mental health disorders in the United States. An estimated 15.7 million (5.9%) of Americans age 12 or older have a past-year AUD diagnosis.[1] These rates are a public health concern, as problem drinking in the United States costs an estimated $249 billion per year[2] and is the fourth-leading cause of preventable mortality.[3]

Perhaps the most striking demographic feature of problem drinking (and various other risky or deviant behaviors) is its nonlinear association with age, characterized by increases during adolescence, peaks around ages 18 to 22, and reductions beginning in the mid-20s.[4] However, studies showing age differences in drinking-related rates for epidemiologic purposes tend to contrast relatively broad age groups, and a finer-grained depiction is informative from a developmental standpoint. Figure 1 shows the results of the authors' descriptive analyses of age-prevalence gradients for different drinking-related outcomes (and other drug-related outcomes included for contrast).

As shown in Figure 1, prevalence rates for a variety of drinking-related outcomes peak in the early 20s. Specifically, in the early 20s, past-year binge drinking and intoxication rates both reach peaks of around 45%, and past-year AUD rates reach a peak of 19%. Although not depicted, similar drinking-related peaks are observed for college students and their noncollege peers, suggesting the peaks are at least partially driven by more general mechanisms beyond college attendance.[5] Regarding historic trends,

drinking-related declines have been observed across adolescent cohorts in recent years. For instance, 12th-grade rates of past 2-week binge drinking decreased from a peak of 32% in 1998 to an historic low of 17% in 2015.[6] However, college students and young adults have had far more modest cohort declines in binge drinking (i.e., from a 39% peak in 2008 to 32% in 2015 for college students, and from a 41% peak in 1997 to 32% in 2015).[6] Similar conclusions regarding historic changes across adolescent and young adult cohorts can be drawn from NSDUH data on AUD.[1]

Figure 1 also shows that, following peak prevalences in the early 20s, reliable age-related reductions in a variety of drinking-related outcomes occur beginning in the mid-20s and continue throughout the remainder of the life span. For instance, after the peak binge drinking rate of 45% in the early 20s, the rate declines to 38% by the late 20s, 29% by the late 30s, 22% by the late 40s, and 14% by the late 50s. For AUD, reductions appear especially dramatic in young adulthood. Specifically, after peaking at 19% in the early 20s, the rate decreases rapidly to 13% by the late 20s, then more gradually to 10% by the late 30s, 8% by the late 40s, and 3% by the late 50s. Of course, such cross-sectional age differences must be interpreted with caution, as differential mortality of problem drinkers and secular changes in prevalence rates could artifactually create the appearance of a developmental age gradient. However, it is unlikely that such factors could plausibly explain the magnitude of the rate changes with age, given the somewhat limited extent of overall mortality and secular variation. Further, researchers have also observed the age-prevalence curve in a number of longitudinal studies assessing how prevalence rates change as a cohort ages.[7]

This robust age-prevalence curve motivates and informs the conceptualization of problem drinking from a developmental psychopathology standpoint.[8,9] Other articles in this

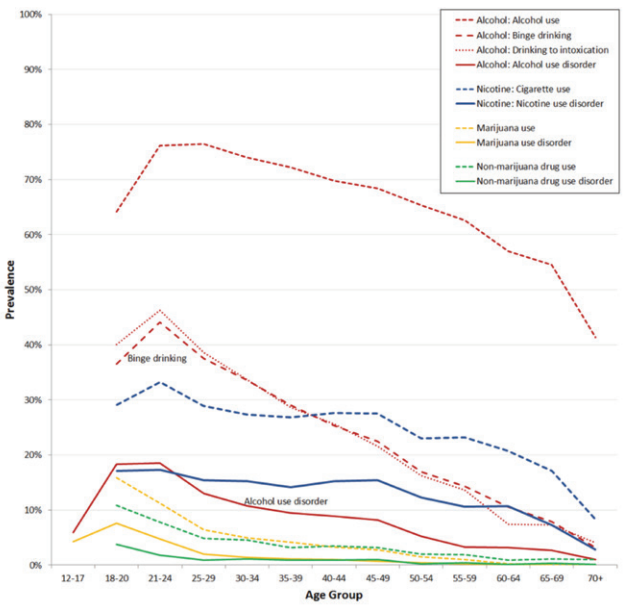

Figure 1 Age-prevalence gradients showing U.S. past-year rates of alcohol-related indices and other drug-related indices across age groups. Prevalence rates for a variety of drinking-related outcomes peak in the early 20s. Following this peak, reliable age-related reductions in a variety of drinking-related outcomes occur beginning in the mid-20s and continue throughout the remainder of the life span. *Note:* Binge drinking was defined as four or more drinks on one occasion for females and five or more drinks on one occasion for males. Disorder rates reflect *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) criteria for abuse or dependence except for nicotine disorder, which reflects DSM-IV criteria for nicotine dependence. *Source:* Prevalence rates for ages 12 to 17 are based on NSDUH 2002 data from Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. *Key Substance Use and Mental Health Indicators in the United States: Results From the 2015 National Survey on Drug Use and Health.* Rockville, MD: U.S. Department of Health and Human Services; September 2016. Prevalence rates for ages 18 to 70+ are based on National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) 2001 to 2002 data from Grant BF, Moore TC, Shepard J, et al. *Source and Accuracy Statement: Wave 1 National Epidemiologic Survey on Alcohol and Related Conditions.* Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism, U.S. Department of Health and Human Services; 2003.

special issue describe factors contributing to the escalation and eventual peak of problem drinking leading up to the early 20s. This article focuses on factors contributing to the later trends toward problem-drinking reductions beginning around young adulthood.

Maturing Out of Problem Drinking

The dramatic age-related reductions in problem drinking that begin in young adulthood have motivated empirical efforts to understand desistance from a developmental perspective. Despite the overall trend toward maturing out after young adulthood, a substantial subset of individuals show persistent or escalating problem drinking beyond this developmental period.[10] Knowledge of what differentiates developmentally limited versus persistent patterns of problem drinking can help clarify the nature of problem drinking and inform public health and clinical interventions.[11] Indeed, in addition to the above evidence that maturing out can include desistance of syndromal AUD, research also suggests that problem-drinking reductions during young adulthood are particularly likely to occur among those who were relatively severe problem drinkers prior to this developmental period.[12,13] These findings support the importance of research aimed at understanding maturing out as a means of guiding future interventions.

The following sections review evidence for different possible mechanisms of maturing out, beginning with effects of adult role transitions (e.g., marriage and parenthood) and personality maturation (e.g., decreased impulsivity and neuroticism) during young adulthood. Further sections then discuss the need for more life span developmental research to explain the later drinking reductions observed in developmental periods beyond young adulthood, noting some mechanisms that may be particularly relevant to desistance in these periods (i.e., "natural recovery" processes and health issues). A key point pertaining to all mechanisms reviewed here is that more research is needed on possible historic changes in how these mechanisms have operated. Preliminary descriptive evidence suggests historic differences across cohorts in the age-related trend of escalation followed by maturing out.[5(pp221-222)] Key public policy insights could be gleaned from in-depth analyses of such cohort changes in age trends and how they may relate to cohort changes in desistance mechanisms (e.g., the prevalence, life-course timing, and impact of adult role transitions). It is also noteworthy that evidence exists for gender, racial, and ethnic differences in both patterns and mechanisms of age-related drinking reductions.[4,7,14] Although discussion of such differences is largely beyond the scope of the current brief review, this should be noted as another important topic in need of further exploration in future research.

Young Adult Role Transitions and Maturing Out

The most commonly offered explanation for maturing out of problem drinking during young adulthood is that it is driven by transitions into adult roles like marriage, parenthood, and full-time employment.[15] Young adulthood is marked by widespread adoption of such roles,[15] and well-established developmental theory views these transitions as key young adult developmental tasks.[16] Role incompatibility theory is often referenced to explain how these roles influence maturing out.[17] The theory holds that, when a state of conflict (i.e., incompatibility) exists between a behavior (e.g., drinking) and demands of a social role, this can initiate a process called role socialization, whereby conflict is resolved through changes in the behavior. However, the theory also posits role selection effects in the opposite direction, whereby individual characteristics and behaviors can influence the likelihood of later role adoption. These are two very different processes through which roles and drinking behaviors can become associated, so research investigating possible role socialization effects must consider role selection as an alternative explanation.

Evidence for Role Socialization

With few exceptions,[18-20] both marriage and parenthood during young adulthood are generally predictive of later problem-drinking reductions. Further, although many studies have tested only effects of either marriage or parenthood in isolation,[21-28] there is also research demonstrating that both marriage and parenthood can contribute uniquely to these reductions.[15,29,30] In contrast, research has often failed to show that employment contributes to reduced problem drinking in young adulthood,[15,24,27] although some evidence for this effect has been found within certain occupational categories (e.g., "professional" jobs).[30]

Evidence for Role Selection

Most studies have failed to show that alcohol use reduces the likelihood of young adult marriage, parenthood, or employment,[21,27] with some findings even suggesting the opposite effect.[15] However, results appear more mixed for more severe indices of problem drinking and for illicit substance use. For example, research has shown that AUD can prevent marriage and parenthood,[31,32] and that illicit substance use can prevent marriage and employment.[15,33-35]

Practical Implications of Role Effects on Maturing Out

In addition to evidence that family roles can spur desistance from AUD,[24,36] there is even evidence that these roles may have especially dramatic effects among those who were particularly severe problem drinkers prior to role adoption.[37] These findings support the clinical significance, not only of maturing out in general, but of role-driven pathways to maturing out in particular. Further, beyond family role effects on drinking-related maturing out, there is mounting evidence from diverse literatures that family roles convey various protective effects that can cascade across many domains of life to broadly spur adaptation and mitigate pathology.[38-41]

However, given the potential importance of these processes from a public health standpoint, it is surprising how little is known about the mechanisms through which roles influence substance-related maturing out. Existing mediational findings show the most robust support for mediation of role effects via reduced socializing with peers, with additional mixed evidence for mediation via changes in drinking-related attitudes and increased religiosity.[27,28,30,42] Mediation via peer involvement is particularly consistent with the popular role incompatibility explanation of family role effects on maturing out (described above), as role demands may restrict socializing opportunities. However, as articulated in Platt's commentary on how to achieve "strong inference," future studies should conduct "riskier" tests of role incompatibility theory.[43] This means testing hypotheses that could potentially provide discriminating support for role incompatibility theory over other plausible explanations, and testing hypotheses that could potentially disconfirm the theory in favor of other explanations. For instance, an explicit assessment of conflict between drinking and role demands (role incompatibility) could provide discriminating support for role incompatibility theory,[37] and this should be tested against other plausible mechanisms, such as the interpersonal support, security, and satisfaction that family roles can provide.[44]

Young Adult Personality Development and Maturing Out

A vast, long-standing literature links personality and drinking, although variability in personality models, definitions, and terminology can sometimes complicate interpretation of this work.[45] For instance, "Big Three" models of the traits that compose personality typically include constraint (related to impulsivity and risk taking), neuroticism (e.g., anxiety, depression, and stress reactivity), and extraversion (e.g., sociability),[46] whereas "Big Five" models typically include neuroticism, extraversion, conscientiousness, agreeableness, and openness (or intellect).[47,48] Within Big Five models, distinct components of impulsivity and constraint (e.g., lack of perseverance and negative affect urgency) are represented as smaller facets of the larger broadband traits (e.g., conscientiousness and neuroticism).[49] It is beyond this brief review's scope to broadly review the many ways these and other models of personality have been linked to drinking, but see Sher and colleagues for an in-depth review of personality and alcohol research.[45]

This review focuses on one particularly relevant burgeoning area of personality research that has emphasized movement beyond a static view of personality, acknowledging that normative changes in personality occur throughout the life span. Importantly, findings include evidence for adaptive (i.e., presumably beneficial) changes in personality traits that have been linked closely to heavy and problematic drinking, including impulsivity, conscientiousness, and neuroticism. Further, maturational changes in these traits appear particularly rapid during the transition to young adulthood (i.e., the 20s and 30s), the period when normative age-related declines in drinking generally begin. For instance, Figure 2 depicts meta-analytic evidence for age-related increases throughout the adult life span in both emotional stability (akin to lack of neuroticism) and conscientiousness.[39,50,51]

Correlated Change in Personality and Problem Drinking

Perhaps motivated by the above evidence for personality maturation, a subsequent series of studies has shown that the normative age-related drinking reductions of young adulthood may be partially explained by age-related personality change.[52,53] Longitudinal growth models showed a reduction in average levels of problem drinking from ages 18 to 35, along with corresponding reductions in impulsivity and neuroticism and increases in conscientiousness. Further, parallel-process growth models showed correlated change such that those with greater age-related maturation in these three personality domains also had greater age-related reductions in problem drinking. A follow-up study using the same data also showed that age-related changes in drinking motives mediated effects of age-related personality change on age-related problem-drinking reductions.[54] Specifically, reductions in neuroticism and impulsivity predicted reductions in coping-related drinking motives, which in turn predicted reductions in problem drinking. These are the only studies, to our knowledge, analyzing correlated change in personality and drinking as an explanation for the normative drinking reductions observed around the developmental transition to young adulthood (i.e., maturing out), although other studies have shown similar correlated change in earlier developmental periods of normative drinking-related escalation (i.e., adolescence to the early 20s).[55]

Directional Effects of Personality on Drinking Over the Course of Young Adulthood

The above studies of correlated change between personality and problem drinking have forged an entirely new avenue for research on drinking-related maturing out, with one important next step being investigation of different possible directions of effects. Toward this objective, Lee and colleagues estimated cross-lag models testing bidirectional effects between personality and problem drinking across four waves spanning ages 21 to 34.[56] Results showed some prospective effects of personality on problem drinking, with lower impulsivity and higher conscientiousness at age 29 both predicting lower problem drinking at age 34 (see Figure 3). In contrast,

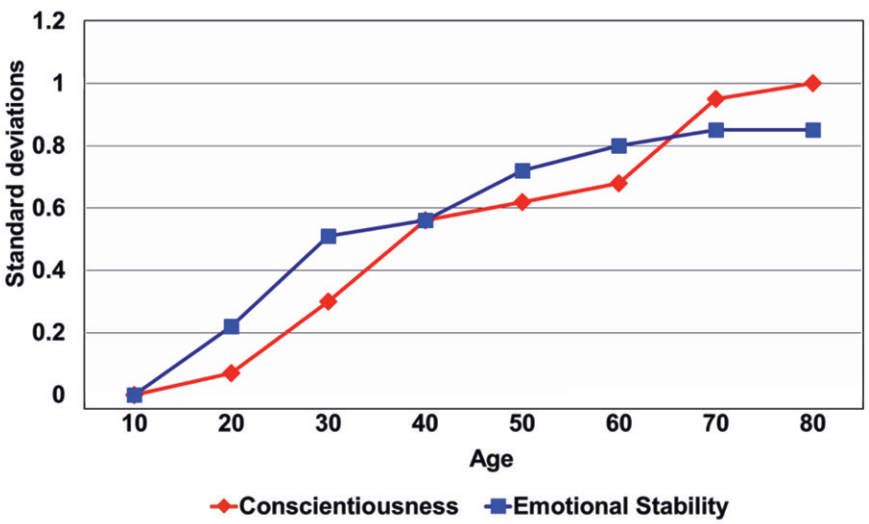

Figure 2 Developmental personality maturation across the life span. Results from a meta-analysis, demonstrating age-related increases throughout the adult life span in both emotional stability and conscientiousness. *Source:* Adapted from Roberts BW, Walton KE, Viechtbauer W. Patterns of mean-level change in personality traits across the life course: A meta-analysis of longitudinal studies. *Psychol Bull.* 2006;132(1):1-25.

results did not show prospective effects of neuroticism on subsequent problem drinking (nor prospective effects in the opposite direction).

Integrating Adult Role and Personality Effects on Maturing Out

Beyond the largely separate bodies of evidence for family role and personality maturation effects on young adult drinking reductions, little work exists advancing an integrated model of these ameliorative processes. Differing views conceptualize personality maturation as unfolding either (1) due to biologically programmed maturation or (2) as an adaptive response to age-increasing contextual demands (e.g., from family roles).[39] These alternative views imply different predictions regarding possible mediated pathways involving role and personality effects on problem-drinking reductions. To investigate these possibilities, the cross-lag models of Lee and colleagues (discussed above) also included transitions into family roles (marriage or parenthood).[56] Results showed that family role transitions mediated personality effects, with higher conscientiousness and lower impulsivity at age 21 predicting transitions into a family role by age 25, which in turn predicted lower problem drinking at age 29 (see Figure 3). In contrast, personality was not found to mediate role effects, as role transitions consistently failed to predict later personality.

Practical Implications of Personality Development Effects on Maturing Out

The notion of interventions targeting personality change has received increased attention in recent literature.[57] The above-discussed research on personality and maturing out has especially highlighted the potential utility of reducing impulsivity and increasing conscientiousness.

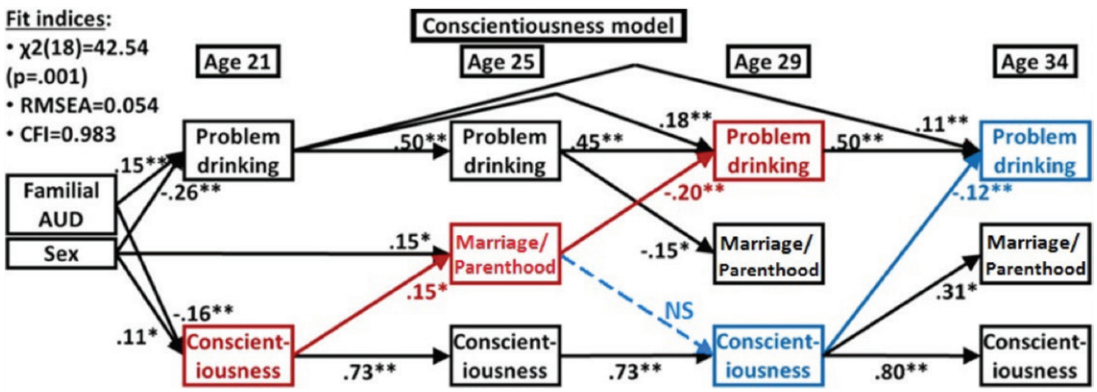

Figure 3 An integrative model of family role and personality effects on young adult maturing out of problem drinking, showing results of a cross-lagged panel model of marriage and parenthood, conscientiousness, and problem drinking across four longitudinal time points. Results of cross-lag models showed some prospective effects of personality on problem drinking, with higher conscientiousness at age 29 predicting lower problem drinking at age 34. Family role transitions mediated personality effects, with higher conscientiousness at age 21 predicting transitions into a family role by age 25, which in turn predicted lower problem drinking at age 29. *Note:* Colors highlight parts of the model testing hypothesized mediation paths. Red variables and paths highlight results confirming the hypothesized mediation of conscientiousness effects on problem drinking via marriage and parenthood. Blue variables and paths highlight results failing to confirm the hypothesized mediation of marriage and parenthood effects on problem drinking via conscientiousness. For marriage/parenthood: 0 = remained never married and a nonparent, 1 = became married or a parent. For family AUD: 0 = family history negative, 1 = family history positive. For sex: 0 = male, 1 = female. *p < .05. **p < .01. *Source:* Adapted from Lee MR, Ellingson JM, Sher KJ. Integrating social-contextual and intrapersonal mechanisms of "maturing out": Joint influences of familial-role transitions and personality maturation on problem-drinking reductions. *Alcohol Clin Exp Res.* 2015;39(9):1775-1787.

Littlefield and colleagues speculated that interventions fostering maturity in these domains might spur relatively durable changes in drinking behaviors.[52] Lee and colleagues noted, based on the above mediation findings, that pre–young adult personality interventions could convey protective effects, in part by aiding successful transitions to family roles in young adulthood.[56] Based on evidence for persistent effects of childhood impulsivity even on midlife outcomes, Moffitt and colleagues argued that universal prevention programs fostering childhood self-control could confer substantial and lasting benefits to most individuals and to an entire population.[58] Indeed, early prevention and intervention programs fostering personality-related maturity could influence many etiologic pathways, thereby conveying protective effects that cascade across multiple developmental stages and domains of life.

However, to bolster confidence in the above implications, additional research is needed to confirm and further characterize the phenomenon of personality maturation and its effects on age-related drinking reductions. Caution is perhaps warranted regarding the use of survey measures to show personality change, as measurement invariance across ages can spuriously influence apparent age-related changes.[59] However, given the magnitude of personality change observed across the life span,[39(p15)] and its associations with changes in various life circumstances,[50] it is unlikely that this phenomenon is largely attributable to a measurement artifact. Nonetheless, confidence could be bolstered by showing this phenomenon with alternative methods. For instance, given the existence of various task-based measures of impulsivity/disinhibition,[60] a key objective should be to confirm age-related changes in these measures and their associations with age-related drinking reductions. Such research could confirm conclusions from survey findings and further inform the practical application of this work.

Further, although clear links have been established among personality maturation, adult role adoption, and drinking reductions, more work is needed to establish directionality of effects within analyses that unambiguously capture developmental change in these constructs. For instance, the cross-lagged panel study by Lee and colleagues[56] addressed the unknown directionality in the growth-modeling studies of Littlefield and colleagues,[52-54] but personality effects in the analyses by Lee and colleagues did not isolate influences of age-related change in personality traits. Thus, creative analytic applications are needed to combine the separate strengths of past research. This work also may require careful conceptualization of the predicted timings and durations of the developmental processes under investigation.

Maturing Out of Problem Drinking Beyond Young Adulthood

As discussed above, age-related drinking reductions are not confined to young adulthood, but instead begin in young adulthood and continue throughout the remaining life span. Beyond the earlier-reviewed epidemiologic evidence, some additional research offers a more precise account of changes in problem drinking across the adult life span. Vergés and colleagues assessed changes across the life span in rates of persistence, new onset, and recurrence of alcohol dependence to understand their unique contributions to overall age-related reductions in alcohol dependence rates.[20] Results showed especially marked age reductions in new onsets (see Figure 4, middle panel). Thus, although the term "maturing out" may be taken to imply age increases in desistance, the continual declines in AUD rates observed throughout the life span instead appear mainly attributable to reductions in new onsets. In contrast, although not emphasized by Vergés and colleagues, rates of desistance appeared to peak in young adulthood. Based on persistence rates in their study, it can be inferred that the rate of desistance peaked at 72% by ages 28 to 32, then declined to a low of 55% by ages 43 to 52 and remained somewhat low thereafter (see Figure 4, upper panel). Thus, an interesting possibility is that risk for AUD onset may continually decline throughout the life span, whereas potential for desistance from an existing AUD may peak in young adulthood. Perhaps confirming and extending the latter notion, ongoing data analyses by the authors[62] have investigated desistance across the life span while differentiating among mild, moderate, and severe AUD (per the *Diagnostic and Statistical Manual of Mental Disorders* [DSM-5] severity grading).[63] Results showed that for those with a severe AUD, desistance rates were substantially higher in young adulthood than in later developmental periods (e.g., severe AUD desistance rates of 46% to 49% at ages 25 to 34 versus 25% to 29% at ages 35 to 55). Of course, given that both above studies used data from

the U.S. National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), these analyses should be replicated in other data sets.

The above evidence for differences across the life span in patterns of desistance suggests there may also be important differences across the life span in mechanisms of desistance. Assessing this possibility should be a key goal of future research, as researchers have clearly gleaned insights through similar attention to developmental variability in etiologic processes of earlier developmental periods (i.e., childhood and adolescence).[64] The following sections consider some specific ways that the mechanisms influencing problem drinking desistance may vary across periods of the adult life span.

Maturing Out Versus Natural Recovery Models of Desistance

Predictions regarding developmental variability in desistance mechanisms can perhaps be made based on Watson and Sher's review highlighting dramatic differences in how desistance is viewed between the "maturing out" and "natural recovery" literatures.[65] As discussed earlier, the maturing out literature focuses on young adulthood and has largely viewed desistance as stemming from contextual changes in this developmental period (e.g., marriage)[15] and accompanying role demands that conflict with alcohol involvement.[17] Importantly, these processes are rarely conceptualized as involving acknowledgment or concern regarding one's drinking.[4,65] A starkly different view of desistance comes from the natural recovery literature, which has investigated

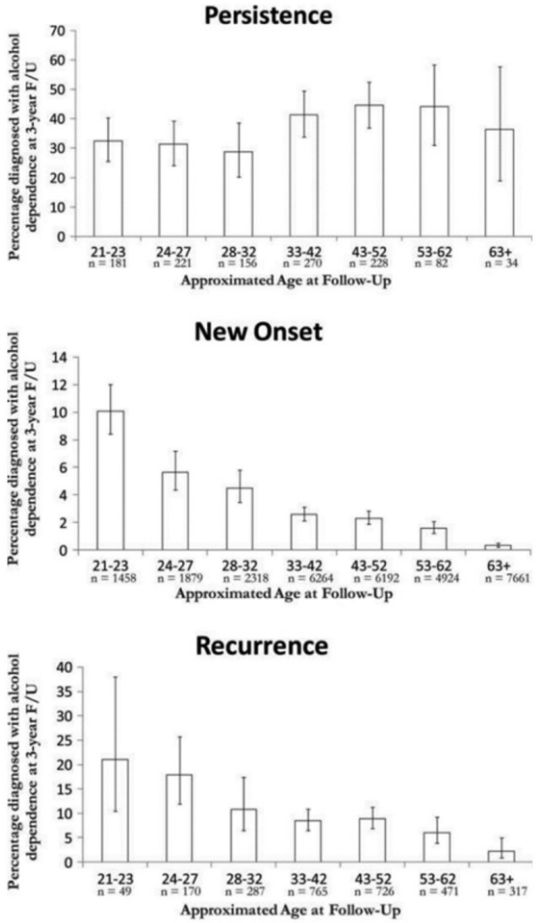

Figure 4 Deconstructing the overall pattern of age differences in alcohol dependence rates, showing separate plots of age differences in persistence (upper panel), onset (middle panel), and recurrence (lower panel) of alcohol dependence, using NESARC data.[61] Brackets show 95% confidence intervals around estimates. *Note:* Persistence rate was defined as the percentage of participants with a past-year alcohol dependence diagnosis at baseline who also had a past-year alcohol dependence diagnosis at the 3-year follow-up. New onset rate was defined as the percentage of participants with no lifetime history of alcohol dependence at baseline who had a diagnosis of past-year alcohol dependence at the 3-year follow-up. Recurrence rate was defined as the percentage of participants with lifetime but no past-year alcohol dependence at baseline who had a diagnosis of past-year alcohol dependence by the 3-year follow-up. *Source:* Adapted from Vergés A, Jackson KM, Bucholz KK, et al. Deconstructing the age-prevalence curve of alcohol dependence: Why "maturing out" is only a small piece of the puzzle. *J Abnorm Psychol.* 2012;121(2):511-523.

precursors of desistance mostly in midlife samples (e.g., mean age = 41 years [*SD* = 9.1] in a review by Sobell and colleagues).[66] Informed in part by models of behavior change (e.g., Stall and Biernacki's stages of spontaneous remission),[67] this literature often views desistance as stemming from an accumulation of drinking consequences that can prompt (1) deliberate reappraisals of one's drinking, followed by (2) self-identification as a problem drinker (i.e., problem recognition), and then (3) targeted efforts to change drinking habits.[68]

Predictions can perhaps stem from an overarching premise that the maturing out and natural recovery literatures may both offer valid conceptualizations of desistance, with maturing out models applying predominantly to young adulthood and natural recovery models applying predominantly to midlife and later developmental periods. That is, desistance in young adulthood may more often stem from the broad cascade of maturational contextual changes that occurs in this period, whereas desistance in later periods may more often stem from more direct processes of deliberate problem recognition and change efforts.

These predictions are consistent with the general idea that contextual effects are stronger earlier in development, whereas intrapersonal effects increase with age[69] as individuals increasingly construct their own environments.[70] It is also noteworthy that there is conceptual similarity between the deliberate reappraisal of one's drinking described in the natural recovery literature and the drinking attitude change believed to mediate personality maturation effects on drinking-related desistance, suggesting a possible point of overlap between natural recovery and personality maturation research. Thus, personality maturation in young adulthood (e.g., conscientiousness increases) may distally potentiate later natural recovery processes of problem recognition and effortful change. Although quite speculative, if the above predictions are supported, this would help bridge divides among different highly influential, yet ostensibly discrepant, views of desistance. More generally, investigating these predictions could help advance the field toward a more unified understanding of desistance across the life span and thereby inform developmental tailoring of public health and clinical interventions.

Older Adult Health and Problem Drinking Desistance

Although health and drinking are, of course, interrelated throughout the life span,[71,72] older adulthood brings various health-related physical and cognitive challenges that may increase in importance as desistance mechanisms in this late developmental stage.[73] There is evidence that more than 50% of U.S. seniors drink at levels deemed risky in the context of co-occurring medical conditions.[74] Further, along with these health issues comes increased use of medications that could interact harmfully with alcohol, with a striking 76% of U.S. seniors using multiple prescription medications.[75] Of the small extant literature on older adult drinking, health issues are among the most commonly reported reasons for desistance.[76] However, studies of prospective effects of health problems on drinking changes are more equivocal,[76,77] perhaps owing to the complex relevance of affect- and coping-related issues to older adult drinking.[78] For instance, there is evidence that health problems can spur drinking reductions except among those who drink to cope, for whom health problems can have the opposite effect.[77,79]

Future studies should expand upon the relative dearth of research in this area. This work should include further study of how affect- and coping-related factors may impede adaptive responding to drinking-related health issues. Attention should also be paid to how these processes are influenced by aging-related increases in alcohol sensitivity[80,81] and changes in social support systems.[73] These questions are particularly important given the increases in older adult problem drinking that are projected to coincide with the aging of the "baby boomer" generation.[82] Indeed, these projections suggest a great future need for research informing policy and clinical interventions for older adult problem drinkers.

Summary of Key Points

Although a distinct peak in problem drinking rates is observed in the early 20s, the reductions that follow (i.e., maturing out) are not confined to the subsequent period of young adulthood. Problem-drinking reductions continue throughout all remaining stages of the adult life span.

In addition to robust evidence that young adult desistance is spurred by transitions into family roles, more recent work shows additional likely influences of developmental personality maturation. Research is needed to further clarify

these ameliorative influences, the mechanisms through which they operate, and how they are interrelated. Such work may yield key practical insights that could inform the design of clinical and public health interventions.

In contrast with developmental models of maturing out, other influential views of desistance (i.e., natural recovery models) place more emphasis on processes of problem recognition and effortful change. A life span developmental perspective on desistance may hold promise for reconciling these ostensibly discrepant models.

More research is needed on health-related mechanisms of problem drinking desistance among older adults.

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NIAAA's College Alcohol Intervention Matrix

CollegeAIM

Jessica M. Cronce, Traci L. Toomey, Kathleen Lenk, Toben F. Nelson, Jason R. Kilmer, and Mary E. Larimer

The College Alcohol Intervention Matrix (CollegeAIM) is a user-friendly, interactive decision tool based on a synthesis of the substantial and growing literature on campus alcohol use prevention. It includes strategies targeted at both the individual and environmental levels. Commissioned by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), CollegeAIM reflects the collective knowledge of 16 separate experts in the field, which makes it unique relative to other summaries of the science. CollegeAIM is designed to help college stakeholders compare and contrast different evidence-based prevention strategies to select a mix of individual and environmental strategies that will work best on and around their campuses. CollegeAIM is a living document, which will be updated to keep pace with the science. Colleges are therefore encouraged to ensure that evaluations of individual- or environmental-focused strategies on their campuses or in their communities make it into the published literature.

Key words: CollegeAIM; college drinking; literature review; prevention; research; underage drinking

Most students (81.4%) have consumed alcohol on at least one occasion by the time they reach college or at some point during their college career.[1] Many college students (63.2%) report alcohol consumption within the past 30 days, with 38.4% reporting "being drunk" at least once during that same time frame.[1] Rates of heavy episodic drinking (i.e., binge drinking), defined in this sample as consuming five or more drinks in a row on at least one occasion in the past 2 weeks for both men and women, roughly mirror the reported rates of being drunk (31.9%).[1]

Of course, students who engage in binge drinking may do so more than once during a 2-week period. In fact, Wechsler and colleagues found that, of the 43% of students who said they engaged in binge drinking (defined in this study as four or more drinks in a row for women or five or more drinks in a row for men during the past 2 weeks), nearly half reported three or more such occasions (44%, or 19% of the total sample).[2] In this study, frequent binge drinking was associated with a host of negative health and social consequences and other risk behaviors, including missing class (53.8%), driving after drinking (40.6%), or engaging in unplanned (49.7%) or unprotected (52.3%) sex (percentages represent the proportion of individuals engaging in frequent binge drinking that endorsed experiencing each consequence). These behaviors have long-term consequences that students can readily identify, including academic failure, injury, legal complications, sexually transmitted disease, and death. Binge drinking also has lasting effects on the brain that produce less recognizable consequences, such as impaired working memory and other changes in mental processes that may be less apparent to the individual engaging in binge drinking or others as long as the person is generally functional, but which nonetheless may derail or impair optimal development.[3] The prevalence of binge drinking, paired with the significant potential for both short-term and lasting harm, is why prevention is paramount in this population.

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) is at the forefront of efforts to prevent underage and harmful alcohol use among college students. NIAAA funds research to develop and evaluate prevention strategies

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and creates dissemination tools to put evidence-based prevention approaches into the hands of college stakeholders.

In 2002, NIAAA's Task Force on College Drinking released a report, *A Call to Action: Changing the Culture of Drinking at U.S. Colleges*, outlining the state of alcohol misuse and prevention science in this area.[4] The report included specific recommendations to help colleges and universities determine which strategies were most likely to produce meaningful changes in alcohol use and consequences on their campuses. The Task Force categorized strategies into one of four tiers, based on evidence of their effectiveness and the nature of the evidence available. The strategies that met criteria for inclusion in Tier 1 had evidence of effectiveness among college students and were individual-focused strategies shown to reduce high-risk drinking behavior and/or negative drinking-related consequences. The strategies that met criteria for inclusion in Tier 2 had evidence of success with general populations and could be applied to college environments, but had not been specifically tested with college students. The multiple strategies assigned to Tier 2 were all environmental in nature, targeting the student body as a whole. Tier 3 strategies were defined as, and comprised, strategies that had logical and theoretical promise but had not been fully evaluated. Tier 4 comprised strategies where there was evidence of ineffectiveness.

In 2004, NIAAA mailed the 2002 report to the president of every college and university in the United States and made it available at no cost to anyone who requested a print copy. The report also was made available online on a dedicated website, www.collegedrinkingprevention.gov, along with a host of resources and supporting documentation.

In 2008, Nelson and colleagues assessed the influence of these dissemination efforts and found that 23% of colleges were not employing any recommended Tier 1 or Tier 2 strategies, and 45% were only employing a single recommended strategy.[5] Two-thirds of institutions surveyed offered a Tier 1 strategy (67%), but most did not report implementing any recommended Tier 2 strategies. This suggests a trade-off between individual and environmental approaches. One possible reason for this is that environmental approaches often are not self-contained within the campus and rely on building partnerships with local law enforcement, businesses within the community, community members, and lawmakers. It also is possible that the tier system created a false hierarchy, making individual strategies assigned to Tier 1 appear more effective than environmental strategies assigned to Tier 2, simply because the latter had not been tested specifically within college populations. This, of course, was not the intent of the tier system, as stated in a report on college drinking research: "Central to the Task Force findings was the recognition that successful interventions occur at three distinct levels . . . [that] must operate simultaneously to reach individual students, the student body as a whole, and the greater college community."[6] Thus, dissemination efforts need to adopt organizational structures that make readily apparent the importance of employing both individual and environmental strategies as part of an overall prevention approach.

CollegeAIM

In the 10 years following the 2002 publication of *A Call to Action*, there was an explosion of research on college alcohol use prevention. There were more than 151 studies published just on individual-focused approaches between 2002 and 2012, compared with only 45 in all the years before 2002.[7-10] This exponential increase in the available science prompted a re-evaluation of the Task Force recommendations: What did the science say about the effectiveness of the recommended strategies now? What new strategies had been shown to be effective and should be added to the list? Was the information provided as part of the original recommendations sufficient for colleges to effectively weigh their options, thus adequately supporting adoption and implementation of evidence-based approaches?

NIAAA had these questions in mind when it commissioned and oversaw creation of CollegeAIM, tapping the expertise of two teams of three researchers: a team at the University of Washington examining individual-focused strategies, and a team at the University of Minnesota examining environmental-focused strategies. Both teams worked together to create a comprehensive list of the practical factors that colleges would likely want to consider when choosing an evidence-based approach, including amount of research support, cost, and potential barriers to adoption and implementation. Each team then reviewed the extant research in their area through 2012, rating each strategy that met their inclusion criteria. For the individual-focused strategies, inclusion criteria required that a strategy had been the subject of at least two peer-reviewed, randomized, controlled clinical trials. In addition, a strategy could only be rated on effectiveness if there were at least three trials. For the environmental-focused strategies, ratings were based on review articles, when available, and all identified studies in other areas.

After the teams completed the ratings, they sent them to 10 leading experts within the alcohol prevention field for multiple rounds of peer review. The teams made edits (e.g., adding specific studies from 2013 that would inform ratings and clarifying how ratings were applied) until they achieved consensus across the teams and reviewers. Thus, CollegeAIM reflects the collective knowledge of 16 separate experts in the field (see Table 1), which makes it unique relative to other summaries of the science.

CollegeAIM is organized into two matrices, one summarizing individual-focused strategies and one summarizing environmental-focused strategies, divided into levels of effectiveness and cost. Each matrix also has a companion table that offers more in-depth information on the specific strategies. CollegeAIM also helps colleges consider both individual and environmental strategies by including a planning worksheet that facilitates a direct comparison of

Table 1 CollegeAIM Contributors

Individual-Focused Strategies Team

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strategies along the various rated factors, both across and within these two broad categories. Although CollegeAIM is largely a selection tool, institutions can use the planning worksheet to organize assessment of currently employed prevention strategies. CollegeAIM urges stakeholders to "see if any new, effective approaches might replace . . . existing strategies."[11] Information in the online version of CollegeAIM directs users to outside resources that can assist with planning and taking action to adopt, implement, and evaluate a given strategy. Each of these steps is necessary for effective campus prevention. Evaluation is of particular importance, since local realities (e.g., differences in campus and community culture, available staff) may influence how effective a strategy actually is on a given campus. A college or university's experience may diverge (for better or worse) from the effectiveness rating in CollegeAIM, which is based on the observed aggregate effect across the campuses and communities where they were tested.

Individual-Focused Strategies

CollegeAIM identified 14 strategies as having some effectiveness in the individual-focused strategy matrices. Of these, the researchers deemed 8 to have higher effectiveness, based on the requirement that 75% or more of the studies evaluating a given strategy reported a reduction in alcohol use and/or alcohol-related consequences. Consistent with *A Call to Action*, the science supported multicomponent alcohol skills training that includes information on what constitutes a standard drink, how to calculate and moderate blood alcohol concentration through protective behavioral strategies such as monitoring and setting limits on consumption, how alcohol outcome expectancies shape behavior following alcohol use, and how perceptions of other people's drinking influences personal drinking. This approach is typified by the Alcohol Skills Training Program (ASTP),[12] which is generally delivered to small groups of students. The ASTP was the precursor to the Brief Alcohol Screening and Intervention for College Students (BASICS),[13] which is the basis for the majority of current brief motivational interventions (BMIs). BMIs are generally one-on-one sessions facilitated by a professional in training (i.e., a graduate student in psychology) or professional (e.g., a master's- or doctoral-level counselor) using personalized feedback summarizing the student's alcohol-related behaviors, beliefs, and experiences to guide the conversation. Although limited research has examined whether undergraduate students (e.g., peer health educators) can deliver BMIs effectively, results are generally favorable; however, there is not enough evidence to conclusively determine the conditions under which peers are as effective as professionals. One factor that is thought to be central to the efficacy of BMIs is fidelity to a motivational interviewing (MI) style,[14] which requires regular supervision and review of taped or audio-recorded sessions that have been rated for adherence to the therapeutic spirit and skills of MI. That said, four of the eight highly effective programs are delivered entirely remotely, in the absence of an MI-trained facilitator.

Relative to BMIs, these nonfacilitated programs have been found to be comparable on most outcomes,[7] although in-person BMIs may hold an advantage over feedback-only

programs in terms of reducing alcohol quantity and negative consequences.[15] Two of these four programs are considered personalized feedback interventions (PFIs), which offer the feedback from a BASICS session delivered online, by email or text, or by mail. It is worth noting that some individual-focused strategies that would be considered PFIs are included as having "too few studies to rate effectiveness," since only two studies had been published when CollegeAIM was launched. Given the success of generic PFIs, as well as eCHECKUP TO GO (the only named and commercially available PFI with higher effectiveness), more research on these approaches is warranted. Another commercially named program rated as having higher effectiveness—AlcoholEdu for College—contains personalized feedback but is not considered a PFI, because it incorporates a number of other interactive elements that go beyond merely providing feedback.

The fourth remotely delivered program constitutes a single component of a PFI: correcting normative misperceptions of peer alcohol use in relation to the individual's own alcohol use, that is, personalized normative feedback (PNF). PNF in the form of birthday cards have been used to target 21st-birthday drinking, a known high-risk drinking event for many students; however, this use of PNF has had overall lower effectiveness.

The final two strategies rated as having demonstrated higher effectiveness include goal/intention setting alone and self-monitoring/self-assessment of drinking alone. Both of these strategies often are a part of the other strategies listed above; however, like PNF, these are considered single-component interventions that, in the absence of other elements, decrease student drinking. As their names imply, the former involves helping students set goals or intentions that are contrary to high-risk drinking, while the latter requires students to complete a one-time assessment or longitudinal daily monitoring of their drinking behavior. Assessment is necessary to create the feedback used for BMIs, PFIs, and PNFs, and creates an opportunity for self-reflection that is thought to be amplified by the associated feedback.

Environmental-Focused Strategies

CollegeAIM identified 19 strategies as having some degree of effectiveness in the environmental-focused strategy matrices. Of these, 5 were deemed to have high effectiveness: retaining the minimum legal drinking age (MLDA) of 21, enforcing the MLDA, increasing taxes on alcohol, retaining a ban on Sunday alcohol sales, and enacting bans on happy hours and other price promotions. Retaining the MLDA of 21 remains one of the most highly effective environmental interventions at the population level in terms of reducing alcohol consumption and alcohol-related fatalities.[16] Retaining the MLDA is beyond the control of any given college, but colleges can describe and promote the existing evidence on the effectiveness of the MLDA and work with community coalitions to ensure the drinking age is not lowered. Furthermore, retaining MLDA laws alone is not sufficient; the MLDA must be enforced through mechanisms such as underage compliance checks. Colleges can directly encourage local law enforcement agencies to regularly conduct compliance checks at alcohol establishments most likely to be frequented by their underage students. Increasing taxes on alcohol sales, retaining a ban on Sunday alcohol sales (if applicable), and bans on happy hours or other price promotions are all policies enacted at the state or local levels. Colleges can partner with other organizations or coalitions that influence policymakers to implement or retain these policies. In addition, college representatives can talk individually with local bars and other venues near campus that serve alcohol and ask them to restrict happy hours and other price promotions. Bars surrounding a campus may attempt to attract students to their establishments by underbidding nearby competitors, which can create a dangerous situation that promotes heavy consumption (e.g., buying one drink and getting one for a discounted price, or promoting discounted shots).

Conclusions

NIAAA developed CollegeAIM to offer colleges and universities an array of evidence-based options to address alcohol use on their campuses. Because the evidence changes with more scientific study, CollegeAIM is necessarily a living document, and NIAAA has committed to updating it every few years for the foreseeable future. The next update is planned for the fall of 2018, reviewing literature published through December 2017. Campus stakeholders are encouraged to facilitate future iterations of CollegeAIM by ensuring that evaluations of individual- or environmental-focused strategies on their campuses or in their communities make it into the published literature. Campus alcohol and drug prevention staff members could partner with graduate students and faculty at their own or nearby institutions to conduct the evaluations and collaborate on the publications. Graduate students, in particular, may be a valuable resource, since they need data for theses and dissertations, and they may therefore be willing and able to contribute time to evaluate the strategies in exchange for use of the data. It is, of course, just as important to publish what doesn't work as what does. CollegeAIM also is meant to help colleges learn what strategies are not effective, to avoid wasting resources.

In sum, CollegeAIM is a user-friendly, interactive decision tool based on a synthesis of the substantial and growing literature on campus alcohol use prevention, including strategies targeted at the individual and environmental levels. It is designed to be a strategy selection tool; however, it also offers resources to aid in strategy planning, implementation, and evaluation. The goal of CollegeAIM is to help colleges and communities use their limited resources in the most cost-effective way possible. The hope is that by using a combination of effective individual- and environmental-focused

strategies, colleges can create sustained reductions in risky alcohol use and related problems among their students.

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The authors declare that they have no competing financial interests.

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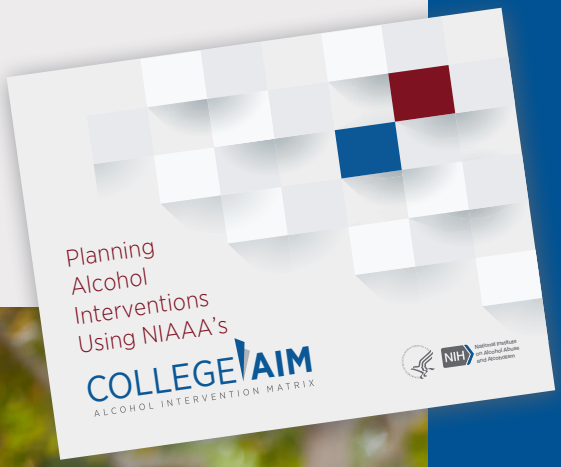
THE COLLEGE ALCOHOL INTERVENTION MATRIX



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High-Intensity Drinking

Megan E. Patrick and Beth Azar

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Binge drinking thresholds have long been set at four or more drinks for women and five or more drinks for men over the course of a few hours. However, a significant number of people regularly consume much higher amounts of alcohol: double or even triple the standard binge drinking threshold. Researchers have begun to distinguish between typical binge drinking and this kind of "high-intensity drinking," which is common among certain types of binge drinkers and is often associated with special occasions, including holidays, sporting events, and, notably, 21st birthdays. To understand the social and physical influences of alcohol consumption, it is important for researchers to set standard definitions for high-intensity drinking and distinguish it from other types of alcohol use.

Key words: Alcohol consumption; binge drinking; college drinking; drinking occasions; drinking patterns; heavy drinking; high-intensity drinking

Consuming alcohol until drunk by guzzling beers, slamming shots, and taking swigs from bottles of booze is common fare in movies and on television, which often portray people drinking to extremes. One study, published in the *British Medical Journal*, calculated that James Bond, of book and movie fame, drank about 45 drinks a week.[1] In the 2006 movie *Casino Royale*, Bond slugged down a stunning 20 drinks just before a high-speed car chase that left him in the hospital for 2 weeks. Researchers typically define binge drinking as four or more drinks in a sitting for women and five or more for men (4+/5+). Due to evidence that some people, like the fictitious Bond, drink far above that cutoff, researchers have begun distinguishing between typical binge drinking and this kind of "high-intensity drinking." They have developed new definitions and have begun examining the special challenges of measuring high-intensity drinking, the frequency with which it occurs, when it is most likely to occur and in which populations, and the consequences of this kind of drinking to the drinker and to the community. This article summarizes the most recent research on high-intensity drinking.

Defining High-Intensity Drinking

In the early 1990s, the College Alcohol Study first applied the term "binge drinking" to the pattern of drinking 4+/5+ drinks in a row during the past 2 weeks.[2] Drinking to this extent became a commonly used measure of increased risk of alcohol-related problems. In 2004, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) evaluated and approved defining binge drinking as 4+/5+ drinks in about 2 hours, because it typically leads to a blood alcohol concentration (BAC) of .08 g/dL, the legal cutoff for driving in the United States.[3] One advantage of the definition has been its use in many studies, making results comparable. However, this definition does not distinguish between drinking levels at or just above this binge threshold and those that far exceed it. It also assigns the same level of risk to everyone who crosses the threshold, regardless of how far beyond it they go.[4] And it does not account for differences in metabolism related to body mass, age, and other factors.[5,6] In fact, Pearson and colleagues[7] point out that average-weight women (about 163 lbs.) and men (about 190 lbs.)[8] in the United States would not reach legal intoxication after consuming 4/5 drinks in 2 hours.

Meanwhile, research indicates that a substantial portion of binge drinkers often drink at levels two or three times the 4+/5+ binge threshold, suggesting the need for another term and clear definition for this heavier binge drinking.[9] Although some articles have used the term "extreme binge drinking,"[10] the field is moving toward the term "high-intensity drinking" as the most accurate way to talk about this level of alcohol use.[11]

There is no firm consensus on exactly how many drinks qualify as high-intensity drinking. However, researchers working in this relatively new area have coalesced around the concept of at least twice the typical binge drinking threshold (i.e., 10+ drinks)[10] or twice the gender-specific binge threshold (i.e., 8+ for women/10+ for men).[9,12] Even using a more conservative measure of just two more

drinks over the typical binge drinking cutoff (6+/7+ drinks), Read and colleagues found significant differences when comparing what they called "heavy binge drinkers" with typical binge drinkers.[13] Specifically, heavy binge drinkers typically got drunker than those closer to the standard binge cutoff; when comparing both binge drinking groups with drinkers who did not binge drink, only heavy binge drinkers differed significantly. In this study, compared with drinkers in either of the other categories, heavy binge drinkers reported, on average, three additional unique types of consequences in the previous year, including impaired control, risk behaviors, academic or occupational consequences, and physical dependence.

How Common Is High-Intensity Drinking?

To date, only a handful of binge-drinking studies distinguish levels of use above binge drinking at the 4+/5+ rate. But those that do, find that a significant percentage of teens and young adults engage in high-intensity drinking at levels that far exceed that cutoff. For example, according to studies reporting on data from the national Monitoring the Future (MTF) survey of high school students and young adults, approximately 10% of U.S. 12th-grade high school students and U.S. 19- and 20-year-olds reported consuming 10 or more drinks in a row at least once in the previous 2 weeks, and an additional 4% to 5% reported consuming 15 or more drinks in a row.[10,14] Those rates are even higher among college students. Patrick and Terry-McElrath reported that 19- to 20-year-olds who attended 4-year colleges and did not live with their parents were significantly more likely to engage in high-intensity binge drinking than other young adults: 12.4% of college students consumed 10+ drinks, and 5.1% consumed 15+ drinks, compared with 9% and 3.5% of 19- to 20-year-olds not attending college (see Figure 1).[14]

In a separate study using MTF data to examine the developmental course of high-intensity drinking, Patrick and colleagues found that high-intensity drinking peaks around age 21, and that the peak tends to be highest for young adults who attend college.[15] Another study found that, among a

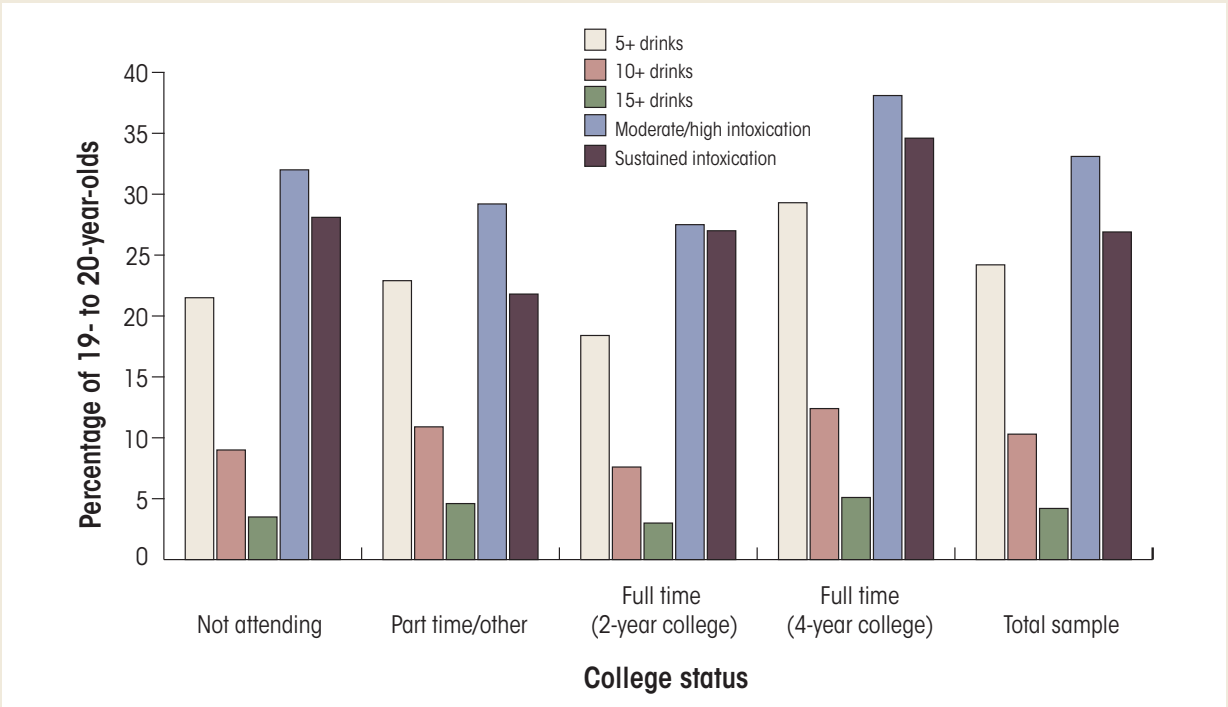

Figure 1 College versus noncollege high-intensity drinking patterns. Young adults who attend a 4-year college full time are more likely to report engaging in high-intensity drinking and binge drinking during the previous 2 weeks than drinkers who do not attend college, attend a 2-year college, or attend college part time. Full-time students at 4-year colleges are also more likely to say that they usually attain moderate/high and sustained intoxication when they drink. *Source:* Figure adapted from Table 1 and Table 3 in Patrick ME, Terry-McElrath YM. High-intensity drinking by underage young adults in the United States. *Addiction.* 2017;112(1):82-93.

sample of 10,424 college freshmen at 14 schools, roughly 20% of males reported consuming 10 or more drinks, and 10% of females reported consuming 8 or more drinks at least once in the 2 weeks preceding the survey.[9] Using the gender-specific high-intensity drinking cutoff of 8+/10+, Patrick and colleagues found that, among a group of 342 college students followed during four 2-week periods over the course of a school year, 67% reported high-intensity drinking on at least one day, and 16.1% of 5,467 drinking days recorded were high-intensity drinking days.[12] These high-intensity drinking days were associated with negative consequences, such as injury, unplanned sex, and aggression.

In addition, Wave 2 data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) reported that 13% of 18- to 20-year-olds drank 15 or more drinks at some point in the previous year, and 3% did so every 2 weeks.[16] Among the 3,718 young adults followed in the MTF analysis by Patrick and colleagues, those who engaged in high-intensity drinking not only drank more per occasion than typical binge drinkers, but they more often engaged in all levels of binge and high-intensity drinking than those who only reported binge drinking.[15]

Although high-intensity drinking appears to peak in the early 20s, it does not disappear. Terry-McElrath and Patrick recently reported that 12.4% of young adults ages 25 and 26 reported drinking 10 or more drinks in a row at least once in the previous 2 weeks.[17] This type of high-risk drinking was most common in people who were male, white, unmarried, employed, nonparents, and who were alcohol users during high school.

Among people who report binge drinking, consuming well in excess of the five-drink threshold is the norm. Naimi and colleagues examined data from the 14,143 adult binge drinkers who responded to the 2003–2004 binge drinking module of the nationally conducted Behavioral Risk Factor Surveillance System.[18] During their most recent binge drinking episode, 70% of respondents said they consumed 6 or more drinks, 38.4% consumed 8 or more drinks, and 16.9% consumed 11 or more drinks. Highest consumption was for respondents ages 18 to 24, who reported drinking an average of 9.5 drinks during a binge drinking episode. Average amounts for ages 25 to 34, 35 to 44, 45 to 54, and 55 and older were 8.0, 7.4, 7.4, and 6.7, respectively.

What constitutes high-intensity drinking may depend on who is drinking. It is largely established that the binge threshold for women should be lower than for men, because women become more intoxicated than men when consuming the same amount of alcohol (even when they weigh the same). Research also suggests that alcohol affects adolescents and young adults differently from adults. The brain undergoes significant growth and change well into young adulthood. Due to developing brain function, adolescents may be less sensitive to alcohol's behavioral effects, such as a staggering walk or sedation. At the same time, teens may be more receptive to the social-interaction effects of alcohol, including feeling more social and having more fun with friends.[6] In addition, adolescents have been shown to reach a BAC of .08 with fewer drinks.[19] Studies in animals and humans suggest that binge doses of alcohol have more severe and potentially permanent effects on adolescent brains and can more readily lead to addiction.[20,21] As for older adults, studies suggest that people over age 60 metabolize alcohol more slowly and are at higher risk of alcohol-related health problems.[22] Although most studies use the standard 4+/5+ definition of binge drinking for all ages, this evidence suggests that such a threshold may more accurately represent high-intensity drinking among older adults. Indeed, some organizations have begun to recommend that binge drinking thresholds be lowered for older adults. A consensus panel created by the Center for Substance Abuse Treatment defines binge drinking for older adults as four or more drinks per occasion for both women and men.[23] If that is indeed the case, high-intensity drinking may be more common among older adults than is currently reported. Parikh and colleagues calculated that almost 10% of a group of 4,815 participants age 65 and older reported drinking above the 4+/5+ threshold over the previous 30 days.[22] To tease apart the rates of high-intensity drinking, it will be critical for studies to use agreed-upon age-group thresholds for binge drinking and high-intensity drinking.

Ritualized High-Intensity Drinking

Many studies find that people intensify their drinking to celebrate special occasions and to bond with friends during holidays. As with much of the binge-drinking research, most of the studies examining when people are most likely to engage in high-intensity drinking revolves around college students. In a study examining the drinking patterns across the seasons among 462 university students, Schuckit and colleagues found that maximum drinks per occasion increased 18% around the time of a popular 1-day campus spring festival, decreased 29% over the summer, and increased another 31% as school resumed in the fall, suggesting that alcohol consumption by college students is highly influenced by annual rhythms and social context.[24] Expanding beyond college students, Bellis and colleagues found that estimates of average weekly drinking among all drinkers in England increased by nearly a quarter—from 13.6 to 17.1 units per person per week—when they included survey questions on special occasion consumption.[25]

Indeed, research finds that there are occasions when high-intensity drinking is much more likely. Not surprisingly, on and off college campuses, drinking tends to peak on Fridays and Saturdays and is particularly high on

holidays such as the Fourth of July and New Year's Eve.[26-29] Research on event-specific drinking has indicated particularly high quantities of alcohol consumed surrounding collegiate sporting events,[30,31] spring break,[32-34] and to celebrate 21st birthdays (at least in the United States).[35,36]

Holidays

Predictably, people tend to drink more on certain holidays. However, increases in high-intensity drinking may depend on the holiday in question. For example, within a sample of 576 young adults ages 18 and 19, both in college and not, Goldman and colleagues demonstrated that on family-oriented holidays such as Thanksgiving and Christmas, the number of young people who consumed alcohol increased but the average number of drinks consumed per person (counting only those who drank) actually decreased.[27] In contrast, on holiday weeks that included a Halloween-like holiday, New Year's Eve, and the Fourth of July, the average number of drinks consumed per drinker increased significantly compared with nonholiday weeks. Because the researchers measured drinks per week, they could not estimate rates of daily high-intensity drinking. However, another study of 1,124 college students found that, compared with a typical nonholiday weekend, more students consumed alcohol and reached higher BACs on their 21st birthdays, New Year's Eve, New Year's Day, the Fourth of July, spring break, and graduation.[29]

As these data suggest, there is some evidence that, at least for young adults, high-risk drinking is more likely during holidays that are centered on friends as opposed to family. Lefkowitz and colleagues examined drinking during a student-created holiday and found that more students drank, and students drank significantly more than they did on several typical weekend days: 51% of students consumed alcohol compared with 29% on a typical weekend, and students consumed an average of 8.2 drinks compared with a more typical 5.3 drinks.[37]

Sporting Events

Sporting events are also associated with particularly heavy drinking. One study found that men, though not women, drink more on Super Bowl Sunday than on a typical Saturday.[38] And among college football fans, particularly men, drinking on days of high-profile football games is as heavy as alcohol consumption on other well-known drinking days, including New Year's Eve and Halloween weekend.[31] In another study, Merlo and colleagues found high rates of heavy drinking, measured as a BAC of .08 or higher, among 466 tailgaters prior to football games at two large universities: 40.2% of tailgaters at one school and 31.9% at the other.[39] In general, studies find that athletes as well as sports fans are more likely than nonathletes and non–sports fans to engage in binge and high-intensity drinking and to have a heavy-drinking style.[30,40,41]

21st Birthdays

In the United States, according to a number of studies, the day young adults become old enough to drink legally is a day they often take very high risks with their drinking. In fact, more than 80% of study participants drink on their 21st birthdays,[35,36] and many drink far more than typical binge drinking. In a survey of 2,518 college students, for example, Rutledge and colleagues reported that 4 out of 5 study participants drank alcohol to celebrate, drinking an average of 12.6 drinks.[36] Moreover, 12% of male and female birthday drinkers reported consuming 21 drinks, and an additional 22% of men and 12% of women reported that they drank more than 21 drinks. An estimate of blood alcohol content (eBAC) suggested that well more than half of birthday drinkers drank enough to raise their BAC to dangerous levels. Specifically, 68% of female and 79% of male birthday drinkers reached the legal limit of .08 or higher; 35% of female and 49% of male birthday drinkers drank enough to have eBACs of 0.26 or higher (a level associated with potentially serious medical outcomes). Another study suggests that birthday drinking is not without consequences.[42] In Ontario, Canada, where the legal drinking age is 19, hospital admissions data for everyone ages 12 to 30 showed that alcohol-related hospital admissions more than doubled during a person's 19th-birthday week, compared with other times during the year.

At least among college students, where most of the research on 21st birthdays takes place, the heaviest drinking is associated with several factors, including overestimating how much one's peers drink during 21st-birthday celebrations, drinking shots, playing drinking games, celebrating with influential peers, and engaging in 21st-birthday traditions such as free drinks at bars.[43,44]

Spring Break

College student spring break is a highly anticipated time of the year when some college students intend to drink excessively. Studies find that college students who travel with friends dramatically increase their alcohol use and face more alcohol-related consequences, but those who stay home or vacation with their parents tend to drink moderately or not at all.[32,33,45] For students who do drink during spring break, their drinking is positively associated with alcohol-related consequences, including having a hangover, vomiting, and being injured as a result of drinking.[34] And, as with the risk of binge drinking, alcohol-related consequences are more likely if students travel: 32% of travelers and 22% of nontravelers reported having a hangover, 23% of travelers and 15% of nontravelers reported being sick to their stomach or vomiting, and 7.5% of travelers and 4% of nontravelers

reported being injured as a result of drinking.[34]

In a longitudinal study of 651 freshmen undergraduate students, Patrick and colleagues confirmed the findings that binge drinking and negative consequences of drinking are common during spring break.[46] They also discovered that previous drinking behavior was among the strongest predictors of alcohol consumption during spring break. In addition, students were more likely to get drunk and experience negative consequences of drinking if, before spring break, they and their friends agreed they would get drunk. And although students going on trips with friends were more likely to have these kinds of understandings, even students who did not go on trips had understandings with their friends about drinking. These findings suggest that the relative freedom of spring break provides many students with the opportunity to experiment with alcohol use. Litt and colleagues also found that whether or not students were willing to engage in high-risk drinking during spring break—drinking enough to black out or pass out—predicted whether they followed through.[47]

Consequences of High-Intensity Drinking

High-intensity drinking is of particular concern because of the adverse consequences associated with it. These consequences include alcohol-related injuries, alcohol poisoning, risky sexual behavior, vomiting, passing out, blacking out, and long-term harm to academic or occupational status. Although this article focuses on alcohol's short-term consequences, some studies have begun to show long-term effects of binge drinking. For example, longitudinal MTF data links binge drinking at age 18 to higher incidence of alcohol abuse disorder at age 35.[46,48]

One study with a cohort of 15,000 college students concluded that the overall frequency of binge drinking increases the risk of negative alcohol-related outcomes.[49] Specifically, students who binge drank three or more times in a 2-week period were twice as likely as students who binge drank once or twice in the same time period to experience alcohol-induced memory losses (27% vs. 54%), to not use protection during sex (10% vs. 20%), to engage in unplanned sex (22% vs. 42%), and to be injured (11% vs. 27%). Both groups were at a 1% risk of needing medical treatment for an overdose.

As mentioned earlier, students who binge drink regularly drink well over the typical binge threshold, making it difficult to determine, at a population level, whether the increase in risk associated with frequent binging results from the number of binge episodes per se, or from the number of drinks consumed in an episode.[4] Wechsler and Nelson concluded that, for individuals, the odds of experiencing alcohol-related harms rise as their level of alcohol consumption increases.[50] Mundt and colleagues reported that, among 2,090 college students, having an alcohol-related injury became 19% more likely for men with each additional day of consuming 8 or more drinks and 10% more likely for women drinking 5 or more drinks.[51] Read and colleagues also found that when they distinguished between nonbinge drinkers, binge drinkers (4+/5+), and heavy binge drinkers (6+/7+) in a sample of 356 college students, only the heavy binge drinkers differed significantly from the nonbinge drinkers on measures of alcohol-related consequences, including blacking out, impaired control, and alcohol dependence symptoms.[13] In a sample of 115 young adults, Jackson found that a threshold of 10 or more drinks was most predictive of hangover when examining the relationship between alcohol-related consequences and different drinking thresholds (from 1+ to 15+ drinks per occasion).[52]

Much of the research on the adverse consequences of consuming alcohol examines global associations between overall drinking levels and overall rates of consequences. Neal and Fromme attempted to assess whether alcohol consumption could be directly associated with specific behavioral consequences by asking college students to monitor their behavior over 30 days.[31] Their analysis included data from 691 women and 422 men on a total of 30,224 days. They concluded that, on a global level, average BAC was significantly correlated with illicit drug use, drinking and driving, engaging in sexual behavior, having unsafe sex, being the victim of coerced sex, being the perpetrator of coerced sex, acting aggressively, and gambling. Their analysis also found strong event-level associations between BAC and several behavioral risks, with the strongest correlations for vandalism, and the weakest for aggressive behavior and unsafe sex. They estimated that every .01 increase in BAC was associated with a 4% to 12% increase in the risk of engaging in these behaviors. Those numbers become significant when people engage in high-intensity drinking, which can increase BAC quickly in a short amount of time.

Several studies indicate that college students who engage in high-intensity drinking are motivated in large part by the expectation that it will lead to positive consequences, including being more social and having fun with friends. And these positive consequences may outweigh any potential negative consequences. In a longitudinal study that surveyed 342 college students over a total of 4,645 days, Patrick and colleagues found that students, in fact, both expected and experienced more positive consequences on days that they engaged in high-intensity drinking.[12] Students also expected and experienced more negative consequences on high-intensity drinking days. Furthermore, the positive consequences were rated as better and the negative consequences were rated as worse on high-intensity drinking days. Students may be motivated by the positive consequences and

accept the negative consequences as part of the drinking experience.

Self-Report of High-Intensity Drinking

When studying binge drinking, or any type of alcohol consumption, it is critical that researchers have access to an accurate and straightforward method for measuring how much alcohol people ingest. Most studies rely on self-reports, although questions have been raised about how valid those reports are at high quantities of alcohol. Recently, studies that compare self-reports with biological measures of alcohol consumption have determined that self-reports are a valid way to assess alcohol consumption.[53] That said, some evidence suggests that self-report data break down after people consume large amounts of alcohol. Northcote and Livingston, for example, found that young adults accurately estimated their alcohol consumption when it was light or moderate but underestimated it after eight or more drinks.[54] These discrepancies may result from a combination of intoxication interfering with memory and a desire to provide a more socially acceptable response.

Conclusions

Research has established that high-intensity drinking is relatively common, especially among teens and young adults, and it appears to peak around age 21. These findings suggest that studies should distinguish between standard binge drinking (4+/5+) and drinking that far exceeds that cutoff. To date, the few studies that measure high-intensity drinking, defined as drinking two or three times as much alcohol (e.g., 10+ or 15+ drinks) as a typical binge episode, suggest that it is far riskier and has major implications for individual and community health. As this field matures, it will be critical to further examine gender-specific measures for high-intensity alcohol use (e.g., 8+/10+ and 12+/15+ drinks for women/men) and to include effects of age in relevant analyses. Indeed, high-intensity drinking behavior is particularly dangerous for teens, whose brains are still developing and who may be more vulnerable to developing alcohol use disorder.

Future research in this area should focus on the initiation and progression of high-intensity drinking.[11] Additional research is also needed to determine whether existing prevention approaches are effective at reducing high-intensity drinking, or whether more prevention and intervention programs are needed to address this more extreme behavior.[11,16] Understanding who is most likely to engage in high-intensity drinking and when and where that drinking occurs will help design prevention programs to specifically target this behavior.

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Gender Differences in Binge Drinking

Prevalence, Predictors, and Consequences

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Just as binge drinking rates differ for men and women, the predictors and consequences of binge drinking vary by gender as well. This article examines these differences and how binge drinking definitions and research samples and methods may influence findings. It also describes the relationship between age and binge drinking among men and women, and how drinking culture and environment affect this relationship. It examines gender-specific trends in binge drinking, predictors of binge drinking for men and women, and binge drinking in the context of smoking. The article reviews current findings on gender differences in the health consequences of binge drinking, including morbidity and mortality, suicidality, cancer, cardiovascular disorders, liver disorders, and brain and neurocognitive implications. It also discusses gender differences in the behavioral and social consequences of binge drinking, including alcohol-impaired driving, sexual assault, and intimate partner violence, and includes implications for treatment and prevention.

Key words: Alcohol and other drugs (AODs); AOD associated consequences; binge AOD use; gender differences; physical health; predictive factors

Introduction

A large research literature shows that women consistently consume less alcohol than men, and they experience fewer social problems resulting from drinking than men, but these gender differences vary culturally, demographically, and historically.[1-3] This literature often has not given close attention to gender differences in binge drinking and its consequences. This lack of attention is unfortunate, because binge drinking is recognized as a major contributor to the social and health burdens of alcohol consumption.[4] Binge drinking has been linked specifically to a wide variety of adverse consequences, acute (e.g., accidents and injuries) and chronic (e.g., liver disease), that harm not only the drinker but also communities and societies as a whole (e.g., productivity losses, crime, and public disorder).[5,6] In this article we review recent research findings on gender differences in the prevalence, predictors, and consequences of binge drinking, and we note how interpretation of these findings has been limited by differences in concepts, measurements, and research methods.

Measurement Issues

There is considerable variation in the research literature as to how binge drinking is measured (4+, 5+, 6+ drinks) and labeled (binge drinking, heavy episodic drinking, or risky single-occasion drinking).[7-10] Furthermore, many studies use gender-specific measures of binge drinking (e.g., 5+ drinks for men and 4+ drinks for women),[11] but many other studies use the same measure for men and

women (e.g., the Alcohol Use Disorders Identification Test uses 6+ drinks).[12-16] Other studies define binge drinking by estimated blood alcohol concentration (BAC) level (e.g., a BAC of at least .08%), which may be a less sensitive criterion for men than for women.[17]

Finally, different studies measure different frequencies of binge drinking over different time periods (e.g., in the past 2 weeks or past 30 days). Measuring the frequency of binge drinking in a given time period (e.g., once in the past 30 days) may produce greater apparent gender differences than measuring binge drinking as any or none. Moreover, using longer time periods for measurement (e.g., a year versus a month) may reduce gender differences when binge drinking is measured as any or none but may magnify gender differences when binge drinking frequency is measured. Because of the inconsistent measurement methods used across the research, we cannot focus our discussion on any one criterion of quantity, frequency, or time period. However, for examination of the consequences of acute and chronic binge drinking, the importance of measurement variation remains uncertain.

Prevalence

There has been widespread alarm in the mass media about the extent of women's binge drinking. A frequent theme is that, traditionally, men have been binge drinkers more than women, but this gender difference is declining rapidly because of a growing epidemic of binge drinking among women.[18,19] However, research evidence indicates that these media stories oversimplify men's and women's patterns of binge drinking.

Recent survey data consistently illustrate that men in the United States and throughout the world binge drink more than women (see Table 1).[20-33] Although studies measure binge drinking in various ways and over various periods of time, the gender difference persists, whether or not studies use gender-specific criteria for defining binges. Another analysis of data from 15 countries reached a similar conclusion.[34] However, binge drinking rates and gender differences vary greatly across populations. One explanation of the difference is that recent changes in binge drinking have not yet erased the sizable gender gap present in many societies. A second explanation is that gender differences in binge drinking cannot be attributed only to biological or cultural differences but may result from a combination of these influences.[3]

Age

One response to these explanations has been concern that gender differences in binge drinking may be disappearing specifically among younger drinkers. In the United States, binge drinking is most prevalent in late adolescence or early adulthood, with rates declining as drinkers grow older.[35] However, a focus on binge drinking in any one age group may be an oversimplification, for several reasons:

- Women's binge drinking has not caught up with men's in any age group in the United States or any other country, judging from large, general-population surveys.
- As drinkers get older, binge drinking (versus none) declines consistently in Europe, North America, Australia, and New Zealand, but these declines do not occur consistently in other areas of the world.[3]
- Frequency of binge drinking by men and women often shows complicated nonlinear relationships with age.[28,36,37]
- Gender-specific associations of age with binge drinking may vary among regions within countries.[38]

Taken together, these findings suggest that how age modifies effects of gender on binge drinking depends on the specific drinking culture and environment where the binge drinking occurs.

Gender-Specific Trends

Complex age effects are one reason why it is difficult to evaluate trends in women's and men's binge drinking. Much of the research and discussion of those trends focuses on two questions:

1. Is binge drinking changing (in recent years) in ways that differ by gender?
2. Are gender-differentiated changes leading to a convergence of men's and women's rates of binge drinking?

In the mass media, the common answers to these questions are that women's binge drinking is increasing faster than men's, and, as a result, men's and women's binge drinking rates are converging.

Research to answer these questions is hard to interpret for many reasons besides age effects. In addition to the variation in how binge drinking is measured, some analyses of binge drinking rates include abstainers, whereas others do not. Some studies analyze changes in binge drinking frequency, whereas others analyze changes in rates of ever/never binge drinking. Furthermore, many studies that measure trends over extended periods do not separate period effects (historical trends in whole populations) from age effects (changes that occur more in one age group than others) and cohort effects (changes that are greater in groups born in one historical period than others).

Nevertheless, a small set of large longitudinal studies has provided consistent answers to the two questions about trends. From 2000 to 2010, large U.S. studies found that any binge drinking (measured as ever or never) in the preceding month increased in prevalence more among women than among men.[35,39,40] This trend was consistent with findings from binge drinking studies that used different

Table 1 Prevalence of Binge Drinking

Source	Population	Binge Drinking Measure	Men	Women
2014 National Survey on Drug Use and Health[20]	United States, ages 18 and older	5+ drinks, 1 occasion, past 30 days	33%	17%
China Chronic Disease and Risk Factor Surveillance, 2007[21]	China, ages 15 to 60	50+ grams (men), 40+ grams (women), ethanol, 1 day, past 12 months	32%	4%
Health Survey for England, 2007[22]	England, ages 16 and older	>2 times recommended daily maximum (>8 units for men, >6 units for women), past week, among drinkers	35%	27%
Kangwha Cohort Study, Korea, 1988[23]	Kangwha County, Korea, ages 55 and older	6+ drinks, 1 occasion, past year	21%	<1%
Moscow Health Survey 2004[24]	Moscow, Russia, ages 18 and older	80+ grams (men), 60+ grams (women), ethanol, 1+ occasion per month	30%	6%
National Health Survey 2004, Singapore[25]	Singapore, ages 18 to 69	5+ drinks, 1 occasion, past month	9%	5%
National survey, Denmark, 2003[26]	Denmark, ages 15 to 99	6+ drinks, 1 occasion, once a month or more	38%	18%
National survey, Mozambique, 2005[27]	Mozambique, ages 25 to 64	5+ drinks (men), 4+ drinks (women), or equivalent drink container, 1 day, past week	25%	11%
National survey, Spain, 2008 to 2010[28]	Spain, ages 18 to 64	80+ grams (men), 60+ grams (women), ethanol, 1 occasion, past month	10%	4%
Nationwide survey on alcohol consumption patterns, Brazil, 2005 to 2006[29]	Brazil, ages 18 and older	5+ drinks (men), 4+ drinks (women), 1 occasion, past year	40%	18%
South African National HIV Prevalence, Incidence, Behaviour and Communication Survey, 2008[30]	South Africa, ages 15 and older	5+ drinks (men), 4+ drinks (women), 1 occasion, past month	17%	4%
Survey, Hong Kong, 2006[31]	Hong Kong, ages 18 to 70	5+ drinks, 1 occasion, past 30 days	15%	4%
Survey of Lifestyle, Attitudes and Nutrition in Ireland, 2007[32]	Ireland, ages 18 to 29	6+ drinks, 1 occasion, past year	92%	79%
Third National Health Examination Survey, Thailand, 2004[33]	Thailand, ages 15 and older	Multiple beverage-specific measures	40%	7%

time periods (a week and a year) and with findings from other countries (England, Finland, Russia, and Singapore).[25,36,41-43] The greater increase in prevalence among women resulted in partial convergence of men's and women's *likelihood* of binge drinking.

In contrast, in the United States, convergence of women's and men's *frequency* of binge drinking more likely occurred because of greater *declines* in frequency among men than among women.[40,44] Furthermore, evidence of men's and women's convergence in the United States often has been stronger in young adults (20s and 30s) than in other age groups.[40,45] Trends in men's and women's binge drinking may be modified by drinking pattern changes in different birth cohorts. In the United States and Finland, evidence has shown that both men and women in more recent birth cohorts have been increasingly likely to become binge drinkers, at least until the 1980s birth cohort.[35,36,44] These patterns indicate that further convergence of women's and men's binge drinking patterns may be hard to predict and cannot be attributed entirely to women's increased binge drinking.[46]

Predictors of Adult Binge Drinking

Childhood Experiences

Childhood experiences are possible early predictors of binge drinking. However, evaluations of gender differences in childhood influences on binge drinking are scarce, particularly in the United States. Most studies lack data on binge drinking, do not analyze effects of childhood experiences on men and women separately, or provide data for only one gender.

Child maltreatment. Child maltreatment (including childhood sexual abuse, childhood physical abuse, and neglect) has consistently been found to be a robust predictor of many adverse mental health outcomes, including high-risk drinking and alcohol use disorder (AUD).[47-51] Typically, research has found that women more often report childhood sexual abuse than men,[52-54] and men more often report childhood physical abuse than women,[55,56] but not always.[57] Gender differences in experienced neglect are uncertain.[58-60]

Given these gender differences in types of child maltreatment, one might infer that childhood sexual abuse is more of a risk factor for women's binge drinking, and childhood physical abuse is more of a risk factor for men's binge drinking. Unfortunately, research has infrequently compared how forms of child maltreatment affect women's versus men's binge drinking. The few relevant studies show inconsistent patterns, suggesting that gender differences in maltreatment effects likely depend on the groups of men and women studied and the measures of binge drinking used.

Widom and colleagues studied men and women with childhood histories of abuse or neglect that resulted in court cases and compared them 30 years later with approximately matched controls (from a Midwest U.S. metropolitan area).[51] The researchers found no significant differences in frequency of past-month binge drinking (defined as 8+ drinks) between men with and without histories of child maltreatment. However, women who had been neglected (with or without other abuse) were more frequent binge drinkers in the past month than same-sex controls. In South Africa, on the other hand, a history of childhood physical punishment nearly doubled the prevalence of binge drinking as the usual behavior on a drinking day, although this effect did not differ significantly between men and women.[61]

Concerning childhood sexual abuse, a Pennsylvania study of adults ages 31 to 41 found a direct effect on binge drinking in women but not in men,[62] whereas a much larger study of U.S. naval recruits found that binge drinking was more prevalent among those men and women who had experienced childhood sexual abuse (and was also more prevalent among those men, but not women, who had experienced childhood physical abuse).[63] The variation in the findings does not allow simple conclusions about how gender may modify connections between childhood maltreatment and adult binge drinking.

Parental problem drinking. Another childhood experience linked to adult alcohol problems is exposure to problematic parental drinking.[64-67] Gender-specific analyses by Merline and colleagues[64] and White and colleagues[67] found that heavy drinking by parents adversely affected the drinking behavior of their male and female adult children. Unfortunately, reports on parental drinking generally have not provided data on gender-specific effects or on binge drinking, and often they have focused only on adolescent drinkers or parents with diagnosed alcohol disorders (e.g., studies of adult children of alcoholics). However, a community study in Finland found that heavy parental drinking was significantly associated with binge drinking at age 42 for men but not for women, when controlling for individual drinking history.[68] In data from the Young in Norway Longitudinal Study, parental binge drinking (not gender specific) was related to adult children's intoxication, or 5+ drink binges at age 28, but there were no significant gender differences for this parental influence.[69] The lack of other recent data means the question of how gender modifies parental drinking effects on binge drinking by adult children remains unresolved.

Early onset of alcohol use. In the United States, early onset of alcohol use is linked to adult alcohol problems,[70,71] although the strength of this relationship has been challenged.[72] Boys in the United States begin drinking earlier than girls, which could increase male risk of later binge drinking, but recent gender differences in age of onset are not large and are not entirely consistent with data from outside the United States.[73-75] The few studies of gender-specific associations between early onset of alcohol use and later binge drinking suggest that gender effects may be culturally dependent. Caetano and colleagues, who studied Hispanic national groups in the United States, found that drinking onset at age 14 or younger versus 21 or older increased the prevalence of binge drinking among women more than among men for Mexican Americans, Puerto Ricans, and South/Central Americans but not for Cuban-Americans.[76] In Korea, both men and women who began drinking at age 17 or younger were more likely to binge on drinking days, and later onset of drinking reduced binge drinking (as typical drinking behavior) among women more than among men.[77] In a Finnish community sample of middle-aged men and women, binge drinking was more frequent among those who began drinking at age 16 or younger, but this effect did not have a clear gender difference.[78]

Psychological Characteristics

The alcohol studies field has a long history of research on associations between personality traits and alcohol use in clinical and nonclinical samples.[79-81] For this article, we selected two clusters of personality characteristics that have known gender differences in prevalence and that may affect men's and women's binge drinking differently: disinhibiting traits (i.e., impulsivity, sensation-seeking, and risk-taking) and affective characteristics (i.e., anxiety and depression).

Disinhibiting traits. Research has shown that heavy or binge drinking in young adulthood is associated with a set of related disinhibiting personality traits, including impulsivity, sensation-seeking, and risk-taking.[82-84] These behavior traits are more prevalent in

men than in women,[85-87] although the size of the gender difference varies across age groups and traits. From these two findings, one could infer that these disinhibiting traits contribute to the excess of binge drinking among men compared with women. However, it is not so clear that disinhibiting traits are associated with men's binge drinking more strongly than with women's. Some studies found stronger associations between disinhibiting traits and frequency of binge drinking or intoxication among men than among women.[88,89] Other studies concluded that disinhibiting traits were more clearly associated with women's heavy drinking.[90,91] The most common finding, however, was that disinhibiting traits were associated with binge drinking, intoxication, or problem drinking among both women and men, with more similar than dissimilar gender-specific effects.[92-95] It is important to be cautious about interpreting such associations causally, because the extent to which a history of heavy or binge drinking facilitates men's and women's impulsivity, sensation-seeking, and risk-taking is unknown.

Anxiety and depression. Anxiety and depression are more prevalent among women than men,[96-99] and some patterns of anxiety and depression, such as patterns defined in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), are associated with some patterns of alcohol consumption, such as AUD.[100-102] However, it is not clear that depression and/or anxiety are associated with binge drinking, specifically. Many studies with gender-specific data have failed to find connections among anxiety, depression, and binge drinking for women or men.[68,103-107] There are some exceptions. A 2006 U.S. Behavioral Risk Factor Surveillance System (BRFSS) survey found that men with current depression were more likely to be binge drinkers than nondepressed men.[108] In a U.S. survey of men and women older than age 56, heavy-drinking or binge drinking men scored higher than other men on a measure of depressive symptoms.[103] The 2006 BRFSS survey also reported that women with lifetime diagnoses of anxiety or depressive disorders or with current depression were more likely to binge drink than women without anxiety or depression, and the severity of depression increased women's (but not men's) odds of binge drinking.[108]

In a national Canadian survey, for both men and women, depression was associated with drinking larger quantities per drinking occasion, but the association was stronger for women.[109] In the large U.S. National Epidemiologic Survey on Alcohol and Related Conditions (NESARC),[105] women's binge drinking was associated only with post-traumatic stress disorder and panic disorder (without agoraphobia). A survey at a large public university found that students with general anxiety disorder were more likely than other students to engage in frequent binge drinking, and students with major depression were less likely than other students to engage in frequent binge drinking.[110] Both of these associations were stronger among men than women. These mixed findings suggest that depression and anxiety do not have simple or gender-determined associations with binge drinking. Studying how drinkers' ages and drinking opportunities differently affect links between binge drinking and anxiety or depression among men versus women may be worthwhile.

Adult Binge Drinking and Smoking

Typically, studies that have examined adult binge drinking and other substance use have focused on tobacco smoking, particularly cigarettes. In the United States, among the whole young adult population,[111] college students,[112] adults ages 18 to 25,[113] and adults older than age 50,[114] binge drinkers consistently have higher odds than non–binge drinkers of being smokers. In the United States and worldwide, smoking is more common among men than among women.[115-117] To the extent that smoking may be part of a lifestyle that encourages or leads to binge drinking, the general patterns described here might contribute to the gender gap in which men binge drink more than women. However, prolongation of smoking may have unknown effects on women's binge drinking, and evidence indicates that women find it more difficult than men to stop smoking.[118-120]

Multiple gender-specific studies worldwide have shown that smoking is strongly related to both men's and women's binge drinking, typically showing stronger connections for women than for men. U.S. surveys have reported that men and women who smoke have three times higher odds than nonsmokers of being binge drinkers,[121] and smokers have a higher probability than nonsmokers of heavy drinking behavior at ages 35 and older.[122] In China in 2007, the majority of men and women smokers were also binge drinkers, an association that was much stronger in women.[21] A separate 2006 study in Hong Kong found that smoking multiplied the odds of binge drinking by 3.7 for men and 12.3 for women.[31] In Brazil, the São Paulo Epidemiologic Catchment Area Study found that men and women who were binge drinkers were more than twice as likely as non–heavy drinkers to be current smokers, and the relationship was stronger for women.[123] In a national Canadian survey, the odds of binge drinking were significantly greater than 1.0 for all women smokers, but only for men who smoked more than six cigarettes a day.[124] The 2004 Moscow Health Survey found that women who were binge drinkers had higher odds of daily smoking than other women, but men who were binge drinkers did not have higher odds of daily smoking than other men.[125] Most of these studies were cross-sectional and could not distinguish the degree that smoking influenced binge drinking or vice versa. These studies also did not

explore the possibility that both smoking and binge drinking were part of a syndrome with shared antecedents. It would be worth examining the extent to which women who both smoke and binge drink are attempting to show independence from older feminine stereotypes that discouraged both behaviors.

Differences in Health Consequences

Research on how gender affects the health consequences of adult binge drinking is scarce, for several possible reasons. Studies of chronic alcohol-related health problems may neglect binge drinking episodes because researchers may assume binge drinking has acute, not chronic, effects. Gender-specific analyses may be neglected because including enough women who binge drink (e.g., in Asian countries) for reliable statistical analysis is often difficult. Research may focus on adolescent rather than adult binge drinking because of greater concern about acute and long-term health consequences for young drinkers. And, investigators may have difficulty distinguishing between effects of binge drinking and effects of chronic heavy drinking, because the two drinking patterns are correlated. Nevertheless, research does suggest where binge drinking has gender-related health effects, and where it does not.

Morbidity and Mortality

Several recent studies have found that binge drinking adversely affects mortality and morbidity for both men and women. In a sample of U.S. moderate drinkers ages 55 to 65, the odds of dying in the next 20 years were twice as great for moderate drinkers who initially reported binge drinking in the preceding month than for moderate drinkers who did not report such binge drinking. No significant difference between genders was found.[126] National U.S. surveys (2008 to 2010) found that among binge drinkers, women reported more days of physical and mental ill health than men, and men and women who had recent heavy binge drinking episodes (7+ drinks for women and 8+ drinks for men) were more likely to report poor health–related quality of life than binge drinkers who drank less.[127]

In contrast, a study that analyzed National Health Interview Survey (NHIS) data from 1997 to 2004 found that episodic heavy drinking (5+ drinks in 1 day) added only modestly to the mortality risk of light and moderate drinkers.[128] And, a population-based study of nearly 27,000 men and women who participated in the Danish National Cohort Study from 1994 to 2005 reported that binge drinking (6+ drinks on an occasion) among male and female moderate drinkers was not associated with increased all-cause mortality when they were compared with moderate drinkers who did not binge drink.[129] The authors suggested that Danish customs around binge drinking (which usually occurs during a long evening of eating and drinking) may account for the results.

A Russian survey asked respondents about the health of close relatives after age 30 and found that men who had engaged in any binge drinking were more likely to have died than other male drinkers, but for women, increased mortality occurred only among those who binge drank at least once a month.[130] In Norway, women and men who binge drank on 10 or more occasions in the past year were more likely to report alcohol-related sickness that caused absence from work than those who binge drank no more than 5 times, and the pattern of more frequent binge drinking was associated with sickness-related absence more strongly for women than for men.[131]

Suicidality

A special case of mortality risk among binge drinkers is the potential effect of binge drinking on suicidal behavior (including thoughts of suicide and suicide attempts). Research has found that suicidal behavior often is associated with chronic heavy drinking,[132,133] which may be a symptom of psychological problems or a way of coping with such problems. For both men and women, completed suicide has been associated with acute alcohol intoxication,[134] which may precipitate or enable the behavior.

How episodic binge drinking as a behavior pattern is related to men's or women's suicidality has been studied much less often. Available research suggests that binge drinking has stronger associations with women's suicidality than with men's. According to U.S. National Violent Death Reporting System suicide data from 2003 to 2011, the likelihood of high postmortem blood alcohol concentrations (BACs) of more than .08 g/dL was much greater than the likelihood of high BACs in general population survey data.[134] Women's postmortem BACs generally were higher than men's, but they were not statistically significantly higher. Data from the 2008 to 2012 U.S. National Survey on Drug Use and Health showed that among women and men who had not experienced major depressive episodes, women's binge drinking was associated with planned and attempted suicide, but men's binge drinking was associated only with suicidal thoughts.[135] These data showed no association between suicidality and binge drinking in men and women who had past major depressive episodes. In a nationally representative sample in France, binge drinking at least monthly predicted suicidal ideation and suicide attempts better for women than for men.[136] And, in a survey of U.S. college undergraduates, reported past suicide attempts were significantly associated with reported past binge drinking among young women but not among young men.[137] However, the time order of binge drinking

and suicidality remains unclear, except as shown in the postmortem data reported by Kaplan and colleagues.[134]

Cancer

A possible life-endangering effect of binge drinking is an increase in women's and men's risks of various forms of cancer. Evidence clearly shows that heavy alcohol consumption is a risk factor for cancers in the oral cavity, pharynx, esophagus, liver, colon and rectum,[138,139] and pancreas.[140-142] In general, research on these cancers has not provided information about binge drinking and its gender-specific effects. One exception is a San Francisco Bay Area population-based case-control study, which found that the risk of pancreatic cancer was higher specifically among men who had a history of binge drinking, particularly if the binge drinking persisted over years and involved large numbers of drinks.[143] Another recent exception is a Korean longitudinal study of differentiated thyroid cancer, which found that acute, heavy alcohol consumption (more than 151 grams of ethanol on one or more lifetime occasions), when compared with no alcohol consumption, doubled men's cancer risk and tripled women's cancer risk.[144]

In studies of gender-specific (or nearly so) cancers, gender-specific effects of alcohol get closer attention. Research on gynecological cancers (i.e., cervical, ovarian, and endometrial/uterine) has consistently found no association between women's drinking and the risks of these cancers.[145-148] In contrast, a large set of evidence has consistently shown that women's risk of breast cancer increases with increased alcohol consumption, even at moderate levels, resulting in more than 100,000 alcohol-related cases of breast cancer worldwide each year.[149,150] (Alcohol is apparently less relevant in the rarer male breast cancer.[151]) Hypothetically, alcohol may increase women's breast cancer risk through multiple processes, including increasing tumor-promoting estrogen levels (now debated) and acting as a cumulative carcinogen (through increased exposure to acetaldehyde and byproducts of the CYP2E1 enzyme, likely activated by binge drinking).[152,153]

Research on associations between binge drinking and breast cancer has been scarce. In the Danish Nurse Cohort Study, data from 1993 to 2001 showed that women who binge drank on weekends (Friday through Sunday) or on the latest weekday had greater risk of breast cancer than women who were light drinkers, even after adjusting for total volume of alcohol consumed.[154] In the U.S. Nurses' Health Study, data from 1980 to 2008 showed that monthly binge drinking was associated with a 33% increase in risk of breast cancer, but controlling for cumulative alcohol consumption weakened the association.[155] A New Zealand case-control study found that weekly binge drinking was associated with a 55% increase in risk of breast cancer among Maori women.[156] A case-control study in North Carolina found a positive association between binge drinking and risk of breast cancer among women who drank an average of 91 grams or more of ethanol per week, but the association was not significant after controlling for other variables, possibly because the sample size was small.[157]

Evaluating the effects of alcohol consumption and binge drinking on male-specific cancers has been difficult. The effects of drinking on testicular cancer are unknown, because no recent or major research on testicular cancer has evaluated the drinking patterns of the men studied. Also, although research on prostate cancer has examined alcohol consumption, the findings conflict. Some studies found that heavier drinking was associated with a greater risk of prostate cancer.[158,159] Some research reported that drinking raised risk only for advanced cancer[160] or only for non-advanced cancer.[161] In other studies, heavier drinking raised prostate cancer risk for men only if they had consumed low amounts of dietary fiber,[162] were African American,[163] or had been lifetime, rather than current, heavy drinkers.[164] And, some large or meta-analytic studies found that drinking had little or no association with prostate cancer.[165-167]

The picture is just as confused for the limited research on associations between binge drinking and prostate cancer risk. In the 1986 to 1998 Health Professionals Follow-Up Study of men ages 40 to 75, men who were binge drinkers (compared with abstainers) had the greatest increase in prostate cancer risk.[168] In this study, binge drinking was defined as drinking 105 grams or more of ethanol on 1 to 2 occasions per week. The older part of the Finnish Twin Cohort study, which surveyed twins (mean age of 40) from 1981 to 2012, found that binge drinkers had a greater risk of prostate cancer than non–binge drinkers.[158] In contrast to these cohort-based studies, case-control data from the 2000 NHIS survey,[169] the U.K. Prostate Testing for Cancer and Treatment (ProtecT) study,[170] and the U.S. Prostate Cancer Prevention Trial[171] showed no connection between binge drinking and prostate cancer. Our conclusion from the conflicting research is that binge drinking does not have simple or unconditional effects on prostate cancer.

Cardiovascular Disorders

Heavy drinking (variously defined) by both men and women consistently has been associated with higher risks of hypertension,[172,173] atrial fibrillation,[174] and stroke.[175,176] Relationships between chronic heavy drinking and coronary heart disease (CHD) have been less consistent. Some studies found that such drinking was a risk factor for both women and men,[177] whereas other studies failed to find such connections.[178-180]

Generally, binge drinking has been associated with a higher risk of

cardiovascular disorders, but reports of such associations often are not gender specific.[181-183] Available gender-specific data have shown that men's risks from binge drinking usually are greater than women's risks. For example, men's risk was greater than women's for CHD and hypertension,[184] death from cardiovascular disease,[185] and death from ischemic stroke.[186] However, findings for women were often limited by small sample size, and some studies found that women and men binge drinkers had similar risks for hypertension[187] and for death after myocardial infarction.[188]

Liver Disorders

Research has shown conclusively that heavy drinking increases risk of a variety of liver diseases and damage.[189-191] From our review of this research, we draw three general conclusions about gender and the effects of binge drinking on the liver:

1. Research on the effects of binge drinking on the liver is scarce and reveals little about gender differences.[192,193]
2. Research on liver damage specifically from binge drinking may be scarce because research has repeatedly found that harm to the liver results from continuous (frequent) drinking rather than episodic drinking (such as binges).[194-196] Binges may merely increase the cumulative toxic exposure to alcohol.
3. The risk of liver damage from chronic drinking is greater for women than for men,[190,197] possibly because of differences in how the body distributes and metabolizes alcohol.[189,198] A European study reported an exception to this gender difference, however. The study found that for men, binge drinking created a higher risk of alcohol-related hepatic steatosis (fatty liver) than it did for women.[199]

In general, not enough research has been conducted to draw any firm conclusions about how gender modifies the adverse effects of binge drinking on the liver.

Brain and Neurocognitive Consequences

Damage that some patterns of alcohol consumption can do to the brain is both well-known and well-studied, particularly in adolescents and individuals with AUD.[200-202] Furthermore, many studies have specifically examined the harmful effects of binge drinking on the brain and neurocognition. However, it is difficult to draw general and reliable conclusions from these studies about gender differences in binge drinking effects on the brain,[203] in part because many of these studies (e.g., those that used functional magnetic resonance imaging) examined small, nonrepresentative samples, which does not allow reliable, within-gender evaluations (i.e., comparing binge drinkers with same-sex controls). Nevertheless, certain patterns have emerged that may guide future gender-specific research and interventions.

One pattern is that binge drinking may alter the anatomy of the young brain in ways that could have persistent adverse effects. In adolescents and college students who have binge drinking histories, studies have shown evidence of poorer integrity (as indicated by lower fractional anisotropy) of white matter in multiple areas of the brain,[204,205] an effect that at least one study found mainly in males and in areas of the brain related to cognitive function and attentional processes.[206] Studies also have shown that adolescent binge drinkers had reductions in white and gray matter in the cerebellum (for both genders)[207] and changes in frontal cortices (thicker for females, thinner for males).[208] In the latter study, the increased cortical thickness was associated with worse performance on visuospatial, inhibition, and attention assessments, possibly reflecting impairment of the normal neuronal pruning process in binge drinking females.[209]

A larger set of studies of cognitive functioning has identified at least three general areas in which binge drinking adolescent and young adult males and females may be impaired.

1. In tasks involving working memory, binge drinking females showed less activation of spatial working memory than same-sex controls, and binge drinking males showed greater activation than controls.[210] In other working memory tasks, the brains of binge drinkers apparently had to work harder to perform at the same level as non–binge drinkers, but no gender differences were reported for those tasks, possibly because of small sample sizes in these studies.[211,212]
2. In studies of response inhibition and monitoring of one's own behavior, binge drinking generally impaired females more than males,[90,213,214] but at least one study found an increase in performance self-monitoring among females, who were possibly compensating for alcohol effects.[215] No such increase was found among male binge drinkers.
3. In evaluations of executive functioning and decision-making, one study found the worst performance in male binge drinkers,[216] another study found males and females were similarly impaired,[217] and a laboratory test of acute impairment reported that males and females performed similarly, although the females had higher BAC levels.[218]

All these performance tests are more descriptive than explanatory, saying little about why gender differences sometimes occur and sometimes do not, or about the extent to which these levels of impairment are reversible or might affect adult life.

Differences in Behavioral and Social Consequences

Research has repeatedly documented and decried multiple adverse behavioral and social consequences of binge drinking.[219-222] This research, however, has not reported much about gender differences for many of these consequences. The research has revealed even less about possible gender-specific links between binge drinking and behavioral or social harm. Our focus here, therefore, is on three major behavioral and social problems for which gender-specific effects of alcohol consumption have been recognized and studied: alcohol-impaired driving (AID), sexual assault, and intimate partner violence (IPV).

Alcohol-Impaired Driving

In recent U.S. research on AID, two gender patterns are clear. Men engage in AID more than women, but the prevalence of both men's and women's AID has been declining since the 1990s, judging from self-reports[40] and the National Roadside Survey.[223] However, from 1982 to 2004, women's arrests for driving under the influence increased (while men's decreased),[224] possibly reflecting changes in laws and law enforcement (including lower limits for BACs) and increases in women's driving.[225,226]

U.S. surveys indicate that more than 80% of AID episodes were self-reported by binge drinkers.[227,228] It is unclear, however, whether binge drinking immediately preceded the episodes of drunk driving, and U.S. reports have not indicated how many binge drinking drivers were men and how many were women. Cultural differences may affect AID gender patterns. In Sweden, men and women arrested for driving under the influence drank a similar amount beforehand (typically more than five drinks).[229] Among Australian drivers killed in single-vehicle crashes, 50% of the males, compared with 29% of the females, had BACs of more than .07 g/dL.[230]

Although AID episodes are very likely to involve binge drinkers, a majority of binge drinkers do not report driving after drinking. In 2003 to 2004 U.S. survey data from self-reported binge drinkers, 13.2% of the men and 8.1% of the women reported driving after drinking.[231] However, tendencies to binge drink and to drive while intoxicated often occur together. The odds of AID are more than 5 times greater for binge drinkers than for other drinkers, and the odds are more than 10 times greater for those who binge drink frequently or who generally drink heavily, and these odds increases may be greater for men than for women.[227,232,233] A study of daily diaries kept by college students estimated that each 0.1% increase in estimated daily blood alcohol level was associated with a 4% increase in men driving after drinking, and a 1% increase for women.[234]

Sexual Assault

Knowledge about how binge drinking is related to sexual assault has three important limitations:

1. Because the great majority of reported sexual assaults involve men assaulting women, research has focused on how alcohol is related to these assaults.[235,236] Little is known about the circumstances in which men are sexually assaulted.[237,238]
2. Most research has focused on assaults among college students and young adults, groups most likely to be both heavy drinkers and sexually active.
3. Research may reveal associations between binge drinking and sexual assaults, but understanding the extent that binge drinking causes or results from the assaults is difficult because of uncertainties about the order of events and time lags between drinking and the assaults.[239,240]

Nevertheless, research findings show several clear patterns in how binge drinking and sexual assaults are likely to be connected.

Perpetration. One repeated finding is that binge drinking among male college students can make them more likely to engage in sexual aggression. In terms of immediate consequences, a study found that men were more likely to engage in sexual aggression if they had BACs of more than .15 g/dL, particularly if they were otherwise light drinkers.[241] Another study determined that the number of drinks men drank in the 4 hours before a sexual encounter affected their odds of aggressive sex with new partners.[242] And, among men who reported perpetrating past sexual violence, having consumed a larger number of drinks at the time led to greater aggression (up to the point where severe intoxication was disabling).[243] One college study found 1-year lagged effects of men's binge drinking on sexual aggression,[244] suggesting that binge drinking as a continuing pattern among men might reinforce recurrent sexual aggression, at least in the college years.

Victimization. There is much evidence that women's drinking, in general, is associated with subsequent sexual assault.[245] A lingering question is whether women's binge drinking increases this apparent risk. Incapacitated rape, which can occur when women have drunk too much to be able to resist an attack, is a major adverse effect of binge drinking. Among college women, a majority of rapes occur when women have drunk enough to be incapacitated.[236,240] Apart from incapacitation and rape, women who binge drink are also at greater general risk of sexual victimization[246-248] for many possible reasons: men's misinterpretation of women's drinking as a sign of sexual availability, miscommunication of women's refusals, and women's underestimation of hazards from male companions.[245] One study of college women found evidence that binge drinkers may overestimate their ability to resist rape attempts.[249]

It is not clear whether experiences of sexual victimization lead women to binge drink, possibly to help cope with the emotional aftereffects of assault. In some studies of women in college[250] and in the general U.S. population,[235] experiences of sexual assault did not predict subsequent binge drinking. Other studies, however, did find that experiences of incapacitated rape[251] or repeated victimization[252] were associated with subsequent binge drinking. These apparent contradictions suggest two more complex patterns:

1. Women's experiences of sexual victimization may perpetuate (not just initiate) binge drinking (and controlling for effects of prior drinking might obscure effects of victimization on subsequent drinking).[247,250]
2. In the short term, such as during college or the young-adult years, women's binge drinking and sexual victimization might become a vicious circle, each making the other more likely, increasing risk of revictimization.[245]

These more complex patterns should be further evaluated.

Intimate Partner Violence

Research on IPV has focused largely on male violence against female partners and the aftereffects for female partners.[253,254] Consistent with this focus, 2005 U.S. survey data have shown that women were roughly twice as likely as men to report being victims of IPV over their lifetimes and in the past year.[255] However, this focus neglects women's violence against male partners, which may be more prevalent at times in some groups, particularly outside the United States.[256-259] It also neglects the degree that IPV is an interactive process in which violence can be reactive and defensive as well as proactive, with both partners as victims and attackers.[260,261] To understand how binge drinking may be related to IPV, therefore, it is important to study binge drinking among both men and women as perpetrators and as victims of IPV.

A large body of research links alcohol use in general to IPV perpetration and victimization.[258,262] One might expect binge drinking, in particular, to increase the likelihood of IPV perpetration through disinhibition and increased aggression.[263] Indeed, in bivariate analyses of survey data, binge drinking was associated with IPV perpetration among men and women in Canada and Costa Rica and among women in Brazil.[258] In bivariate analyses of U.S. survey data, rates of IPV perpetration were doubled for male binge drinkers and nearly tripled for female binge drinkers.[264,265] However, in multivariate analyses of U.S. data, the associations between binge drinking and IPV either disappeared[264,265] or became too small to be meaningful.[266]

Binge drinking might also increase women's vulnerability to IPV victimization. In surveys in Brazil, Canada, Mexico, and Peru, binge drinking women were more likely to report being victims of IPV.[258] A meta-analysis of three longitudinal U.S. studies found that women's binge drinking significantly increased the odds of their subsequent IPV victimization,[267] but other U.S. studies either could not confirm such a relationship[265,268,269] or found only very weak relationships.[266] These mixed findings about perpetration and victimization, particularly from multivariate analyses, suggest that binge drinking (as distinct from other drinking patterns) may not be a direct cause of IPV, but it may be an indicator of other personality and behavior patterns that may lead to IPV (e.g., antisocial traits).[270,271]

Research shows, somewhat more consistently, that a history of IPV victimization increases the likelihood that women will engage in binge drinking after varying time lags.[267,272,273] However, this relationship is not always evident or strong,[268,269] possibly because many women who are victimized cope with the distress in other ways. Indeed, male victims of IPV might be more likely to use binge drinking as a stereotypically male method of coping, but few studies have looked for or found evidence of men's binge drinking behavior after IPV victimization.[274,275] If binge drinking is becoming more prevalent among women (as noted earlier), there may be a greater need for interventions to reduce the use of alcohol as a coping mechanism.

Alcohol's Harm to Others

To date, alcohol research has focused mostly on how drinking harms the drinker.[276] Limited previous research on harm to people other than the drinker has focused mainly on AID,[277,278] fetal development,[279,280] and IPV,[281,282] largely neglecting broader harm to others' mental health, quality of life, living conditions, and resources. An Australian study has suggested that costs of such harm to others may be double those experienced by drinkers themselves.[283]

Some studies of alcohol's harm to others (AHTO) have examined gender differences in the types of harm caused and harm received. A common finding has been that women are considerably more likely than men to experience marital and family harm, and men are significantly more likely than women to experience physical assault from strangers and other crime victimization.[284-286] However, with a few exceptions,[287,288] AHTO research has focused on harmful effects of others' drinking or heavy drinking without exploring possible associations between specific drinking patterns (e.g., heavy episodic or binge drinking) and specific types of harm. Such associations might include relationships between binge drinking and AID, crashes, and fatalities, or relationships between binge drinking and increased risk of fetal alcohol effects. The harm to others paradigm is a relatively new development in alcohol epidemiology.[289] As this perspective matures, we hope

that greater attention will be given to associations between specific drinking patterns, such as binge drinking, and specific types of harm, as well as possible gender differences in those associations.

Possible Implications

Treatment

Our research literature search on gender differences in alcohol treatment outcomes found very little information specifically relevant to binge drinking. Nonetheless, research on gender-specific alcohol treatment is helpful when considering strategies to reduce binge drinking. Before the early 1990s, most alcohol and drug treatment programs were developed for and served primarily men.[290] However, more recent research on gender-sensitive treatment has focused on treatment strategies that may be particularly appropriate and effective for women. Much of this evolution of gender-sensitive treatment has been informed by empirical evidence of gender differences in treatment needs. This evidence includes research demonstrating higher prevalence among women of (1) comorbidity of substance use disorders and other psychiatric disorders (e.g., mood, anxiety, and eating disorders), (2) trauma exposure and associated physical and mental health needs, and (3) the central role of relationships (with children, intimate partners, and others) in women's addiction and recovery.[291-293] A number of studies have reported a general tendency for women to respond somewhat better to a variety of psychosocial interventions[294-296] and to show a less consistent or harder-to-detect response to some pharmacological treatments.[297,298] There is general agreement on the need for more well-controlled randomized clinical trials that examine the effects of gender-specific treatment.

Integrated Interventions for Binge Drinking and Smoking

Given the strong associations between binge drinking and smoking described in this article, there may be promise in combined interventions that target both smoking cessation and binge drinking. Indeed, preliminary data presented by Ames and colleagues suggest the potential value of integrated smoking cessation and binge drinking interventions, particularly for young adults.[299] Environmental interventions that disengage alcohol use and tobacco use (e.g., smoking bans in bars) may also help to reduce hazardous drinking behavior. Evidence from several countries indicates that female smokers find it more difficult than male smokers to stop smoking,[118-120] so combined interventions to reduce both smoking and binge drinking could prove especially helpful to women who both smoke and binge drink.

Prevention

In our search for prevention programs that specifically target binge drinking, we found an article that described gender-specific prevention strategies focused specifically on binge drinking college women.[300] Aimed primarily at nurse practitioners, this article argued that for women college students, several common consequences of binge drinking (e.g., sexually transmitted infections, sexual assault, and other physical injury) bring them into contact with health care providers, offering opportunities for intervention. The author suggested several intervention strategies that may be particularly effective for female binge drinkers, including brief motivational interventions.[294,301] She speculated that Web-based interventions may be particularly effective for women, perhaps due to women's greater involvement with electronic programs[302] and the greater feeling of anonymity online programs may provide for women who feel stigmatized by their alcohol use or misuse.[303]

Considerable anecdotal evidence,[304-306] supported by qualitative studies in several countries,[307-310] suggests that one motivation for binge drinking among women—younger women in particular—may be that "drinking like a man" produces feelings of power, status, and gender equality. To date, in all countries studied, men drank more alcohol than women, and men engaged in extreme forms of drinking, such as high-volume drinking and heavy episodic or binge drinking, more than women. In many traditional societies, heavy alcohol consumption symbolizes and enhances men's greater power relative to women, serving as an emblem of male superiority and a privilege that men have often denied to women.[311] Indeed, in contemporary higher-income countries, numerous studies of young men have reported associations among endorsement of traditional masculine norms, heavy and binge drinking, and adverse drinking consequences.[312,313] With changing gender roles in many societies, and increasing opportunities for women, increased access to and consumption of alcohol understandably may seem like an expression of liberation and empowerment for many young women.

To our knowledge, prevention scientists have not tried to reduce binge drinking in young women by changing the significance of heavy alcohol consumption as a symbol of gender equality. A critical question is how best to persuade women that alcohol is a poor way to demonstrate gender equality—clearly not through simple educational approaches[314] or by trying to frighten or shame them, such as with warning labels.[315] One modest policy step might be to restrict advertising that links drinking to liberation from traditional feminine roles and stereotypes.[316] It is possible, also, that mass media and marketing methods could be used to sell the positive advantages of abstention or

low-risk alcohol consumption. A powerful message might be that women do not gain status or express liberation by emphasizing their sameness with men or by trying to outdrink them, but by setting their own standards—in their drinking decisions and in other areas of their lives.[305,317] Such messaging may be most effective if it provides gender-specific information about drinking norms[318] and is reinforced by multiple community sources.[319]

Parallel prevention strategies could be targeted to men, especially younger men, to weaken associations among traditional constructions of masculinity, heavy episodic drinking, and other risk-taking behavior. Specific strategies might include media literacy training to recognize and resist media images that link masculinity and excessive alcohol use, and interventions designed to change expectancies about alcohol's effects on sexuality, aggression, and other dimensions of traditional masculinity.[313]

Future Research Needs

When attempting to review gender differences in the prevalence, predictors, and consequences of binge drinking—and gender-sensitive strategies to reduce binge drinking—we became aware of many gaps that future research could fill. Some of the major gaps and challenges in this area are listed and discussed briefly in this section.

First, the use of different *definitions and measures* of binge drinking poses a serious challenge to research on many aspects of binge drinking. For researchers interested in gender similarities and differences, the use of more consistent definitions and measures would permit much firmer conclusions about gender-related patterns in binge drinking prevalence (across types of populations sampled and in various cultural contexts), as well as about gender-linked predictors of binge drinking and the consequences of binge drinking for men's and women's behavior and health.

Second, although a majority of prevalence studies have disaggregated binge drinking rates by gender, many studies of predictors and consequences of binge drinking have not. In some cases, studies have focused only on men or only on women, whereas other studies sampled both males and females but did not conduct or report gender-specific analyses. In the United States in the 1990s, actions by the National Institutes of Health led to increases in female research participants in both human[320] and animal studies.[321] Despite these increases, many researchers, from diverse scientific fields, fail to consider the role of (biological) sex and (culturally defined) gender when designing, analyzing, and reporting research. In addition to continued pressure on funding agencies to require sampling of both genders when appropriate for the research question being studied, editors and reviewers for scientific journals can play an important role in requiring adequate analyses and reporting of sex and gender differences in research publications.[322] A greater understanding of gender-differentiated aspects of binge drinking is one of many benefits that could result from development of new, and greater enforcement of existing, guidelines for attention to sex and gender in scientific research.

Third, the majority of studies reviewed in this article were cross-sectional, limiting inferences that can be drawn about time order and causality. Some of the many questions that well-designed longitudinal research could begin to answer are:

- The persistence or nonpersistence into adulthood of effects of adolescent and young-adult binge drinking on brain structure and function
- The extent that psychological characteristics such as impulsivity, anxiety, and depression precede and predict binge drinking versus being consequences of binge drinking or outcomes of some third factor that also predicts binge drinking
- Temporal and causal linkages (including possible bidirectional relationships) between smoking and binge drinking, binge drinking and suicide attempts, binge drinking and sexual assault, and binge drinking and intimate partner violence

Fourth, we were unable to find recent binge drinking literature, other than studies addressing age differences, that examined interactions of gender with other major demographic variables, such as race/ethnicity, sexual orientation, or socioeconomic status. Future research should give increased attention to such variables' associations with binge drinking prevalence, predictors, and consequences.

Finally, very little research has tested strategies specifically designed to reduce or prevent binge drinking. There are major conceptual and methodological challenges to designing and evaluating intervention strategies that specifically address binge drinking, as compared with more general interventions to reduce or prevent chronic heavy drinking or AUDs. Nonetheless, our review suggests that there may be promise (and possibly gender differences in effectiveness) in intervention strategies that specifically target the combination of binge drinking and smoking, as well as in strategies that attempt to weaken perceptions, expectancies, and norms that link men's binge drinking with ideals of traditional masculinity or women's binge drinking with feelings of status, power, and gender equality. In addition, the emerging perspective of AHTO may eventually suggest approaches for preventing or reducing binge drinking linked to gender-related harm, such as IPV and adverse fetal alcohol effects.

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Binge Drinking's Effects on the Developing Brain—Animal Models

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Adolescence typically is a time of experimentation, including alcohol use and, particularly, binge drinking. Because the brain is still developing during adolescence, such exposure could have long-lasting effects. Animal models and adolescent intermittent ethanol exposure (AIE) paradigms have been used to help elucidate the consequences of adolescent binge drinking. These studies have identified cognitive deficits, particularly in challenging cognitive tasks, and behavioral alterations such as greater risk preferences, impulsivity, and disinhibition. AIE also is associated with changes in affect when the animals reach adulthood, including increased social anxiety and, sometimes, general anxiety. Animal models have demonstrated that AIE can result in retention of certain alcohol-related adolescent phenotypes (i.e., reduced sensitivity to alcohol's aversive effects and increased sensitivity to alcohol's rewarding effects) into adulthood, which may motivate continued elevated alcohol use. The detrimental effects of adolescent alcohol exposure extend to a diversity of lasting alterations in the brain, including reduced neurogenesis, increased proinflammatory responses, changes in gene expression through epigenetic mechanisms, and alterations in the activities of various neurotransmitter systems. Further exploration of these mechanisms in animal models and humans may lead to improved prevention and intervention efforts.

Key words: Adolescence; alcohol exposure; alcohol use disorder; animal studies; binge drinking; brain development

Adolescence typically is a time of experimentation and emulation of adult behaviors, and many adolescents initiate alcohol and other drug (AOD) use during this developmental period. Brain development continues during adolescence, which could render the adolescent brain particularly vulnerable to alcohol's effects. Consequently, adolescent alcohol exposure could result in long-lasting changes in neuropsychological function and increased risk of developing alcohol use disorder (AUD). To better understand and minimize these risks, it is crucial to comprehensively study alcohol's impact on the adolescent brain. Such studies in humans face a number of challenges, however. For example, ethical constraints prevent the administration of alcohol to underage youth. Moreover, in human adolescents it is difficult to discern whether observed correlations between alcohol use and the behavioral or neuropsychological measures under investigation reflect causes or consequences of alcohol use or are purely coincidental. Finally, despite significant progress in noninvasive imaging technologies, the complexity of the human brain and technical limitations of brain analyses hamper researchers' abilities to fully investigate how alcohol influences adolescent brain structure and function.

Animal models using laboratory animals such as mice and rats can help circumvent some of these problems. However, their use also is associated with certain limitations. Most importantly, no currently available animal model can fully represent complex human behaviors such as alcohol use and addiction. Certain factors that influence adolescent neurobehavioral function and AOD misuse are not amenable to analysis using animal models, including variables such as verbal ability and language, and influences such as self-esteem, culture, media, or even parenting styles. Despite these limitations, much of what is currently known about the intricacies of brain development, neural substrates of AOD use and misuse, and adolescent responses to AODs has been obtained using animal models. This article summarizes some of the characteristics of animal models for studying alcohol's effects on the adolescent brain and reviews the findings of studies using those models that have shed light on functional and structural alterations

associated with adolescent alcohol use, the alcohol-induced persistence of adolescent phenotypes into adulthood, and the impact of adolescent alcohol use on later alcohol consumption.

Characteristics of Animal Models

The potential usefulness and validity of animal models, especially for complex behaviors such as alcohol misuse and its consequences, depend primarily on the specific research questions being asked. The validity of such models can be assessed on three levels:[1]

- Face validity assesses whether the phenomenon under study in the model resembles the targeted human behavior in terms of its behavioral, cognitive, and physiological features. However, it is important to realize that even if certain behaviors or other effects appear similar across species, they may not share the same underlying mechanisms.
- The measure of construct validity focuses on the relevance of the phenomenon under investigation in the animal model to the concept being modeled. Investigators seek to determine how similar the animal model is to the biological foundation and neural underpinnings of the human behavior being modeled. This concept also considers the impact of moderators, such as previous experiences or the environment.
- The concept of predictive validity reflects how effectively the animal model predicts experimental findings or treatment outcomes in humans.

Assessment of the validity of animal models of adolescent alcohol consumption and its consequences is an ongoing, iterative process, as research in these areas escalates in both human adolescents and laboratory animals. The current research supports cautious optimism in the use of such models. For example, findings have shown signs of consilience between human adolescents and rodent models of adolescence when comparable assessment measures of alcohol sensitivity and consequences were used.[2]

Animal Models of Alcohol Use and Its Consequences

One of the main factors for using rodent animal models for alcohol research is that these animals voluntarily self-administer AODs when given free access. For example, rodents often orally self-administer substantial amounts of alcohol, particularly if they are offered beer or sweetened beverages. Laboratory animals and humans exhibit similar behavioral and cognitive responses to acute AOD administration. Laboratory animals effectively model a broad diversity of alcohol effects seen in humans, ranging from euphoria and social stimulation at low alcohol levels to intoxication, motor impairment, sedation, and memory impairment at higher doses.[3] In addition, animals that are chronically exposed to AODs can develop physical dependence, characterized by dysphoria and physical signs of withdrawal (e.g., tremor, anxiety, insomnia, and even seizures) when access is terminated.[4] Such physical dependence can be accompanied by a tendency for relapse, particularly after re-exposure to the drug or exposure to stressors or drug-related cues. Experiments that used a conditioned place preference approach demonstrated that laboratory animals, even without physical dependence, can develop a preference for contextual cues associated with drug use.

Not only are the behavioral consequences of alcohol exposure often similar in humans and in animal models, but the neural substrates underlying these effects also exhibit across-species similarities. Numerous studies have identified sufficient similarities in brain structure and function between rodents and humans to support the validity of animal models in assessing the consequences of alcohol use on the brain. For instance, consider the prefrontal cortex (PFC), a brain region that comprises a notably greater proportion of the total brain matter in humans and other primates than in rodents. In humans, the PFC is thought to play a central role in executive functions, such as working memory, temporal processing, planning, flexibility, and decision-making, which influence behaviors such as drug self-administration and dependence. Comparative studies have indicated that rats also engage in these behaviors, and that the PFC is critical for mediating these processes in rodents, nonhuman primates, and humans.[5,6] In rats and humans, the PFC can be divided into subregions that are associated with similar cognitive functions across species.[5] Experimental animal models have been used successfully to reproduce features of neuropathological and neurochemical changes observed in humans who had neurodegenerative and psychiatric disorders that affected their cognitive function.[7]

Extensive studies also have established the relevance of animal models for investigating drug use behaviors and the consequences. For instance, brain reward systems using the neurotransmitter dopamine, including dopamine projection regions of the nucleus accumbens (NAc), amygdala, and PFC, are critically involved in drug self-administration and dependence in humans and animal models.[8-10] In addition, in humans and laboratory animals, specific brain structures and neurochemical systems are critical for different aspects of alcohol use and misuse (e.g., producing dependence or mediating craving and relapse).[11]

However, differences exist between the rodent and the human and nonhuman primate brains that should be considered when translating findings from animal studies to the neurological substrates and consequences of alcohol use in humans. For example, electrophysiological studies have suggested that the medial PFC in the rat brain combines elements (i.e., the anterior cingulate cortex and the dorsolateral PFC) that are separated in the primate brain.[12]

Animal Models of Adolescence

Adolescence—that is, the transition from dependence on parents to the independence of adulthood—is not unique to humans and is, to some extent, experienced by all mammals. Similar biological changes, including alterations in the brain, are seen across a variety of mammalian species during adolescence.[13-15] Adolescence-associated neural alterations include regionally specific reductions in the number of synaptic connections between neurons and declines in the relative volume of certain cortical and subcortical areas.[14] Speed of information flow across distant brain regions increases,[14] as does the reactivity of some subcortical brain regions, including the NAc and amygdala.[13,15]

Adolescence-associated changes in dopamine-terminal regions, such as the amygdala and NAc, are particularly important in the context of adolescent AOD use, because these regions are critically involved in processing and responding to rewarding, aversive, and emotionally arousing stimuli, including social stimuli. In adolescents, when compared with adults, these brain regions often react in an exaggerated way to motivational stimuli.[13,15] In contrast, maturation of cognitive control regions in the PFC and other frontal regions occurs gradually during adolescence.[16] This maturational dissociation is thought to contribute to adolescent-characteristic behaviors, such as increased risk-taking and exploratory drug use.[17]

Such developmental alterations have been observed in humans and in animal models and have been matched by analogous behavioral changes in various species. Adolescent rats, for instance, show more peer-directed interactions, novelty-seeking or risk-taking behaviors, and consummatory behavior; find social stimuli, novel stimuli, and pleasant tastes particularly reinforcing; and voluntarily consume two to three times more alcohol than adult rats.[18-21]

Despite such similarities, there are, of course, marked differences between humans and rodents in the duration of this developmental period. Adolescence is relatively brief in rodents and in other mammals with a short life span. Adolescence in rats has been estimated to last only about a month (i.e., postnatal day [P] 25 to P55), with early to mid-adolescence ending at about P42, and late adolescence occurring from P43 to P55.[22] The experimental designs used to study adolescent alcohol use and its consequences, such as analyses involving operant self-administration, must be adapted to this relatively short time period.

To ensure the face validity of models, experimental designs for modeling human alcohol use and its consequences in animals must consider human drinking patterns. For example, alcohol misuse among human adolescents typically takes the form of binge drinking on weekends rather than daily drinking. This human adolescent behavior can be modeled by intermittent alcohol exposure. However, alcohol misuse among adults often involves more regular drinking patterns, which may be better represented by more continuous exposure models.

Despite these constraints, judicious use of animal models can complement studies in human adolescents and address questions that are ethically or technically not amenable to study in humans. Studies using animal models have identified numerous functional alterations associated with adolescent alcohol use, as well as a variety of neural alterations.

Functional Alterations Associated With Adolescent Alcohol Exposure

Studies of the lasting consequences of repeated alcohol exposure during adolescence in animal models have identified numerous functional alterations across domains, ranging from cognition and behavior, to affect, and to later alcohol consumption. These studies typically use alcohol exposure levels that produce blood ethanol concentrations of .08% or more—the level required to meet the definition for binge drinking specified by the National Institute on Alcohol Abuse and Alcoholism[23] (see **Drinking Patterns and Their Definitions** in this issue). Blood ethanol concentrations in these studies often average .15% to .20%, which is well within the binge-drinking range observed in field studies of human adolescents.[24] Usually, each alcohol exposure during a rat's adolescence is followed by a short period of abstinence before the next exposure period, a design sometimes called adolescent intermittent ethanol exposure (AIE).

Cognitive and Behavioral Alterations

Animal studies have helped identify a variety of cognitive deficits resulting from repeated adolescent alcohol exposure, particularly deficits in tasks that are thought to require hippocampal functioning.[25] Other identified deficits reflect aspects of executive functioning, where prefrontal cortical brain regions are thought to play a particularly important role.[16] Interestingly, the observed effects are highly specific. Learning of some less cognitively challenging tasks, such as passive avoidance or simple operant conditioning tasks, does not seem to be affected by adolescent alcohol exposure.[26,27] Alcohol-exposed animals sometimes exhibit deficits on more challenging tasks, such as conditional discrimination and object recognition tasks.[28] For adolescent animals exposed to ethanol, tasks that demand some degree of cognitive flexibility or self-control seem to be particularly vulnerable to performance impairment. These tasks include reversal learning,[29] extinction, and set-shifting tasks.[30] Adolescent alcohol exposure also is associated with a greater vulnerability to disruptions in spatial memory that are induced by ethanol challenge in adulthood.[25]

Other studies have assessed the effects of AIE on risk-taking behavior, impulsivity, and disinhibition, all behavioral propensities that could promote experimentation with AODs. Such studies have demonstrated that animals with adolescent alcohol exposure exhibited greater risk preferences on a probability-discounting task.[31,32] AIE has been associated with increased impulsivity and greater disinhibition, as indicated by an increase in time spent in open or lighted test areas.[30,32-34]

Changes in Affect

Animal studies also have demonstrated changes in measures of affect in adult animals that were exposed to alcohol as adolescents. For example, AIE animals exhibited depression-like signs, such as reduced consumption of a sugar solution or increased immobility in a swim test.[35-37] Similarly, alcohol exposure during early to mid-adolescence was associated with reliable increases in social anxiety in adulthood.[38,39] Interestingly, this effect seems to be sex-specific and is only observed in males. Other studies in male rats after AIE have detected increases in general anxiety, as indicated by decreased time on the open arms (relative to time on the closed arms) of an elevated plus maze.[37,40,41] However, increases in general anxiety have not always been observed.[36,42]

It is challenging to distinguish disinhibition and anxiety in animal studies. For example, although the elevated plus maze test was developed and validated as a test of anxiety, results from it are sometimes interpreted in terms of disinhibition. Increased time spent in an environment that animals perceive as more risky (i.e., the open arm of an elevated maze) could indicate either greater disinhibition, decreased anxiety, or some interaction of the two, with increases in disinhibition perhaps contributing to a suppression in anxiety.[30,34] In studies of adolescent alcohol exposure, AIE has been found to increase open-arm time in some studies, suggesting greater disinhibition, but to decrease open-arm time in others, a pattern of findings consistent with a profile of increased anxiety. It is possible that adolescent alcohol exposure can be characterized by profiles of both increased anxiety and disinhibition. Competition between these propensities—depending, for example, on the perceived stressfulness of the situation or the animals' previous handling—may explain these reliable but opposing outcomes.[43]

Retention of Adolescent Phenotypes Into Adulthood

One surprising long-lasting consequence of adolescent alcohol use observed repeatedly in AIE studies is the retention of adolescent phenotypes into adulthood. In rodent studies, adolescents have been shown to differ from adults in a variety of alcohol-related phenotypes. In instances where researchers could assess similar effects in human adolescents, the analyses uncovered comparable age-related differences.[2] For example, like their human counterparts, adolescent animals often voluntarily consume significantly more alcohol per drinking occasion than adults.[18,44,45] This elevated alcohol intake is particularly notable in male animals and mirrors intake by human adolescents.[46]

Adolescents often differ from adults in their sensitivity to alcohol's effects, with the direction of these differences dependent on the effect studied. Adolescents are less sensitive to many of alcohol's undesired effects, such as alcohol-induced motor impairment, sedation, aversion, and social impairment, which normally serve as cues to limit intake.[47] Adolescents are also less sensitive to acute withdrawal (i.e., hangover effects) after moderate to high alcohol consumption. In animal models, this effect has been reflected in reduced levels of withdrawal-associated anxiety.[48,49] In contrast to the attenuated sensitivity of adolescents to many of alcohol's undesired effects, adolescents are often more sensitive to certain desired effects of alcohol, such as its rewarding and social facilitating effects.[47] Adolescents are also usually sensitive to the disruptive effects of acute alcohol intoxication on learning and memory.[25] Collectively, adolescent-associated attenuated sensitivity to aversive effects and increased sensitivity to desirable effects of alcohol could contribute to enhanced susceptibility to the initiation and escalation of alcohol use during adolescence,[47] with intoxication having pronounced disruptive effects on learning and memory.[25]

Animals given repeated alcohol exposure during adolescence often retain adolescent-typical phenotypes into adulthood.[50] This persistence can be observed through baseline behavioral, cognitive, electrophysiological, and neuroanatomical assessments, as well as in the animals' responses to alcohol challenges in adulthood.[51] For example, animals exposed to alcohol during adolescence maintained an enhanced sensitivity to alcohol's rewarding and stimulatory effects into adulthood.[38,52-54] This persistent sensitivity could promote alcohol consumption in adulthood. In other studies, animals that experienced AIE retained their adolescent-typical insensitivities to alcohol's sedative, motor-impairing, and aversive effects, which could permit the maintenance of elevated alcohol drinking during adulthood.[53,55-58] Also, the decline in sensitivity to alcohol-induced deficits in spatial working memory that normally occurs between adolescence and adulthood did not occur in animals exposed to alcohol in adolescence.[59] As a result, adult animals exposed to AIE retain adolescent-like vulnerability to alcohol-induced memory impairments and show more memory disruption under the influence of alcohol than adults without a history of adolescent alcohol exposure.

Generally, retention of these adolescent phenotypes into adulthood is associated with alcohol exposure during adolescence; equivalent alcohol exposure during adulthood does not induce similar effects.[55,58] Moreover,

adolescent phenotypes are more pronounced if adolescent alcohol exposure is episodic, rather than continuous, reflecting typical adolescent binge-drinking consumption patterns.[55] An episodic exposure pattern can result in withdrawal episodes following each exposure, which could result in escalating withdrawal signs (e.g., increased anxiety-like behavior, lower seizure threshold, and more severe seizures), particularly in adolescents.[60,61]

Researchers are trying to uncover the neurobiological mechanisms that underlie the retention of adolescent phenotypes after adolescent alcohol exposure. One line of investigation has explored whether animals exposed to AIE retain into adulthood an immature balance of enhanced excitation to inhibition in the brain. Some analyses have assessed the role of gamma-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the brain. Studies found that in the hippocampus, inhibitory effects of GABA responsible for baseline levels of tonic inhibition normally are attenuated in adolescents; however, after AIE, this attenuation is maintained into adulthood.[50,62] Ethanol potentiation of this tonic inhibition is more marked in adolescents than adults—an effect that is maintained into adulthood after AIE.[50,62,63] These adolescent-typical neurophysiological characteristics and their persistence into adulthood may contribute to alcohol's enhanced memory-impairing effects in adolescents and to long-lasting memory impairment seen in adulthood after AIE.[51] More work is needed to identify the overall prevalence of persistent adolescent-typical immaturities after adolescent alcohol exposure under various baseline and challenge conditions, and to further characterize the mechanisms underlying these persisting effects.

Effects on Later Ethanol Consumption

Another potential long-term consequence of adolescent alcohol exposure that may reflect the persistence of adolescent phenotypes is elevated alcohol consumption during adulthood. Findings are mixed as to whether adolescent alcohol exposure increases adult alcohol consumption. The hypothesis is supported by findings that alcohol-preferring rats given free access to ethanol in their home cages throughout adolescence acquired an operant self-administration task for alcohol in adulthood more quickly than animals that did not have access to alcohol during adolescence.[64,65] Moreover, these animals exhibited greater resistance to extinction of the operant task, more spontaneous recovery of self-administration, and elevated response levels during reacquisition of the operant task compared with animals with no history of alcohol exposure. Similar findings were obtained in mice. Animals that had voluntary access to alcohol throughout adolescence consumed more alcohol as adults than mice whose access to alcohol was delayed until adulthood.[66] Rats exposed to alcohol through intermittent intraperitoneal administration in early to mid-adolescence later exhibited increased alcohol consumption, an effect that was not apparent when alcohol exposure was delayed until late adolescence.[41,67]

The findings of increased adult consumption levels following adolescent exposure are not universal, however. In some studies, adolescent rats exposed to alcohol vapor, and mice or rats given free access to alcohol in their home cages did not exhibit increased alcohol consumption during adulthood.[44,68,69] Other researchers found that animals given free access during adolescence to alcohol through an operant task demonstrated no increased operant response during adulthood, although they did show increases in some alcohol-related responses.[30,42]

Several variables may influence whether adolescent alcohol exposure increases adult alcohol consumption, which may explain the diverse findings. These variables include the sex of the animals, genetic background (i.e., the strain of rats or mice used), amount and mode of adolescent alcohol exposure, and assessment method of adult alcohol intake.[43] Also, when adolescent rats were given either a sweetened alcohol solution or the sweetened solution without alcohol, both groups later increased intake only of the solution they were exposed to during adolescence, not the alternate solution.[70] This suggests that increased alcohol intake during adulthood after consuming alcohol during adolescence may reflect increased acceptability of a familiar solution, rather than alcohol-specific effects. Although the existing data suggest that in some cases adolescent alcohol exposure can lead to increased consumption during adulthood, researchers still need to further clarify the circumstances in which these intake-enhancing effects emerge.

Neural Alterations

Alcohol exposure during adolescence has detrimental and potentially long-lasting effects not only on cognition, affect, and behavior, including future alcohol consumption, but also on the structure and function of the brain. Particularly pronounced effects include reductions in the formation of new brain cells (i.e., neurogenesis), long-lasting neuroinflammation, changes in gene expression through epigenetic mechanisms, and alterations in the activities of neurotransmitter systems in several vulnerable brain regions.

Neurogenesis and Cell Death

Adolescence is associated with a variety of neuroanatomical changes, including enhanced neurogenesis in some brain regions (e.g., the hippocampus).[71] Reductions in the numbers of neurons and in the connections between neurons (a process known as pruning) may occur in other regions of the brain (e.g., the PFC).[72] One of the most consistent neurological findings associated with adolescent alcohol ex-

posure is a reduction in neurogenesis and a region-specific increase in cell death and cell damage in the brain. The regions most commonly affected include the frontal cortex, hippocampus, amygdala, NAc, and cerebellum—regions that also undergo significant developmental changes during adolescence.[71,73-75] The adolescent brain seems to be particularly vulnerable to the effects of alcohol exposure because similar disruptions were not observed after equivalent exposure in adulthood.[73] The effects of binge-like exposure during adulthood occurred in different regions of the brain and were less pronounced than the effects of exposure during adolescence.[74]

Adolescent alcohol exposure affects not only the overall number of brain cells in specific brain regions but also their connections with each other. Recent studies investigated the effects of AIE on the structure and function of synapses in the hippocampus, a brain region associated with learning and memory.[76] The analyses found that AIE resulted in a greater proportion of immature relative to mature dendritic spines (specialized sites on neurons that receive and amplify input from signal-emitting neurons) in the brains of AIE animals compared with those of nonexposed adult animals. Animals with AIE also manifested more robust long-term potentiation as adults when they were compared with nonexposed animals, a pattern of neurophysiological activation similar to the pattern normally seen in adolescents. Long-term potentiation is the strengthening of synaptic connections when the synapses are repeatedly activated. Although this process is necessary for learning, greater than normal long-term potentiation has been linked to memory deficits and other learning-related behavioral changes.[76]

Neuroinflammation

Adolescent alcohol exposure has been shown to induce long-term increases in expression of several neuroimmune genes that encode proinflammatory signaling molecules.[77] Adolescent exposure also has been shown to activate Toll-like receptor 4 (TLR4), a receptor in the innate immune system that plays a central role in initiating innate immune responses throughout the body.[77] Ethanol-induced TLR4 activation triggers the expression of various transcription factors that, in turn, promote the expression of proinflammatory cytokines and other mediators of inflammation. In the short term, such proinflammatory responses may be adaptive. However, when these responses are maintained over longer periods, the result is long-lasting neuroinflammation.

In the brain, ethanol-induced activation of TLR4 and its subsequent actions can contribute to brain damage associated with excessive alcohol exposure.[77] For example, in animal studies, activation of TLR4 using a bacterial compound (i.e., lipopolysaccharide) induced a long-lasting reduction in neurogenesis similar to that observed after AIE.[71] In mice that did not produce TLR4, adolescent alcohol exposure did not result in the characteristic inflammatory, cognitive, and behavioral consequences usually associated with this exposure.[40,77]

The role of TLR4 and neuroinflammation in the functional and neural consequences of adolescent alcohol exposure is supported by findings that treatment with an anti-inflammatory compound (i.e., indomethacin) prevented the typical cell death and behavioral deficits seen after AIE.[28] These observations suggest that anti-inflammatory agents may represent a new class of pharmacotherapeutic interventions for preventing, ameliorating, or even reversing some of the long-term consequences of adolescent alcohol exposure.

Epigenetic Mechanisms

Adolescent alcohol exposure also influences gene expression by modifying epigenetic regulatory mechanisms. Adolescent animals exposed to alcohol show alterations in histone acetylation, which, in turn, influences DNA methylation and the level of gene expression.[41,78,79] Such epigenetic alterations have been identified in the amygdala, NAc, and PFC, which are brain structures involved in memory processing, decision-making, and emotional reactions. For example, rats with AIE exhibited persistent increases in histone deacetylation and reductions in histone acetylation in the amygdala,[41] resulting in reduced expression of certain genes (e.g., brain-derived neurotrophic factor [BDNF]). When the alcohol-induced deacetylation was prevented by treatment with a histone deacetylase inhibitor, histone acetylation levels in the amygdala normalized, and the transcription of BDNF was restored.[41] The effects of AIE on histone acetylation levels also may contribute to observed behavioral and neural effects of AIE. Treatment with the deacetylase inhibitor attenuated anxiety-like behaviors, reversed the increase in alcohol intake during adulthood, and normalized the decline in neurogenesis usually exhibited by AIE animals.[41,80]

Neurotransmitter Systems

Alcohol exerts its dose-dependent and region-specific effects largely through direct or indirect interactions with the major neurotransmitter and neuromodulatory systems in the brain, including the GABA system discussed earlier, as well as the dopamine, serotonin, glutamate, acetylcholine, and endocannabinoid systems.[81] However, there is specificity in these effects, and not all systems and brain regions are equally vulnerable. Many of these alcohol-sensitive neurotransmitter and neuromodulatory systems and affected brain regions undergo developmental transformations during adolescence, and they may be especially vulnerable to alcohol-induced perturbations during development. Indeed, AIE has been shown to be associated with alterations in several of these systems, including:

- **Changes in the activity of the dopamine system in the NAc.** Several studies have reported enhanced dopamine function in neurons projecting to the NAc, a pivotal component of the brain's reward system, following AIE. These neurons exhibited increased dopamine-mediated neurotransmission under normal conditions and after an alcohol challenge.[78,82,83] The neurons also exhibited higher basal extracellular dopamine levels.[78,84] Given the critical role that dopamine plays in facilitating reward-related motivation and behaviors, these findings suggest that AIE may enhance the rewarding experiences associated with alcohol, which could promote further alcohol ingestion.
- **Changes in the activity of the glutamate system.** Glutamate is the primary excitatory neurotransmitter in the brain and acts via several types of receptors, including the N-methyl-D-aspartate (NMDA) receptor. AIE has been reported to increase NMDA receptor binding in the frontal cortex, as well as the expression of one subunit of this receptor (i.e., the NR2B subunit).[85] Other research has reported a decrease in the subunit's phosphorylation.[78] Altered NMDA functioning in the PFC has been suggested to disrupt functioning of that brain region and to contribute to the impulsive behavior and the lack of control over drinking that is characteristic of individuals with AUD.[78]
- **Changes in the acetylcholine system in the basal forebrain.** One reliable consequence of AIE observed in rodent studies is a long-lasting decrease in the basal forebrain of the number of neurons that exhibit activity of the choline acetyltransferase enzyme, which is required for synthesis of the neurotransmitter acetylcholine. This effect is seen following adolescent, but not adult, alcohol exposure.[29,31,36,86] These findings suggest that adolescent alcohol exposure impairs the normal cholinergic neurotransmission in the basal forebrain that is crucial for ensuring cortical plasticity and learning. Hence, AIE-induced deficits in the cholinergic system may contribute to future cognitive deficits.

Repeated alcohol use during adolescence induces specific alterations in a variety of neural systems that play critical roles in neural, cognitive, and behavioral function. It is possible that some of these neural alterations reflect positive adaptations to AIE to mitigate long-term consequences of the alcohol exposure. Yet, these potential compensations do not appear to be sufficient, given the growing list of long-term consequences of AIE on later neurocognitive and behavioral function.

Conclusions and Future Directions

Adolescence is characterized by social and emotional development and often is accompanied by experimentation with AODs. Brain development continues during adolescence, and, increasingly, adolescence is being viewed as a period of enhanced brain plasticity and experience-related brain sculpting. Many adolescent experiences (e.g., education, sports, and positive social interactions) provide beneficial long-term sculpting. Other influences, such as repeated exposure to alcohol, can be detrimental and have long-term effects on neural functioning, cognition, and behavior, including enhanced AOD consumption, that persist into adulthood.

Studies conducted primarily using rodent models of adolescence have shown that propensity for the initiation and escalation of alcohol use during adolescence may be promoted by adolescents' greater sensitivity to the socially facilitating and rewarding effects of alcohol, combined with a reduced sensitivity to other effects (e.g., social and motor impairment, and sedative and aversive effects) that likely serve as cues to terminate intake. Animal studies have shown that repeated exposure to alcohol during adolescence, especially AIE that mirrors binge-drinking patterns observed in human adolescents, induces specific patterns of sustained neurobehavioral alterations that may promote further drinking. Particularly worrisome are reports that adolescent alcohol exposure may lead to the retention of adolescent phenotypes—including adolescent-typical responses to alcohol—into adulthood. Other cognitive, behavioral, and affective consequences have been reported after AIE, including impaired performance of executive functions, memory impairment, reduced cognitive flexibility, greater risk preference and disinhibition, and elevated social (and sometimes general) anxiety. In many cases these effects are specific to adolescent alcohol exposure and are not evident after equivalent alcohol exposure during adulthood.

Animal studies also have identified lasting neural alterations induced by AIE that may contribute to behavioral and cognitive changes. These changes include reduced neurogenesis, increased neuroinflammation, epigenetic alterations, and alterations in numerous neurotransmitter systems, including glutamate, GABA, the balance between these excitatory and inhibitory systems, dopamine, and the basal forebrain cholinergic system. When different age groups were compared, the consequences typically were more pronounced after adolescent alcohol exposure than after equivalent adult exposure. Likely anatomical targets for these long-term effects include the hippocampus, amygdala, NAc, and PFC. These neural systems underlie the developmental shifts in sensitivity to drug rewards and drug aversion that normally occur during adolescence and adulthood. These systems are also involved in neurodevelopmental processes related to socioemotional

functioning and advanced aspects of cognitive functioning.

Despite the progress achieved using animal models for understanding the consequences of adolescent alcohol exposure and, particularly, the intermittent, binge-like exposures characteristic of this age, many questions remain. For example, additional research is needed to elucidate how AIE affects the neural mechanisms underlying the enhanced reward and attenuated aversive sensitivities that are normally seen during adolescence and are maintained into adulthood after AIE, as well as how these mechanisms contribute to later alcohol consumption. It also will be crucial to determine if lasting functional consequences of adolescent alcohol exposure can be prevented, attenuated, or reversed by blocking alcohol-induced neural alterations. Similarly, researchers need to further elucidate the persistence of adolescent phenotypes into adulthood that has been reported after adolescent alcohol exposure. The breadth and limitations of this adolescent-like persistence across different functional domains, its stability over time, and whether it can be reversed or modified all need to be examined. It is undoubtedly useful and necessary to use animal models to study contributors to and consequences of adolescent-typical behaviors such as alcohol consumption. Nonetheless, the findings are only useful if they prove valid, applicable to predicting the effects of adolescent alcohol exposure in humans, and ultimately relevant to prevention and treatment.

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Effects of Binge Drinking on the Developing Brain

Studies in Humans

Scott A. Jones, Jordan M. Lueras, and Bonnie J. Nagel

Binge drinking is a pattern of alcohol drinking that raises a person's blood alcohol concentration to at least .08%, which amounts to consuming five alcoholic drinks for men and four alcoholic drinks for women in about 2 hours. It is the most common form of alcohol misuse in adolescents and young adults. Heavy drinking includes the same criterion as binge drinking, but with higher frequency (i.e., 5 or more days in the past 30 days). Although binge drinking or heavy drinking alone is insufficient to meet the criteria for an alcohol use disorder (AUD) diagnosis, there are neurobiological changes, as well as an increased risk of developing an AUD later in life, associated with this form of alcohol misuse. This review describes the recent neuroimaging findings in binge drinking and heavy-drinking adolescents and young adults, a developmental period during which significant neuromaturation occurs.

Key words: Alcohol misuse; binge drinking; college drinking; neurodevelopment; neuroimaging; young adults

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It has been well established that the brain undergoes significant maturation during adolescence that continues into young adulthood.[1] Studies using structural magnetic resonance imaging have described linear and nonlinear changes in cortical gray-matter volume and thickness[2-5] and increases in white-matter volume and integrity[2,6-9] occurring during development. Gray-matter volume peaks earlier in females (i.e., around age 11) than in males (i.e., around age 12) and declines during adolescence due to pruning of unused synaptic connections in order to promote efficient communication between neurons.[6] Furthermore, gray matter has been shown to reach earlier maturation in the sensorimotor cortices, whereas the frontal and temporal cortices mature later in development.[4] The prefrontal cortex, which is central to executive control, matures later compared with earlier developing limbic structures thought to be more involved in reward and emotional processing.[6,10,11] The asynchronous development of the prefrontal cortex and emotional and reward circuitry has been hypothesized to result in increased risk-taking behavior during adolescence, such as alcohol use.[12-15] This is especially of concern because ongoing neurodevelopment may render the adolescent brain particularly vulnerable to the neurotoxic effects of alcohol, as has been shown repeatedly in animal models.[16-19]

Binge drinking is a pattern of alcohol drinking that raises a person's blood alcohol concentration to at least .08%, which amounts to consuming five alcoholic drinks for men and four alcoholic drinks for women in about 2 hours.[20] It is the most common pattern of alcohol consumption in adolescents and young adults. As of 2014, 1.5 million adolescents ages 12 to 17 (6.1%) and 13.2 million young adults ages 18 to 25 (37.7%) in the United States reported binge drinking.[21] Heavy drinking includes the same criterion as binge drinking, but with higher frequency (i.e., 5 or more days in the past 30 days).[21] In the National Survey on Drug Use and Health, 257,000 adolescents (1%) and 3.8 million young adults (10.8%) reported heavy drinking.[21] Although binge or heavy drinking alone is insufficient to meet criteria for an alcohol use disorder (AUD) diagnosis, there are neurobiological changes, as well as an increased risk of developing an AUD later in life, associated with this form of alcohol misuse.[22] This article reviews neuroimaging studies assessing the effects of binge and heavy drinking on brain structure and function in adolescents. Studies in which participants met criteria for AUD were not included. Further, the age range included studies in adolescents and young adults, which extends up to a mean age of 25, because brain matu-

ration continues to occur well into the late 20s.[2]

Effects on Brain Structure—Gray Matter

Volume

Cross-sectional studies in binge drinking adolescents and college-age individuals have demonstrated regions of both more and less gray-matter volume compared with nondrinking peers, with volumes often related to frequency and quantity of alcohol consumption. For example, a recent study found that adolescents and young adults who consumed moderate to high levels of alcohol had smaller total-brain, frontal-lobe, and temporal-lobe volumes than their nondrinking peers; however, they also found that a greater number of lifetime drinks was positively associated with greater temporal-lobe volume.[9] In support of the notion that binge drinking is associated with lower gray-matter volume, a study of college-age binge drinkers found that higher Alcohol Use Disorders Identification Test (AUDIT) scores, indicative of greater reported frequency and quantity of alcohol consumption and alcohol-related problems, were associated with smaller frontal-lobe volumes.[23] An association between alcohol use and smaller gray-matter volume also was supported by another study that identified smaller precuneus volumes in a group of college-age binge drinkers compared with alcohol-naïve controls.[24] Further, greater AUDIT scores again were associated with smaller gray-matter volumes in the amygdala and hippocampus.[24] Additionally, among binge drinking adolescents, greater peak number of drinks in the past 3 months was associated with decreased cerebellar gray-matter volume.[25] Together, these findings suggest that binge drinking during development is associated with various regions of lower cortical, subcortical, and cerebellar brain volume, and that these changes often are associated with alcohol drinking characteristics.

Contrary to findings of smaller brain volumes, Howell and colleagues reported greater ventral striatal, thalamic, and lingual-gyrus volumes in college-age binge drinkers compared with control subjects.[24] A study on binge drinking, college-age participants also found increased frontal, occipital, anterior cingulate cortex (ACC), and posterior cingulate cortex volumes compared with nondrinking control subjects.[26] In this study, larger dorsolateral prefrontal cortex (DLPFC) volumes were positively associated with speed and quantity of alcohol consumption and negatively associated with age of onset of alcohol use.[26] It is worth noting that these individuals reported binge drinking for a minimum of 3 years prior to neuroimaging sessions, suggesting that volumetric increases in regional gray matter may be associated with long-term binge drinking.

In addition to these disparate findings in gray-matter volume, sex-specific effects also have been observed in college-age binge drinkers. Kvamme and colleagues noted a significant sex-by-drinking status interaction in numerous prefrontal, parietal, temporal, and striatal regions, such that binge drinking males had smaller volumes than alcohol-naïve males, whereas binge drinking females had larger volumes than alcohol-naïve females.[23] Although these sex-specific effects partially may explain the bidirectional effects seen in previous studies, there are likely many other factors that could contribute to these disparate findings, including the inability of cross-sectional designs to capture alterations in nonlinear developmental trajectories.[2-5]

To better address volume-related changes associated with drinking, longitudinal studies have begun to investigate gray-matter volume both before and after binge drinking. The first of such studies examined heavy-drinking adolescents with a baseline magnetic resonance imaging scan when the subjects were alcohol naïve and a follow-up scan approximately 3 years later, after binge drinking. At baseline, adolescents who later transitioned into heavy drinking had smaller ACC, posterior cingulate cortex, and inferior frontal gyrus (IFG) gray-matter volumes.[27] Furthermore, heavy-drinking adolescents showed accelerated reductions in the thalamus/hypothalamus, inferior temporal gyrus, middle temporal gyrus (miTG), caudate, and brain stem, with greater lifetime alcohol use associated with a greater reduction in gray-matter volume in the left caudate and brainstem.[27]

A follow-up to this study that investigated gray-matter volumes in heavy-drinking adolescents at baseline and during multiple follow-ups found that heavy drinkers exhibited greater reductions in overall neocortex volume, as well as in frontal, lateral frontal, and temporal cortex volumes.[28] Finally, Whelan and colleagues used machine-learning techniques to classify adolescents before and after initiation of binge drinking.[29] They reported that before alcohol use, binge drinking adolescents had lower gray-matter volume in the superior frontal gyri (SFG) and greater volume in the premotor cortex compared to nondrinking control subjects. After alcohol initiation, however, smaller ventral medial prefrontal cortex (PFC) and IFG volumes were observed compared with nondrinking controls.[29] Taken together, these findings suggest that binge drinking during development may result in accelerated decreases in gray-matter volume, above and beyond what is seen in typical maturation, likely caused by the neurotoxic effect of alcohol. It also is possible, based on evidence from cross-sectional studies in college-age individuals (described above), that a longer duration of alcohol use into young adulthood may result in greater gray-matter volumes in young adults who binge drink, potentially because of impaired synaptic pruning. Additional longitudinal studies with multiple time points will be necessary to elucidate alcohol's

effects on the full developmental trajectory across adolescence and young adulthood.

Cortical Thickness

Generally, studies investigating cortical thickness in binge drinking adolescents have supported findings of decreases in gray matter. Similar to their gray-matter volume findings noted above, Pfefferbaum and colleagues noted that alcohol-consuming adolescents had thinner total, frontal, temporal, and cingulate cortices than nondrinkers; moreover, the number of binge drinking episodes in the past year was negatively associated with frontal and parietal cortex thickness.[9] This finding is in agreement with another cross-sectional study of young adults, which determined that binge drinkers had thinner cortical measures in the ACC and posterior cingulate cortex compared with light drinkers (i.e., consuming one or two drinks per week, but no binge episodes).[30] Further, ACC cortical thickness was negatively correlated with the number of drinking occasions and number of drinks per occasion in the past 3 months, indicating that greater frequency and quantity of use is associated with thinner cortices.[30]

Similar to the volumetric study previously cited, sex-specific effects also have become apparent when investigating cortical thickness in binge drinking adolescents.[23] A cross-sectional study in binge drinkers identified sex-by-drinking status interactions for cortical-thickness measures in four frontal regions (i.e., frontal pole, pars orbitalis, medial orbital frontal, and rostral anterior cingulate). Thus, binge drinking males had thinner cortices than alcohol-naïve control subjects, whereas binge drinking females had thicker cortices than alcohol-naïve control subjects.[31] The directionality of these findings is consistent with those of Kvamme and colleagues.[23] The findings suggest that during this particular window of development, alcohol may have differential effects for boys and girls, likely resulting from underlying sex differences in the rate and timing of synaptic pruning in adolescents.[6]

In a longitudinal investigation of the effects of binge drinking on cortical thickness, Luciana and colleagues found that adolescents who initiated alcohol use showed a significantly greater decrease in middle frontal gyrus (miFG) cortical thickness between baseline and revisit compared with adolescents who remained alcohol naïve,[32] suggesting that alcohol has a neurotoxic effect on frontal lobe development. However, this study found no differences in cortical thickness prior to initiation of alcohol use, contrary to a subsequent study observing differences in baseline gray-matter volume.[27] Other studies have investigated the effects of binge drinking on cortical thickness in a longitudinal manner, but without an alcohol-naïve baseline. Jacobus and colleagues examined cortical thickness over 3 years and found that concomitantly binge drinking and marijuana using adolescents had thicker cortices across time in five frontal, eight parietal, one temporal, and one occipital region compared with alcohol- and marijuana-naïve control subjects.[33] Moreover, in three frontal regions, control subjects showed a decrease in cortical thickness across time, whereas concomitantly binge drinking and marijuana using adolescents did not. A prior study had suggested that these effects persisted following abstinence, because concomitantly binge drinking and marijuana using adolescents showed greater thickness in the ACC, medial temporal gyrus, lingual gyrus, and occipital cortex both before and after 28 days of monitored abstinence.[34]

Taken together, these studies suggest that, when combined with marijuana use, binge drinking may result in increases, as opposed to decreases, in cortical thickness, that these increases are cumulative with prolonged use, and that they persist even following a month of abstinence. Furthermore, although these studies contradict some literature,[9,30,32] they may help provide an alternative explanation for the equivocal findings in gray-matter volume described above. In fact, in the longitudinal study by Squeglia and colleagues, although a greater number of lifetime alcohol-use occasions was associated with greater reductions in caudate and brainstem volume, a greater number of lifetime marijuana uses was associated with increases in caudate volume.[27] This provides further evidence that although gray-matter volume and thickness typically decrease in binge drinking adolescents and young adults, concomitant marijuana use may result in observed increased volume and thickness.

Effects on Brain Structure—White Matter

Volume

As opposed to the varied findings in gray-matter volume, results in white-matter volume have been more parsimonious. Cross-sectional studies have shown that a greater number of lifetime drinks was associated with smaller central white-matter volume,[9] and peak number of drinks during a binge episode in the past 3 months was associated with smaller cerebellar volumes.[25] Longitudinal studies tell a similar story, with binge drinking adolescents showing reduced white-matter volumes both before[27] and following initiation of binge drinking.[28,32] Squeglia and colleagues found that heavy-drinking adolescents had lower baseline cerebellar white-matter volumes compared with control subjects, but the investigators identified no regions where white-matter volume changed differentially across time.[27] However, in a follow-up study, heavy-drinking adolescents exhibited significantly attenuated white-matter growth in the pons and corpus callosum between baseline and follow-up scans, compared with controls.[28] Luciana and colleagues reported similar findings, such that alcohol-naïve controls showed an increase in vol-

ume in white-matter regions of the precentral gyrus, miTG, SFG, and lingual gyrus between baseline and follow-up, whereas binge drinking adolescents did not.[32] Taken together, these observations suggest that reduced white-matter volume may precede alcohol use, and that alcohol use during adolescence attenuates the typical maturational increase in white-matter volume observed in adolescence in a dose-related fashion.[2,6-8]

Microstructure

Varied differences in white-matter microstructure have been observed between binge drinking adolescents (with and without concomitant marijuana use) and non–alcohol using controls. First, a cross-sectional diffusion tensor imaging study investigating fractional anisotropy (FA)—a measure thought to reflect white-matter myelination and axonal integrity and coherence—found that binge drinking adolescents had lower FA than control subjects in seven frontal, three parietal, two temporal, four subcortical, and two cerebellar regions. Furthermore, in six of these regions, lower FA was associated with significantly greater lifetime hangover symptoms and higher estimated peak blood alcohol concentrations.[35]

In a second cross-sectional study, concomitant binge drinking and substance using adolescents had lower FA than control subjects in 10 separate frontal, parietal, temporal, and subcortical regions, and reduced FA in these regions was associated with greater lifetime alcohol use.[36] Interestingly, the investigators also noted three regions (i.e., the superior longitudinal fasciculus, internal capsule, and occipital lobe) where FA was greater in concomitant binge drinking and substance using adolescents than in control subjects, and they found that greater FA in these regions was associated with greater lifetime alcohol use.

Finally, a third cross-sectional study of binge drinking adolescents and concomitant binge drinking and substance using adolescents found that binge drinking adolescents, again, had lower FA than control subjects in eight different regions, including the superior corona radiata (SCR), inferior longitudinal fasciculus, superior longitudinal fasciculus (SLF), inferior fronto-occipital fasciculus (IFOF), and cerebellar peduncle.[37] Those with concomitant substance use, in contrast, only had significantly lower FA (compared with control subjects) in three regions, including the SCR and SLF, and they had significantly higher FA than binge drinking adolescents in four regions (i.e., the SCR, SLF, IFOF, and cerebellar peduncle). In this study, greater marijuana use frequency was associated with greater FA in the SCR and SLF, whereas a greater number of lifetime drinks was associated with greater FA in the SLF. Together, these findings suggest that binge drinking during adolescence is associated with reduced FA, but that concomitant marijuana use may interact with the effects of alcohol, resulting in an alteration of this effect.

These cross-sectional findings have been corroborated by numerous longitudinal studies. Luciana and colleagues reported that compared with control subjects, adolescent binge drinkers showed significantly diminished normative increases in FA in the dorsal caudate and IFOF between baseline and follow-up visit.[32] Another study found that concomitant binge drinking and substance using adolescents had reduced FA in the corpus callosum, prefrontal thalamic fibers, and posterior corona radiata at follow-up, compared with control subjects, with no differences reported at baseline.[38]

A series of studies examined FA in a group of binge drinking and concomitant binge drinking and substance using adolescents and young adults at baseline and follow-up.[39-41] First, they found that binge drinking adolescents both with and without concomitant substance use showed a significant, widespread decline in FA across the three visits, resulting in lower FA after 3 years of use compared with control subjects.[39] Moreover, lower FA in the fornix and SCR at baseline in concomitant binge drinking and substance using adolescents predicted greater subsequent use at the first follow-up, above and beyond baseline substance use.[40] It is important to note that in these two studies,[39] adolescent binge drinkers and substance users were not drug and alcohol naïve at baseline; rather, they were drinking and using marijuana throughout the entirety of the study. Lastly, Jacobus and colleagues identified 20 regions in the brain where there was a significant group-by-time interaction, such that adolescents who used both alcohol and marijuana concomitantly showed a sharper decline in FA between baseline and 3-year follow-up than those who only binge drank.[41] In combination, these findings suggest that whereas binge drinking during adolescence and young adulthood appears to be associated with reduced FA, results tend to be less clear when adolescents concomitantly use marijuana. Whereas Jacobus and colleagues found that binge drinkers with concomitant marijuana use initially had had greater FA than those who only binge drank,[37] a longer history of concomitant marijuana use, extending into young adulthood, may eventually result in a steeper decline in FA across development.[41]

Effects on Brain Function

Verbal Encoding

Learning and memory abilities are crucial for an adolescent's success, and development of those abilities may be altered or attenuated by alcohol use. Verbal encoding/learning, using a verbal paired-association task, has been used to investigate the impact of alcohol on learning and memory in binge drinking adolescents with and without comorbid marijuana use. A preliminary study found that binge drinking adolescents had greater activation in the SFG, superior parietal lobule,

inferior parietal lobule (IPL), and the cingulate, as well as lower activation in one cluster encompassing the cuneus, precuneus, lingual gyrus, and parahippocampal gyrus (PHG) during novel word encoding.[42]

In a follow-up investigation, Schweinsburg and colleagues found that binge drinking and concomitant binge drinking and substance using adolescents, when compared with marijuana-only users and control subjects, showed greater encoding-related activation in the postcentral gyrus, IPL, and SFG, and less activation in the fusiform gyrus, PHG, cuneus, precuneus, IPL, IFG, precentral gyrus, and cingulate.[43] They also identified regions of the brain (i.e., the IFG, miFG, SFG, and cuneus) where users of either alcohol or marijuana showed greater brain response than nonusers during novel word encoding, whereas users of both substances resembled nonusers. Because performance on the task was the same between binge drinkers and control subjects,[42,43] these findings suggest that alcohol use during adolescence may cause adolescents to adopt a different neural strategy (e.g., heavier prefrontal-cortex recruitment) to achieve the same successful verbal encoding. Because of the cross-sectional design, it is unknown whether these differences were present prior to or developed as a consequence of alcohol consumption.

Working Memory

Brain response during working memory also has been shown to be altered in binge drinking adolescents and young adults. In a preliminary study, Tapert and colleagues found that brain response during a visual working memory task was negatively associated with subjective response to alcohol, such that adolescents who reported that a greater quantity of alcohol was needed to feel an effect showed greater activation in the SFG, cingulate, cerebellum, and PHG during memory retrieval.[44] A subsequent study showed that binge drinking adolescents had greater activation in the medial frontal gyrus (meFG), SFG, IPL, and supramarginal gyrus, as well as less activation in the middle occipital gyrus, when compared with control subjects.[45] Furthermore, in longitudinal analyses, binge drinking adolescents actually had lower activation in the IPL and meFG at baseline (i.e., prior to drinking), but when compared with control subjects, they showed a greater increase across time. These greater increases in brain activation were associated with a greater peak number of drinks in the past year, more past-month drinking days, and greater withdrawal/hangover symptoms at follow-up.[45] Further, less premorbid activation in the meFG and IPL predicted a higher peak number of drinks and drinking days in the year preceding follow-up.[45] This suggests that binge drinking not only affects neural response during working memory, but that baseline differences in brain activation during working memory may be useful in identifying adolescents who may go on to drink.

These findings also are supported by cross-sectional work using other working memory tasks. One study found that during verbal working memory, binge drinking young adults had greater activation in the parietal cortex (pre–supplementary motor area) than control subjects.[46] Moreover, more drinks per drinking occasion were associated with greater dorsal medial PFC activation, whereas more drinking occasions per week were associated with greater cerebellar, thalamic, and insular activation. In contrast, Squeglia and colleagues reported that binge drinking adolescents had lower activation in the SFG and IFG compared with control subjects.[47] However, this study differed in two ways from the previous studies. Squeglia and colleagues used a spatial working memory task and also reported significant sex differences, such that binge drinking females showed less activation than control subjects, and binge drinking males showed greater activation than control subjects in the SFG, IFG, ACC, miFG, miTG, superior temporal gyrus, and cerebellum. These findings suggest that, in general, adolescents show alcohol-related increases in activation, particularly in fronto-parietal networks during working memory; however, at least for spatial working memory, these findings may be sex specific. Further work is necessary to tease out the different elements (e.g., spatial versus verbal) of working memory and the effects of alcohol on their associated neural responses.

Risk Taking and Reward Response

Because adolescence is a time of increased risk taking, including experimentation with alcohol, it may come as no surprise that binge drinking adolescents show altered brain response during various phases of risk taking. Whereas some investigators have attempted to elucidate binge drinking's effects on a particular aspect of risk-taking behavior,[48-50] others have investigated risk taking more broadly.[51] In a study looking at risk-taking behavior using the Iowa Gambling Task, binge drinking adolescents had greater risk-related activation in the amygdala and insula compared with control subjects, and they had more reported drinking problems related to less activation in the orbitofrontal cortex (OFC) and more activation in the insula.[51] Two recent studies separately investigated the effects of binge drinking during adolescence during decision making and reward receipt. In the first study, binge drinking adolescents, compared with control subjects, showed reduced cerebellar response during reward receipt following initiation of binge drinking, a finding that remained significant when controlling for premorbid activation, and which was associated with more drinks per drinking day in the past 90 days.[48]

A longitudinal investigation found that binge drinking adolescents, compared with control subjects, had lower

activation in the IFG, IPL, miTG, and superior temporal gyrus across time, suggesting a different pattern of brain activation that occurs prior to binge drinking and persists after alcohol initiation.[49] There also was a significant group-by-time interaction in the dorsal caudate, such that binge drinking adolescents showed similar risky decision-making–related brain responses as controls at baseline, but they showed a reduced response following binge drinking. This reduction was associated with a greater number of drinking days and heavy drinking days in the previous 3 months.

Further, Worbe and colleagues used a novel risk-taking gambling task in binge drinking young adults to investigate brain responses during the decision-making and feedback phases of both reward and loss gambles.[50] During decision making in conditions with both a low and high potential for a loss, the study found that binge drinkers had greater activation in the OFC, superior parietal cortex, and DLPFC compared with control subjects. This finding was accompanied by more risky decisions during high-loss selections. Furthermore, although giving feedback during the task reduced the amount of risky decisions in binge drinking young adults, it also was associated with greater activity in the IFG and IPL, when compared with control subjects.

In addition to studies looking at adolescent risk-taking behavior, a study by Whelan and colleagues investigated brain responses during reward anticipation and receipt outside of the context of risk, using the monetary incentive delay task.[29] The study demonstrated that, compared with control subjects, adolescent binge drinkers had greater activation during reward receipt in the SFG prior to initiation of binge drinking, but they had reduced activation during reward anticipation and receipt in the ventral medial PFC and IFG after binge drinking. Taken together, these findings suggest that binge drinking during adolescence and young adulthood is associated with alcohol-related alterations in brain response during decision making and reward/consequence notification. Further, group differences in fronto-parietal brain response during risky decision making and reward receipt that occur prior to drinking may serve as a risk factor for future drinking.[29,49]

Inhibition

Several longitudinal studies have used a standard go/no-go procedure to investigate the effects of binge drinking on brain response during inhibition. One study found that, at baseline, adolescents who went on to engage in heavy drinking had reduced brain response during successful inhibition in the DLPFC, miFG, SFG, IFG, meFG, paracentral lobules, cingulate, putamen, miTG, IPL, and pons, compared with adolescents who remained alcohol naïve.[52] In another study, less activation during successful inhibition in the ventral medial PFC predicted more alcohol dependence symptoms in heavy-drinking adolescents at 18-month follow-up.[53] Meanwhile, in a study investigating the failure to inhibit responding, greater activation in the premotor cortex served as a risk factor for adolescents who later went on to engage in binge drinking.[29] Together, these studies suggest that lower engagement of numerous regions, particularly within the fronto-parietal network, during successful inhibition, as well as greater engagement of premotor regions during unsuccessful inhibition, may precede the onset of binge drinking.

Furthermore, compared with alcohol-naïve control subjects, heavy-drinking adolescents were shown to have significantly lower levels of brain activation during inhibition in the miFG, IPL, putamen, and cerebellum at baseline.[54] They also showed greater increases in inhibition-related brain responses, compared to controls, following initiation of heavy drinking. Greater increases in brain response during response inhibition between baseline and follow-up were associated with more lifetime drinks. The same group of researchers also found that these patterns of activation differed in adolescents who experienced alcohol-induced blackouts. Prior to initiation of heavy drinking, adolescents who did and did not experience alcohol-induced blackouts showed less activation in the IPL compared with control subjects.[55] However, adolescents who went on to experience alcohol-induced blackouts showed greater activation during inhibition in the miFG, miTG, cerebellum, and parietal cortex (pre–supplementary motor area) compared with those who did not experience blackouts. These findings suggest that adolescents who later experience alcohol-induced blackouts show patterns of brain activation during inhibition, which may render them more vulnerable to the memory-impairing effects of alcohol.

Lastly, a recent study in binge drinking young adults found that those who escalated drinking over a 12-month period had greater fronto-parietal activation during inhibition compared with young adults who maintained stable drinking levels.[56] Taken together, it appears that hypoactivation of the fronto-parietal network during inhibition may serve as a risk factor for alcohol use initiation; however, after alcohol use initiation, hyperactivation of the fronto-parietal network during inhibition may serve as a risk factor for escalation of drinking.

Cue Reactivity

Two recent studies have looked at brain activation elicited by an alcohol cue (i.e., cue reactivity), using an alcohol pictures task, in binge drinking adolescents and young adults. Dager and colleagues found that young adults who transitioned from moderate to heavy drinking over a 1-year follow-up had greater activation at baseline in the caudate, ACC, medial prefrontal cortex, precentral gyrus, insula, IFG, and OFC, compared with those who

remained moderate drinkers or heavy drinkers throughout the study.[57] Furthermore, brain activation in this network of regions predicted future drinking and alcohol-related problems, above and beyond baseline drinking characteristics. This suggests that changes in how the brain responds to alcohol cues may help predict which individuals may transition from light to heavy drinking and may be more informative than simply comparing heavy drinkers with control subjects. In another study, heavy-drinking adolescents had greater cue-elicited brain response in the dorsal striatum, cerebellum, PHG, and thalamus than control subjects prior to abstinence; however, the group differences in the cerebellum and ACC no longer remained significant after 28 days of abstinence.[58] This suggests that although cue-elicited brain response may be a predictor of future drinking, if adolescents manage to maintain abstinence, they may be able to reduce that cue-elicited response. This finding has important implications for future intervention strategies.

Effects on Behavior and Cognition

Many of the structural and functional differences observed in adolescent binge drinkers also are associated with changes in cognition and behavior. Several studies have examined neurocognitive changes related to binge drinking and reported poorer performance in many domains, including attention,[59,60] learning and memory,[59,61-66] and visuospatial functioning.[60] Neuroimaging studies have found that the poorer sustained attention observed in binge drinking adolescents is associated with thicker PFCs[31] and lower FA in the inferior longitudinal fasciculus[67]—regions where thickness and FA differed significantly between binge drinking adolescents and control subjects. This suggests that binge drinking during adolescence may cause a delay in the maturation of both gray and white matter, resulting in poorer sustained attention.

Furthermore, binge drinking adolescents and young adults have demonstrated impaired performance on a variety of learning and memory tasks.[59,61,62,64,65] These findings also have been associated with changes in brain structure in binge drinking adolescents in regions of the brain where these adolescents differ from control subjects. Binge drinking–related deficits in working memory also have been demonstrated,[61,63] with one study showing that after 3 years of binge drinking, greater gray-matter volume in the DLPFC was positively associated with working-memory errors.[26] Further, decreased FA in the inferior longitudinal fasciculus in binge drinking and substance using adolescents has been shown to be associated with poorer working-memory performance.[67] In addition, although an initial study found that the number of drinking days in the past year predicted greater reductions in performance on a visuospatial task,[60] a follow-up study showed that thicker frontal cortices corresponded with poorer visuospatial performance in binge drinking females.[31] These findings suggest that delayed cortical maturation may underlie the effects of binge drinking on visuospatial performance.

Binge drinking adolescents also demonstrate impaired, or riskier, decision making,[68] likely resulting from impairments in impulsivity[69] and inhibition.[64] One study found that young adults who showed stable, high levels of binge drinking made riskier choices on the Iowa Gambling Task compared with adolescents who engaged in stable, low levels of binge drinking.[68] Other studies have reported that heavy-drinking adolescents show greater impulsivity than light drinkers[69] and that binge drinking adolescents show impaired inhibition compared with control subjects.[64]

Neuroimaging studies have helped shed some light on the mechanisms underlying this impaired decision making and impulse control. Structurally, greater impulsivity in adolescent binge drinkers has been shown to be associated with smaller DLPFC and IPL volumes and greater dorsal cingulate and precuneus volumes,[70] whereas reduced FA in the fornix of concomitant binge drinking and substance using adolescents has been shown to predict greater amounts of risky behavior a year and a half later.[40] Functionally, riskier behavior on the Iowa Gambling Task in binge drinking adolescents has been accompanied by greater activation in the insula and amygdala, when compared with control subjects.[51] Also, as described above, greater activation in the OFC, superior parietal cortex, and DLPFC, when compared with controls, has been associated with more risky decisions when there was a high potential for loss.[50] Taken together, these findings suggest that the underdevelopment of control regions (e.g., smaller DLPFC and IPL volumes) and hyperactivation of reward-salience regions (e.g., amygdala), both of which are hallmarks of adolescent neurodevelopment, may be exacerbated in adolescents who binge drink and may underlie the observed increase in risk-taking behavior in binge drinking adolescents.

Conclusions

Although evidence is still emerging on how binge drinking during adolescence and young adulthood affects the brain, many general conclusions can be drawn from current literature (for a summary of all replicated findings in binge drinking adolescents and young adults, see Figure 1). First, binge drinking during adolescence appears to result in a decrease in both gray-matter volume and cortical gray-matter thickness,[9,30] with longitudinal studies suggesting that some of these differences may be present prior to binge drinking and continue to worsen as adolescents initiate alcohol consumption.[27,28,32] Although it must be noted that some studies show increased gray-matter volume or thickness in binge drinking

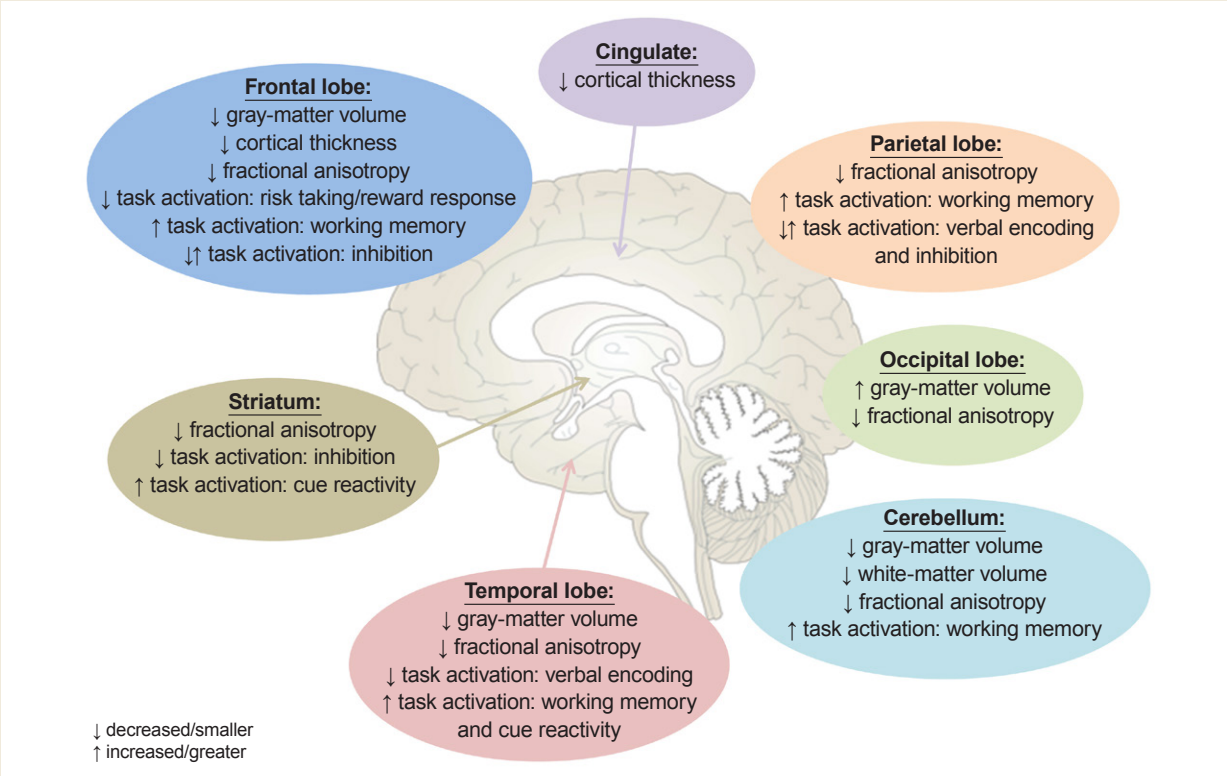

Figure 1 Replicated findings in binge drinking adolescents and young adults.

adolescents, it is plausible that these contradictory findings either are caused by the influence of concomitant marijuana use[33,34] or are the result of examining the effects of binge drinking on a nonlinear developmental pattern[2-5] in a cross-sectional manner.[24,26]

Second, multiple studies consistently have shown that the developmental increases in white-matter volume, often observed in adolescents,[2,6-8] appear to be attenuated in adolescents who binge drink,[27,28,32] and that this attenuation is associated with the degree of substance use.[9,25] However, studies demonstrating altered white-matter microstructure in binge drinking adolescents have yielded mixed results, showing both increases and decreases in FA. Again, it appears that this may partially be explained by the presence of concomitant marijuana use in adolescence.[36,38-41] More studies comparing concomitant users to those using only alcohol or marijuana likely are necessary to completely disentangle these effects.

Functionally, binge drinking during adolescence appears to affect brain responses in numerous regions, across a variety of tasks. Cross-sectional work has identified both increased and decreased brain activation in multiple task domains (e.g., verbal learning, working memory, risk taking, cue reactivity, and inhibition) and demonstrates the necessity of longitudinal studies to determine which effects are a result of alcohol consumption and which reflect an underlying risk phenotype for those who will go on to binge drink. Longitudinal work, specifically in working memory[45] and response inhibition,[52,54] suggests that binge drinking adolescents demonstrate similar or lower levels of brain activation in task-relevant regions at baseline, followed by an exacerbated increase in activation, above and beyond that seen in control subjects, after initiation of binge drinking. A failure to recruit task-relevant regions at baseline in future binge drinkers could lead to poorer task performance, while hyperactivation following alcohol use suggests that binge drinking adolescents require more recruitment of task-relevant networks to achieve desired cognitive outcomes.

Meanwhile, similar or lower levels of brain activation during risk-taking behavior (i.e., risky decision making and reward response) also have been observed in binge drinking adolescents.[48,49] However, unlike during working memory and response inhibition, binge drinking adolescents have lower levels of brain response over time during risky decision making and

reward response. This may suggest not only a pattern of activation during risky decision making that may serve as a risk factor for future drinking,[49] but also a diminished brain response to risky stimuli and rewards following binge drinking.[48,49] This decreased brain response may be what causes binge drinking adolescents to show greater risky behavior and may enhance reward seeking.

Understanding these altered neurobiological features in binge drinking adolescents is extremely relevant, because changes in both brain structure and function have been related to changes in cognition in binge drinking adolescents.[26,31,40,50,51,60,67,70] Moreover, not only do differences in task activation serve as risk factors for future drinking,[45,49,52,54] but neurobiological features, such as fronto-parietal hyperactivation during inhibition and atypical white-matter microstructure, may serve as risk factors for escalated drinking and risk-taking behavior in adolescents who are already drinking.[40,56] Adolescent onset of alcohol use has been associated with an increased risk for developing an AUD later in life;[22] thus, understanding neurobiological markers that are associated with both initiation and escalation of alcohol use is important for advancing future prevention and intervention strategies in an effort to reduce the rates of AUD.

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The authors declare that they have no competing financial interests.

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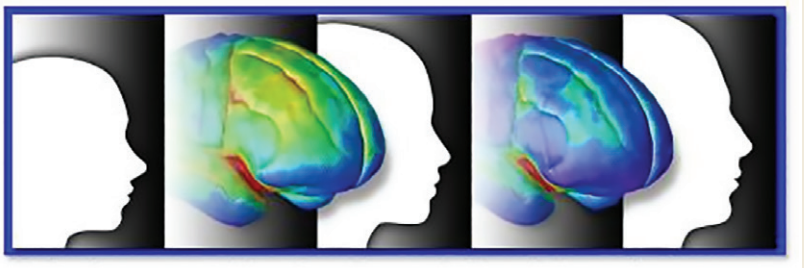
NIH's Adolescent Brain Cognitive Development (ABCD) Study

Alcohol Research: Current Reviews Editorial Staff

Adolescence is the stage of life during which most people begin using alcohol, and it is also a time of considerable social, psychological, and physiological change. The brain, particularly the frontal cortex, continues to develop throughout adolescence and does not fully mature until early adulthood. Adolescent alcohol exposure can impair brain development, compromise short- and long-term cognitive functioning, and increase the likelihood of developing alcohol-related problems during adolescence and later in life. Furthering our understanding of the developing brain—as well as how differences in brain structure and function that exist prior to alcohol and other substance use contribute to substance use disorders—is a high priority for the National Institutes of Health (NIH).

In September 2015, NIH launched the Adolescent Brain Cognitive Development (ABCD) Study, the largest long-term study of brain development and child and adolescent health in the United States. The ABCD Study will recruit more than 11,000 9- to 10-year-olds to capture data before children begin using alcohol or other addictive substances. It will integrate structural and functional brain imaging; genetic testing; and neuropsychological, behavioral, and other health assessments of study participants conducted over a 10-year period, yielding a substantial amount of information about healthy adolescent brain development. Data gathered from participants will allow the creation of



baseline standards for typical brain development (similar to those that currently exist for height, weight, and other physical characteristics). These data are expected to illuminate how brain development is affected by substance use and other childhood experiences, such as patterns of sleep, use of social media, and engagement in sports and with video games. It may also reveal neurobiological, cognitive, and behavioral precursors of substance misuse and other risk behaviors, and ultimately inform preventive and treatment interventions.

The ABCD Consortium consists of a Coordinating Center, a Data Analysis and Informatics Center, and 21 research sites across the country. Recruitment, which began in September 2016, is expected to span 2 years. ABCD workgroups have established standardized and harmonized assessments of neurocognition, physical and mental health, social and emotional functions, and culture and environment. They also have established multimodal structural and functional brain imaging and bioassays. Brain imaging and biospecimen collection for genetic and epigenetic analyses will be done every other year, and the remaining assessments will be conducted semiannually or annually.

One important goal of the ABCD Study is to create a unique data resource for the entire scientific community by embracing an open science model. Curated, anonymized data will be released annually to the research community, along with the computational workflows used to produce the data, beginning 1 year after data collection begins.

ABCD is supported by the National Institute on Alcohol Abuse and Alcoholism, the National Institute on Drug Abuse, the National Cancer Institute, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Institute of Mental Health, the National Institute on Minority Health and Health Disparities, the National Institute of Neurological Disorders and Stroke, the NIH Office of Behavioral and Social Sciences Research, and the Division of Adolescent and School Health at the Centers for Disease Control and Prevention.

For more information, visit http://abcdstudy.org/index.html.

NIAAA ALCOHOL TREATMENT NAVIGATOR

Pointing the way to evidence-based care

In any given year, about 15 million adults in the United States meet the diagnostic criteria for alcohol use disorder (AUD), but less than 10 percent of them receive treatment. Often, finding quality AUD care can be complicated, and many people aren't aware of available treatment options.

In response, NIAAA developed the online tool, Alcohol Treatment Navigator℠, which makes this complicated process easier by telling people what they need to know, what to do, and how to recognize quality care. This landmark resource is comprehensive but also easy-to-use. We hope you will explore the site and then share it widely.

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Binge Drinking's Effects on the Body

Patricia E. Molina and Steve Nelson

Studies have focused on the effects of chronic alcohol consumption and the mechanisms of tissue injury underlying alcoholic hepatitis and cirrhosis, with less focus on the pathophysiological consequences of binge alcohol consumption. Alcohol binge drinking prevalence continues to rise, particularly among individuals ages 18 to 24. However, it is also frequent in individuals ages 65 and older. High blood alcohol levels achieved with this pattern of alcohol consumption are of particular concern, as alcohol can permeate to virtually all tissues in the body, resulting in significant alterations in organ function, which leads to multisystemic pathophysiological consequences. In addition to the pattern, amount, and frequency of alcohol consumption, additional factors, including the type of alcoholic beverage, may contribute differentially to the risk for alcohol-induced tissue injury. Preclinical and translational research strategies are needed to enhance our understanding of the effects of binge alcohol drinking, particularly for individuals with a history of chronic alcohol consumption. Identification of underlying pathophysiological processes responsible for tissue and organ injury can lead to development of preventive or therapeutic interventions to reduce the health care burden associated with binge alcohol drinking.

Key words: Alcohol and other drug (AOD) intoxication; alcoholic hepatitis; alcoholic liver cirrhosis; alcohol-induced disorders; binge drinking; blood alcohol content

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Introduction

Alcohol misuse is the fifth-leading risk factor for premature death and disability worldwide,[1] and, adjusting for age, alcohol is the leading risk factor for mortality and the overall burden of disease in the 15 to 59 age group.[2] According to the World Health Organization, in 2004, 4.5% of the global burden of disease and injury was attributable to alcohol: 7.4% for men and 1.4% for women.[2]

Alcohol can permeate to virtually all tissues in the body, resulting in significant alterations in organ function, which leads to multisystemic pathophysiological consequences. The effect of alcohol misuse on multiple organ systems outside the liver, mediated through direct and indirect effects beyond those associated with alterations in the nutritional state of the individual, has been well-established.[3,4] The resulting tissue injury has increasingly been recognized and examined as a contributing factor to alcohol-related comorbidities and mortality. Several pathophysiological mechanisms have been identified as causative factors of tissue and organ injuries that resulted from excessive alcohol consumption, including acetaldehyde generation, adduct formation, mitochondrial injury, cell membrane perturbations, immune modulation, and oxidative stress (Figure 1). Some of these mechanisms are the result of direct alcohol-induced cell perturbations, whereas others are the consequence of tissue alcohol metabolism (Figure 2). The oxidative stress caused by excess production of reactive oxygen species (ROS) or a reduction in reducing antioxidant equivalents in tissue has been consistently demonstrated to be an overall mechanism of the tissue injury that results from chronic alcohol misuse. Dose-dependent relationships between alcohol consumption and incidence of diabetes mellitus, hypertension, ischemic heart disease, dysrhythmias, stroke, pneumonia, and fetal alcohol syndrome have been reported.[4] However, recognition of alcohol as an underlying causal factor in comorbid conditions remains a challenge in the clinical setting.

Several factors associated with alcohol consumption, including pattern, amount, and frequency, and the type of alcoholic beverage, may contribute differentially to the risk for alcohol-induced tissue injury. The question of whether all types of alcohol produce similar pathophysiological consequences remains to be answered.

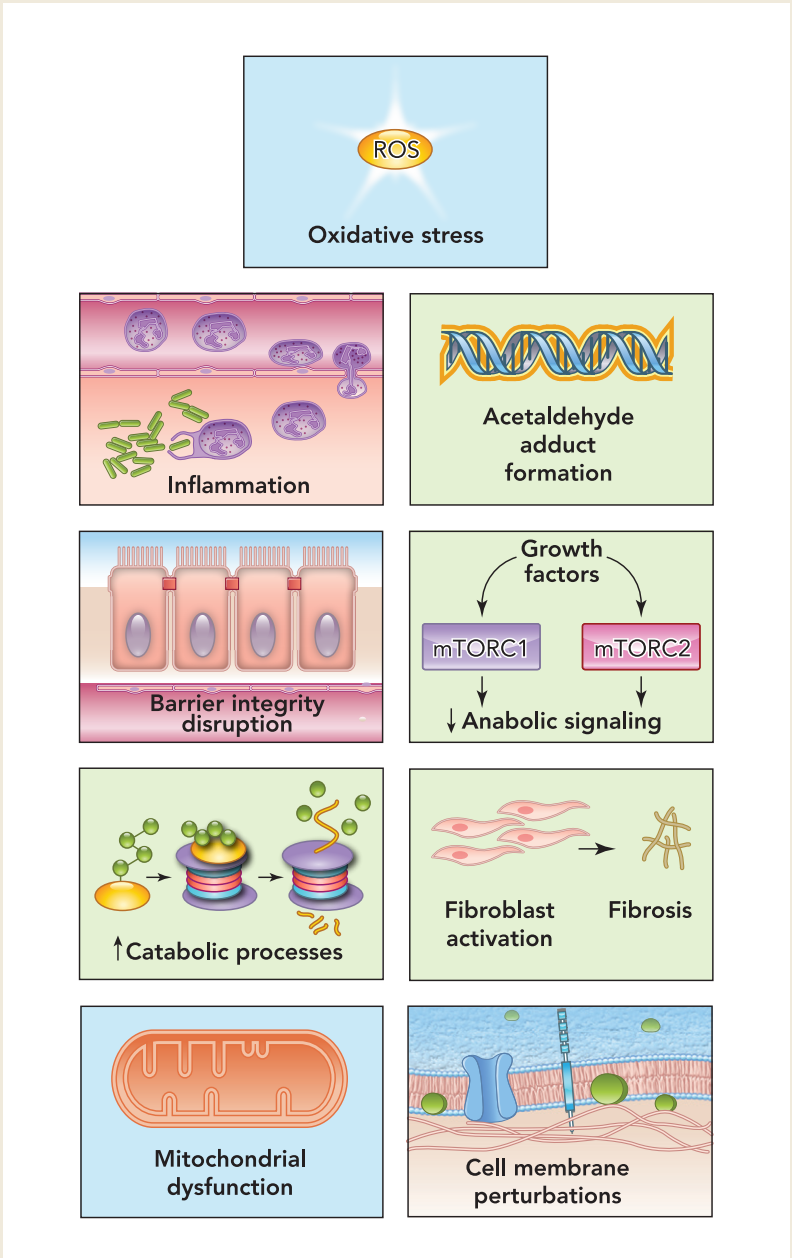

Figure 1 Mechanisms of alcohol-induced tissue injury. Alcohol contributes to tissue injury directly and indirectly through mechanisms including oxidative stress, inflammation, acetaldehyde adduct formation, barrier integrity disruption, decreased anabolic signaling, enhanced catabolic processes (particularly through the ubiquitin proteasome pathway), profibrotic changes, mitochondrial dysfunction and injury, and cell membrane perturbations. *Note:* mTORC1, mammalian target of rapamycin complex 1; mTORC2, mammalian target of rapamycin complex 2; ROS, reactive oxygen species. *Source:* Molina PE, Gardner JD, Souza-Smith FM, et al. Alcohol abuse: Critical pathophysiological processes and contribution to disease burden. *Physiology*. 2014;29(3)203-215.

However, the particularly detrimental effects of binge drinking have increasingly gained attention. Binge drinking, as defined by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), is a pattern of alcohol consumption that brings blood alcohol concentration to .08 g/dL, which typically occurs following the intake of five or more standard alcohol drinks by men and four or more by women over a period of approximately 2 hours.[5] Results from the 2015 National Survey on Drug Use and Health show overall prevalence of binge drinking (during the past 30 days) of 26.9% among U.S. adults ages 18 and older.[6] Those data show that binge drinking prevalence and intensity are highest among those ages 18 to 24 but also occur in high frequency among older individuals (ages 65 and older). Thus, binge drinking prevails in two vulnerable segments of the population, raising their risks for greater severity of injury and frequency of comorbidities.

Understanding the Biomedical Consequences of Binge Drinking

A limitation to our understanding of the consequences of binge alcohol consumption on organ injury is the lack of information on the time period, duration, and number of binge occurrences that describe the long-term practice of binge drinking. Preclinical studies conducted under controlled conditions provide opportunities to examine quantity and frequency variables in the investigation of the effects of alcohol consumption on organ injuries. However, interpreting, comparing, and integrating the patterns of alcohol consumption described in clinical reports is difficult because of the different types of data collected across studies. This difficulty underscores the need for researchers to perform more rigorous comprehensive and systematic data collection on alcohol use patterns. The Timeline Followback (TLFB) tool, for example, uses a calendar and

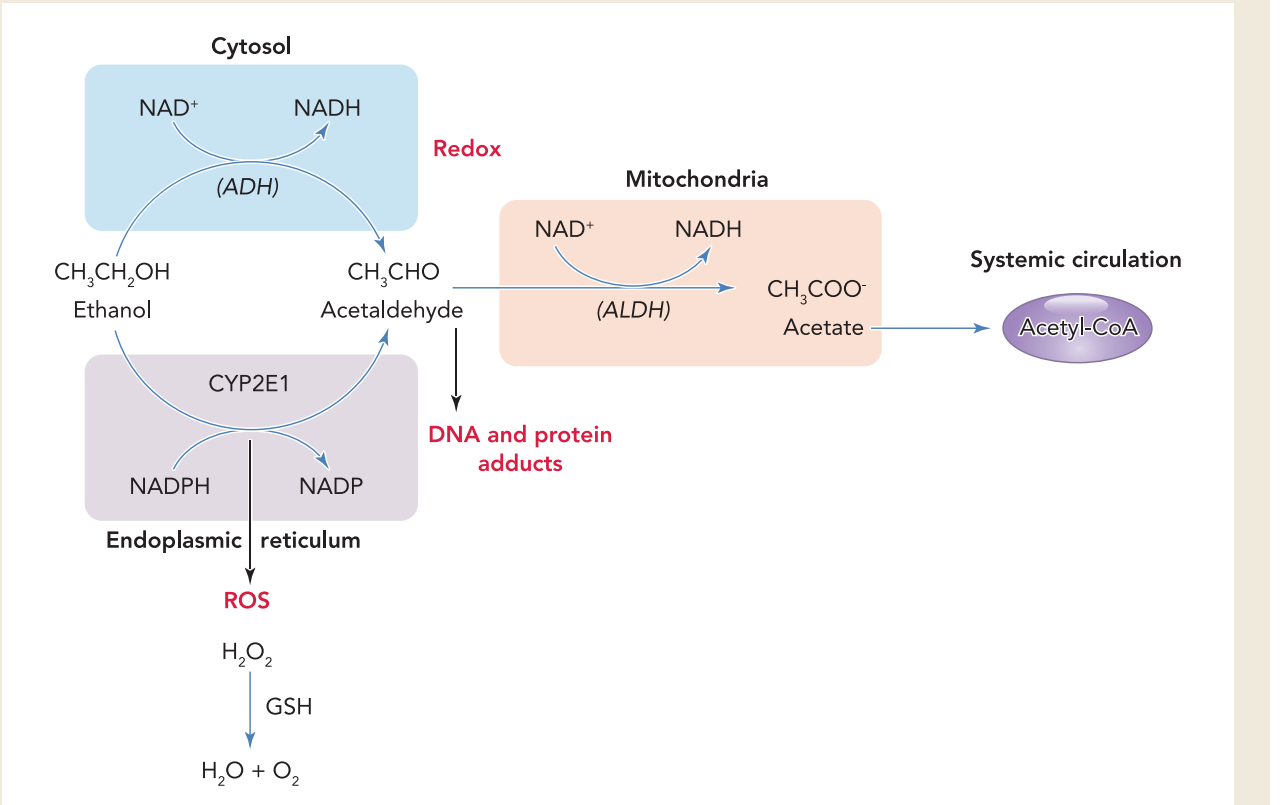

Figure 2 Tissue alcohol metabolism contributes to tissue and organ injury through altered redox potential, generation of ROS, and generation of metabolites, such as acetaldehyde, that form DNA and protein adducts. Alcohol (ethanol) is metabolized to acetaldehyde primarily by ADH in the cytosol and CYP2E1 in the endoplasmic reticulum. Acetaldehyde is converted to acetate in the mitochondria by the enzyme ALDH. Acetaldehyde can form adducts with DNA and proteins that can produce injury through activation of immune responses. During the oxidative process, both ADH and ALDH reactions reduce NAD+ to NADH, shifting the cellular redox ratio. In addition, the cytochrome P450 enzymes, particularly CYP2E1, contribute to the oxidation of alcohol to acetaldehyde, particularly at increasing alcohol concentrations, as well as following their induction by chronic alcohol misuse. The pathway of alcohol oxidation results in the production of large amounts of ROS, including H_2O_2, and is thought to be an important mechanism contributing to alcoholic liver injury. ROS are eliminated by antioxidants like GSH under normal conditions. Alcohol depletes cellular GSH stores, thereby exacerbating ROS-mediated injury. ROS can interact with lipids, producing lipid peroxidation, which leads to formation of reactive molecules such as MDA and HNE, which can then form protein adducts. *Note:* Acetyl-CoA, acetyl coenzyme A; ADH, alcohol dehydrogenase; ALDH, acetaldehyde dehydrogenase type 2; CYP2E1, cytochrome P450 2E1; GSH, glutathione; H_2O, water; H_2O_2, hydrogen peroxide; HNE, 4-hydroxy-2-nonenal; MDA, malondialdehyde; NAD+, nicotinamide adenine dinucleotide (oxidized); NADH, nicotinamide adenine dinucleotide (reduced); NADP, nicotinamide adenine dinucleotide phosphate (oxidized); NADPH, nicotinamide adenine dinucleotide phosphate (reduced); O_2, oxygen; ROS, reactive oxygen species. *Source:* Molina PE, Gardner JD, Souza-Smith FM, et al. Alcohol abuse: Critical pathophysiological processes and contribution to disease burden. *Physiology.* 2014;29(3)203-215.

a structured interview to collect retrospective information on the types and frequency of alcohol use over a given time period.[7,8] Nevertheless, accounting for a lifetime pattern of binge alcohol consumption remains challenging when conducting clinical studies. Alcohol consumption patterns should be taken into consideration for future development of alcohol use screening tools, because binge drinking has been suggested to result in greater alcohol-related harm.[9]

Different types of alcoholic beverages consumed in binge drinking episodes could also differentially affect the health consequences associated with binge drinking. Epidemiological studies that compared the prevalence of coronary heart disease in "wine-drinking countries" and beer- or liquor-drinking countries have proposed that red wine, but not beer or spirits, consumed with a meal may

confer cardiovascular protection.[10] The proposed protective effects of red wine include decreased blood clot formation, vascular relaxation, and attenuation of low-density lipoprotein (LDL, or bad cholesterol) oxidation, an early event preceding formation of cholesterol-filled plaque. These effects are attributed to polyphenols, especially resveratrol, and their antioxidant properties.

However, not all reports support the link between consuming a specific beverage type (i.e., wine vs. beer or spirits) and health benefits. Some reports suggest that beverage amount is more directly linked to health outcomes.[11,12] The differential contribution of alcoholic beverages to beneficial or detrimental health outcomes remains to be examined in both preclinical and clinical studies. In binge drinking episodes, the form of alcohol consumed most frequently is beer (67.1%), followed by liquor (21.9%) and wine (10.9%).[13] Moreover, beer accounts for most of the alcohol consumed by drinkers who are at the highest risk of causing or incurring alcohol-related harm, including drinkers ages 18 to 20, those with more frequent binge episodes per month, and those drinking 8 or more drinks per binge episode. Therefore, dissecting how pattern of drinking and type of alcoholic beverage contribute to overall outcomes is challenging.

The Gastrointestinal Tract, Liver, and Pancreas

Of all tissues affected by binge-like alcohol consumption, the gastrointestinal tract bears the greatest burden due to its direct exposure to high tissue concentrations of alcohol following ingestion (Figure 3). Binge drinking often occurs apart from meals, which may also contribute to its deleterious effects on organs. Food consumed at the time of alcohol consumption influences not only the alcohol absorption rate and blood alcohol concentration, but also the direct effect of alcohol on the gastrointestinal mucosa. Hence, binge drinking is more likely to contribute to organ injury than paced, moderate alcohol drinking that is associated with a meal.

The gut mucosa is particularly susceptible to alcohol-induced injury, and alcohol consumption can result in a loss of intestinal barrier integrity. Several direct and indirect mechanisms have been identified that disrupt the structural and functional components involved in maintaining the integrity of the gut mucosal barrier. Alcohol and its breakdown products directly damage epithelial cells through generation of ROS and through disruption of tight junction protein expression and signaling.[14] This process disrupts the integrity of the intestinal barrier, allowing bacteria and toxins to reach the bloodstream. Acute alcohol binge drinking in healthy human volunteers can produce a significant increase in serum endotoxin levels and bacterial 16S ribosomal DNA, suggesting the gastrointestinal microbial origin of endotoxin.[15-17]

More recently, attention has focused on the changes in intestinal microbiome that contribute to alcohol-associated intestinal inflammation and permeability. Alcohol promotes both dysbiosis (decreased diversity or an imbalance in the types of microbes) and bacterial overgrowth in the gastrointestinal system.[18-21] Alcohol alters the balance between bacterial strains, decreasing the presence of beneficial bacteria, such as *Lactobacillus* and *Bifidobacterium*, and increasing that of Proteobacteria and Bacilli.[19] This imbalance adds to the possibility that bacterial overgrowth may contribute to local mucosal inflammation through bacterial metabolism of alcohol and enhanced local production of metabolites such as acetaldehyde.[22] Moreover, increased bacterial load, together with shifts in intestinal bacterial strains, brings about diverse profiles of bacterial-derived metabolites.

How these shifts in bacterial strains, load, and metabolites contribute to organ injury remains to be fully elucidated. However, it is reasonable to speculate that greater bacterial burden and altered bacterial profiles, together with increased permeability of the gut mucosa, would lead to continuous entry of bacterial toxins into the systemic circulation. These changes could produce chronic and sustained activation of immune responses that, in turn, could lead to immune exhaustion and dysfunction. Preclinical studies show that binge-on-chronic alcohol feeding alters the gut microflora at multiple taxonomic levels, influencing hepatic inflammation, neutrophil infiltration, and liver steatosis,[23] which highlights the need for clinical investigation into the relationship between gut microflora and hepatic liver disease.

Local and Systemic Consequences of Gut Injury

Toxins and bacterial products leaked from the gastrointestinal tract can be transported through the lymphatic system. This route of dissemination, which escapes hepatic clearance, may prove critical in the enhanced systemic delivery of toxins. Preclinical studies have shown that repeated binge-like alcohol intoxication increases lymphatic permeability and inflammation in the adipose tissue that immediately surrounds the mesenteric lymphatics. Inflammatory response in mesenteric perilymphatic adipose tissue is associated with altered adipose tissue insulin signaling and circulating adipokine profiles, which suggests a link between lymphatic leak, adipose tissue inflammation, and metabolic dysregulation.[24]

Whether chronic alcohol consumption not in a binge pattern produces similar alterations in lymphatic permeability and mesenteric adipose inflammation remains to be determined. However, localized alterations in mesenteric adipose tissue metabolic regulation, including insulin signaling, may prove to be relevant to the enhanced risk for metabolic syndrome that is associated with binge alcohol consumption.[25] After burn injury

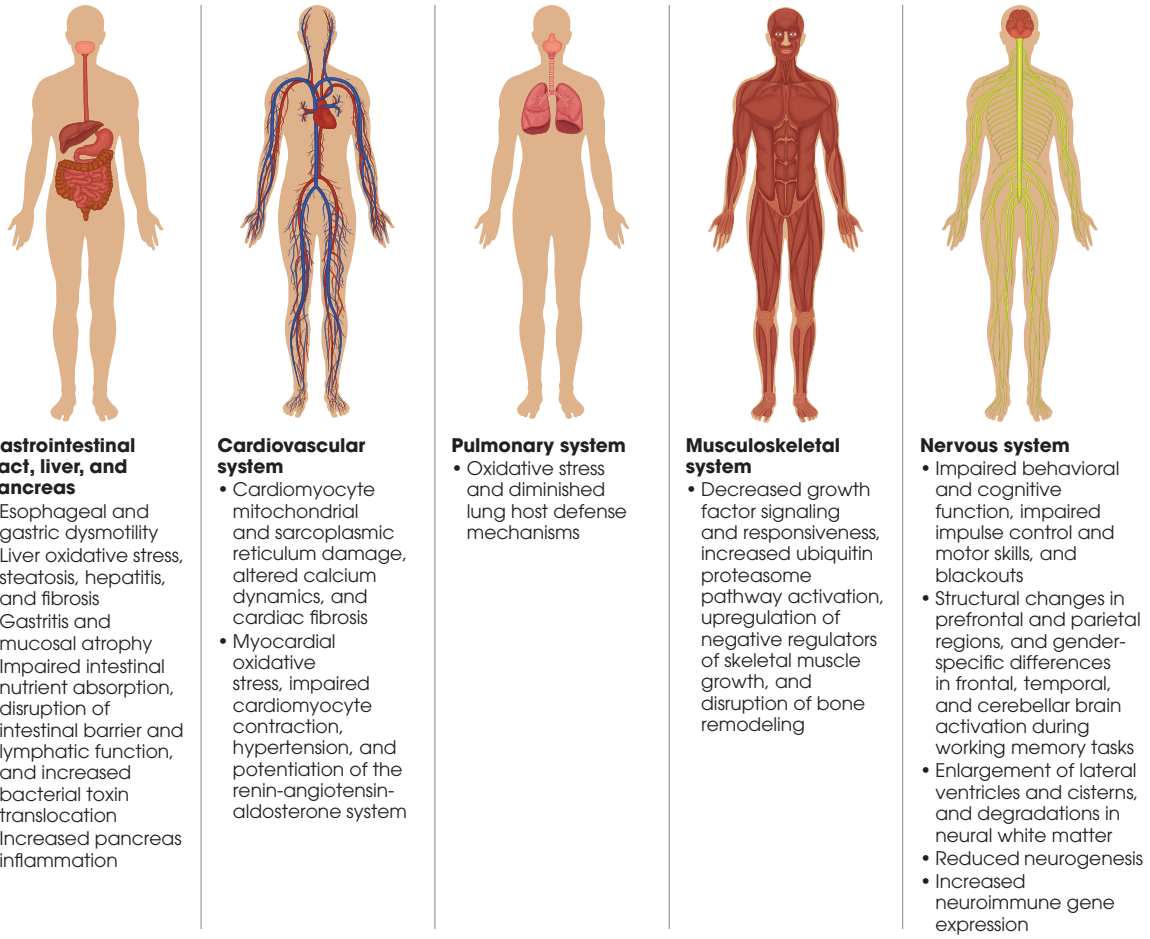

Figure 3 The systemic effects of chronic binge alcohol consumption and the principal organ systems affected.

and a binge-like pattern of alcohol intoxication, rodents showed similar exacerbation of adipose tissue inflammation.[26] This suggests that a possible synergism between binge-like alcohol intoxication and injury promotes a dysregulated adipose environment conducive to insulin resistance, and potentially metabolic syndrome, if these alterations are sustained beyond the immediate period following binge drinking or burn injury.[3]

Second to the gastrointestinal tract, the liver has the most exposure to high alcohol concentrations during periods of binge drinking. Hepatocellular metabolism of alcohol and the resulting ROS generation; acetaldehyde formation and the resulting adducts; immune response activation, particularly in Kupffer and stellate cells; and alterations in cell signaling are all proposed as mechanisms that underlie liver injury associated with binge-like alcohol consumption. For people with chronic alcoholism, binge drinking augments liver injury[27,28] and is a major trigger for the progression from steatosis to steatohepatitis.[29-31] In one study, rodents that received binge-on-chronic alcohol exposure had accentuated elevation in liver enzymes (alanine aminotransferase), hepatic steatosis, and inflammatory cytokine expression compared to rodents subjected only to chronic or to acute alcohol exposure.[32] These results demonstrate that binge-on-chronic alcohol exposure results in greater insult than either chronic or acute alcohol exposure alone. Clinical studies have provided evidence of associations among alcohol binge drinking patterns, immune activation (high CD69 and low TLR4, CXCR4, and CCR2 expression), and decreased chemotactic responses to SDF-1 and MCP-1.[33] These associations reflect an altered immune profile that may be as-

sociated with liver injury and increased susceptibility to infection. More recently, attention has been drawn to the potential greater liver injury in individuals with metabolic syndrome. A population-based study showed a direct association between binge drinking frequency and liver disease risk, after adjusting for average daily alcohol intake and age.[34] In this study, binge drinking and metabolic syndrome produced supra-additive increases in the risk of decompensated liver disease. Because of increasing rates of obesity and metabolic syndrome, research on the effects of alcohol misuse and the biomedical consequences is needed for this particular segment of the population.

Located strategically between the liver and the gastrointestinal tract, the pancreas also has high susceptibility to alcohol-induced tissue injury. Heavy, chronic alcohol consumption is a recognized contributing factor in the development of pancreatitis. However, how dose and pattern of alcohol consumption affect pancreatic function and structure is not known. Studies show that alcohol consumption of more than 40 g per day is increasingly detrimental for any type of pancreatitis.[35] Retrospective clinical studies have shown that binge alcohol drinking is associated with aggravation of first-attack severe acute pancreatitis, which is reflected in higher admission levels of serum triglycerides, Balthazar computed tomographic score, and Acute Physiology and Chronic Health Evaluation II score, as well as higher mortality and incidence of complications.[36]

Insight into the mechanisms involved in pancreatic injury is derived from preclinical studies that show detrimental effects of binge alcohol exposure on the pancreas. These effects include tissue edema, inflammation, acinar atrophy and moderate fibrosis, endoplasmic reticulum stress, oxidative stress, and apoptotic and necrotic cell death. These structural changes are associated with pancreatic dysfunctional changes, which are reflected by altered levels of alpha-amylase, glucose, and insulin, strongly suggesting a detrimental effect of acute binge alcohol exposure on the pancreas. Specifically, preclinical studies have proposed that, alone, chronic and binge alcohol exposure caused minimal pancreatic injury, but chronic plus binge alcohol exposure resulted in significant apoptotic cell death; alterations in alpha-amylase, glucose, and insulin; pancreatic inflammation; and protein oxidation and lipid peroxidation, which are indicative of oxidative stress.[37] The pathogenesis of alcoholic pancreatitis involves acinar cell alcohol metabolism. The direct toxic effects of alcohol and its metabolites on acinar cells, in the presence of an appropriate trigger factor, may predispose the gland to injury. In addition, pancreatic stellate cells are implicated in alcoholic pancreatic fibrosis.[38] Thus, experimental and clinical data suggest that alcohol consumption alone does not initiate pancreatitis, but it sensitizes the pancreas to disease from other insults, including smoking, exposure to bacterial toxins, viral infections, and binge alcohol consumption.[39]

Cardiovascular Consequences

The effect of alcohol consumption on cardiovascular function has been the subject of much debate. The relationship between alcohol consumption and cardiovascular health is not linear and is thought to follow a J-shaped curve, with low amounts of alcohol consumption frequently reported as cardioprotective.[40] However, data suggest that binge drinking is associated with transient increases in systolic and diastolic blood pressure (Figure 3).[41-43] The prevalence of hypertension has been reported to be higher in individuals who consume more than six drinks per day. However, the pattern of alcohol consumption was not considered in these studies.[44] The effect of even a modest rise in blood pressure is considerable, as it is a recognized risk factor for cardiovascular mortality.[45,46] Binge drinking has been associated with increased risk of cardiovascular comorbidities, including hypertension, stroke, myocardial infarction, and sudden death, and this risk may extend to the younger population as well.[47-51] Acute elevations in blood alcohol levels resulting from binge alcohol consumption are associated with an increased risk of new-onset atrial fibrillation, a most common arrhythmia strongly associated with adverse cardiovascular events and sudden death.[52] A higher risk for myocardial infarction has been reported after 1 day of heavy alcohol consumption (which could reflect a binge-like pattern of alcohol consumption).[53]

Few preclinical studies have examined the effect of binge drinking on cardiac function. In one study, over a 5-week period, rodents received repeated episodes of alcohol administration that modeled a binge drinking pattern.[54] These rodents did not show changes in cardiac structure, but this drinking pattern resulted in increased phosphorylation of myocardial p38 mitogen-activated protein kinase and transient increases in blood pressure, which became progressively higher with repeated episodes of binge drinking. These effects were partly mediated by adrenergic mechanisms. More recently, the combined binge-on-chronic pattern of alcohol feeding to rodents has been shown to result in alcohol-induced cardiomyopathy, characterized by increased myocardial oxidative/nitrative stress, impaired mitochondrial function and biogenesis, and enhanced cardiac steatosis.[55,56] The role of oxidative stress has been confirmed by other preclinical studies.[57]

Pulmonary Consequences

Preclinical studies have identified impairments in multiple aspects of lung function after chronic and binge-like alcohol administration, including altered epithelial barrier function, suppressed immunity, impaired bacterial clearance, depleted glutathione (GSH),

and impaired pulmonary epithelial ciliary function (Figure 3).[58,59] Moreover, alcohol binge drinking increases the risk for sustaining traumatic injuries and aggravates outcomes from traumatic injuries,[60] such as burns,[26,58,61-63] bone fractures,[64] and hemorrhagic shock.[65] For alcohol-intoxicated hosts, similar detrimental effects have been reported on bacterial pneumonia outcomes, a frequent comorbid condition associated with traumatic injury.[66] Binge-like alcohol administration impairs innate and adaptive immune responses in the lungs, thereby increasing infection susceptibility, morbidity, and mortality.[61,62] It is possible that, in hosts previously exposed to chronic alcohol consumption, binge drinking detrimentally affects pulmonary outcomes from traumatic injury by priming host defense mechanisms. This combined effect may prevent clear isolation of binge alcohol consumption effects from chronic alcohol consumption effects.

Musculoskeletal Consequences

The incidence of skeletal muscle dysfunction (i.e., myopathy) resulting from chronic alcohol misuse surpasses that of cirrhosis.[67] This progressive loss of lean mass is multifactorial and involves metabolic, inflammatory, and extracellular matrix alterations, which promote muscle proteolysis and decreased protein synthesis (Figure 3).[68] An additional severe complication of binge drinking is the development of acute muscle injury, rhabdomyolysis. Binge drinking that precedes coma or immobility can lead to rhabdomyolysis and, consequently, to renal injury, as documented in case reports in the literature.[69-71] The mechanisms are not well-understood, but they may involve acute hypokalemia.[72] This phenomenon may warrant further study, as environmental factors such as high ambient temperature and individual drug-drug interactions can obscure presentation and hinder management of alcohol-induced rhabdomyolysis.

Preclinical studies suggest that, after binge-like alcohol administration, physical exercise may ameliorate cognitive impairment and suppressed neurogenesis.[73] The effect of binge alcohol consumption on exercise performance and recovery remains to be systematically investigated. One clinical study reported no change in isokinetic and isometric muscle performance, central activation, or creatine kinase release during or after acute moderate alcohol intoxication.[74] Short-term reductions in lower-extremity performance were reported in a study that investigated athletes after an alcohol drinking episode and the associated reduced sleep hours.[75] Another study found that alcohol consumption following a simulated rugby game decreased lower-body power output but did not affect performance of tasks requiring repeated maximal muscular effort.[76] However, the same researchers found that alcohol consumption following eccentric exercise accentuated the losses in dynamic and static strength in males.[77]

In contrast, alcohol consumption following muscle-damaging resistance exercise did not alter inflammatory capacity or muscular performance recovery in resistance-trained women,[78] suggesting possible gender differences in alcohol's modulation of exercise performance and recovery. These studies were conducted using healthy volunteers and athletes. Other studies that investigated patients with alcoholic liver disease showed lower muscular endurance, maximal voluntary isometric muscle strength, and total work of knee extensors.[79] Controlled studies are needed, particularly in light of the popularity of binge drinking events frequently associated with collegiate and professional sports.

Neuropathological Consequences

The behavioral and cognitive effects of binge drinking include difficulties in decision-making and impulse control, impairments in motor skills (e.g., balance and hand-eye coordination), blackouts, and loss of consciousness (Figure 3).[80] All of these effects have serious health consequences ranging from falls and injuries to death.[81] In particular, adolescents are vulnerable to the cognitive manifestations and memory loss associated with binge drinking. National estimates suggest that significant numbers of people who binge drink report at least one incident of blacking out in the previous year.[82,83] Blackouts, defined as short periods of amnesia during which a person actively engages in behaviors (e.g., walking or talking) without creating memories for them, often occur at blood alcohol concentrations exceeding .25 g/dL.[84,85] Blackouts are common among college students who drink alcohol. Estimates suggest that up to 50% of students that engaged in drinking reported a blackout episode during the past year.[86,87] The pattern of rapid consumption of large doses of alcohol, frequently on an empty stomach, is characteristic of the adolescent period.[88]

The consequences of binge drinking are not short-lived or limited to the period of intoxication. Imaging studies of binge drinking adolescents document long-lasting changes. Reports indicate structural changes in the prefrontal and parietal regions, as well as in regions known to mediate reward, and these changes are thought to reflect long-lasting effects of alcohol bingeing on critical neurodevelopmental processes.[89] Functional imaging studies of the brains of binge drinking and nondrinking adolescents found that binge drinking adolescents showed greater responses in frontal and parietal regions, no hippocampal activation to novel word pairs, and modest decreases in word-pair recall, which could indicate disadvantaged processing of novel verbal information and a slower learning slope.[90] In another study, adolescent binge drinking resulted in gender-specific differences in frontal, temporal, and cerebellar brain activation during a special working memory

task, reflecting differential effects of binge drinking on neuropsychological performance and possibly greater vulnerability in female adolescents.[91] Other researchers have reported that degradations in neural white matter were linked with impaired cognitive functioning in adolescents who binge drank.[92]

Adolescent rodent intermittent ethanol exposure that modeled human adolescent binge drinking produced a range of pathophysiological and neurobehavioral sequelae, including altered adult synapses, cognition, and sleep; reduced adult neurogenesis; increased neuroimmune gene expression; and increased adult alcohol drinking associated with disinhibition and social anxiety.[93] Preclinical studies indicated that binge drinking could produce brain structural abnormalities. Binge alcohol administration to rodents produced increases in cerebrospinal fluid volume in the lateral ventricles and cisterns, decreased levels of *N*-acetylaspartate and total creatine, and increased choline-containing compounds, glutamate, and glutamine, all of which recovered during abstinence.[94] Moreover, preclinical data suggested that adolescent binge drinking sensitized the neurocircuitry of addiction, possibly inducing abnormal plasticity in reward-related learning processes, which could contribute to adolescent vulnerability to addiction.[95]

Summary

Although the effects of chronic alcohol consumption and the mechanisms of tissue injury underlying alcoholic hepatitis and cirrhosis have received much attention, less attention has been focused on the pathophysiological consequences of binge alcohol consumption. The differential duration of the intoxication period, excessive concentrations of alcohol at the tissue level, accelerated alcohol metabolism and generation of ROS and alcohol metabolites, and acute disruption of antioxidant mechanisms are some of the salient differences between chronic and binge-like alcohol-mediated tissue injury. Because of the differences in male and female alcohol metabolism rates, it is possible that greater tissue injury is produced in females who consume alcohol in binge-like patterns. Furthermore, in an aging population already riddled with polypharmacy, there is heightened potential for toxicity during an alcohol binge (Figure 4). Also, pre-existing comorbid conditions such as cardiovascular disease, renal failure, or steatohepatitis may predispose binge drinkers to accelerated tissue injury.

Additional research is needed to better recognize the differential effects of binge, chronic, and binge-on-chronic patterns of alcohol consumption. Animal models that reflect these patterns of alcohol exposure are needed. In addition, greater effort toward documenting a history of alcohol consumption, including the frequency, quantity, and quality of alcoholic beverages consumed, should help us better understand the effects of binge drinking on biological systems.

Figure 4 Factors that contribute to disease processes associated with binge alcohol drinking. For individuals who drink alcohol, factors such as type of alcohol, pattern of consumption, duration of alcohol misuse, and the age and diet of the drinker contribute to the incidence and severity of tissue injury. Another factor, polypharmacy, particularly affects the older adult population, as multiple medications increase the potential for toxicity during an alcohol binge. Similarly, pre-existing comorbid conditions may predispose binge drinkers to accelerated tissue injury. Finally, genetic predisposition and environmental toxins are likely to be determining factors that affect the incidence and severity of tissue and organ injury.

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The authors declare that they have no competing financial interests.

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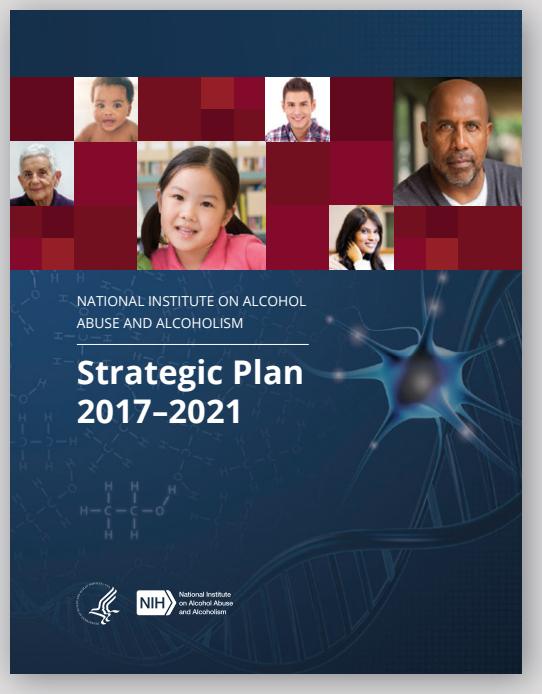
NIAAA Strategic Plan

Charting a Course for the Next Five Years of Alcohol Research



As scientific advances continue to expand our understanding of how alcohol affects human health and point to ways to address alcohol-related harm, NIAAA has released its 2017–2021 strategic plan for research. The new plan serves as a road map for optimizing the allocation of NIAAA's resources to areas of alcohol research most likely to benefit from additional support, translating scientific discoveries for the benefit of the public, and continuing to build on NIAAA's position as the nation's key source of evidence-based information on alcohol and health.

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