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NIAAA 50th ANNIVERSARY FESTSCHRIFT

AUD Risk, Diagnoses, and Course in a Prospective Study Across Two Generations: Implications for Prevention

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Acknowledgments
This paper was developed from my tribute to NIAAA that was delivered as a lecture at the NIAAA 50th Anniversary Science Symposium on November 30, 2020. That meeting was personally meaningful to me because my scientific career began with help from NIAAA's precursor at NIH, and the work presented here was supported by NIAAA over the years. Particularly the San Diego Prospective Study would not have been possible without the institute's support, both financially and intellectually, and their dedicated staff. It has been a privilege for me to have received this support as well to have this opportunity to share some aspects of our program of research supported by NIAAA.
I was introduced to research and the importance of alcohol problems as a medical student at Washington University, St. Louis Medical School through mentoring by Eli and Lee Robins, Sam Guze, George Winokur, and Donald Goodwin. During that experience I received additional important mentorship through interactions with Jack Mendelson and Nancy Mello at the NIH. The work described in this article has been supported by NIAAA since the mid-1970s and was enriched by my interactions with institute directors over the years, especially Enoch Gordis, Ting Kai Li, and George Koob. The data were developed through ongoing interactions with my colleague Tom Smith and could not have been produced without his close collaboration. Whatever I have been able to accomplish is a tribute to these mentors and friends and the NIAAA itself.
Parts of this paper were extracted from papers developed over the course of our research and published in the *Journal of Studies of Alcohol and Drugs* and *in Alcoholism: Clinical and Experimental Research* and as cited within this manuscript.[18,23,43,46,47] This work was supported by NIAAA grants U10AA008401 and R01AA021162.

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This article was based on a presentation at the NIAAA 50th Anniversary Science Symposium, "Alcohol Across the Lifespan: 50 Years of Evidence-Based Diagnosis, Prevention, and Treatment Research," held on November 30–December 1, 2020. Links to the videocast are available on the NIAAA 50th Anniversary Science Symposium agenda webpage.
Opinions expressed in contributed articles do not necessarily reflect the views of the National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health. The U.S. government does not endorse or favor any specific commercial product or commodity. Any trade or proprietary names appearing in *Alcohol Research: Current Reviews* are used only because they are considered essential in the context of the studies reported herein.

This article is part of a Festschrift commemorating the 50th anniversary of the National Institute on Alcohol Abuse and Alcoholism (NIAAA). Established in 1970, first as part of the National Institute of Mental Health and later as an independent institute of the National Institutes of Health, NIAAA today is the world's largest funding agency for alcohol research. In addition to its own intramural research program, NIAAA supports the entire spectrum of innovative basic, translational, and clinical research to advance the diagnosis, prevention, and treatment of alcohol use disorder and alcohol-related problems. To celebrate the anniversary, NIAAA hosted a 2-day symposium, "Alcohol Across the Lifespan: 50 Years of Evidence-Based Diagnosis, Prevention, and Treatment Research," devoted to key topics within the field of alcohol research. This article is based on Dr. Schuckit's presentation at the event. NIAAA Director George F. Koob, Ph.D., serves as editor of the Festschrift.

KEYWORDS: alcohol; genetics; sensitivity; prevention

A large proportion of the population consume alcoholic beverages at some time in their lives. For most people, alcohol consumption is low to moderate and is not associated with harmful physiological, psychological, or social outcomes. However, for a substantial number of individuals, alcohol consumption increases over time; leads to the development of tolerance and alcohol-related life problems; and, ultimately, results in a diagnosis of alcohol use disorder (AUD). The reasons why some people develop harmful drinking behaviors and AUD are complex and still not entirely understood.

One crucial tool for identifying factors that influence alcohol consumption and its consequences are longitudinal studies that follow individuals over long periods of time, sometimes including evaluating family members over several generations. Among the most important alcohol-related longitudinal studies are the San Diego Prospective Study (SDPS), the Collaborative Study on the Genetics of Alcoholism (COGA) and the Avon Longitudinal Study of Parents and Children (ALSPAC), each of which have been supported by the National Institute on Alcohol Abuse and Alcoholism (NIAAA). This article briefly summarizes some findings from these studies, particularly the SDPS. After reviewing the contribution of genetic and environmental influences in AUD, it will introduce a low level of response (low LR) to alcohol as a risk factor for AUD. The article will then describe the 40-year SDPS in more detail, as well as its main conclusions regarding the contributions of genes and environment on the low LR and AUD, and summarizes an AUD prevention program based on the low LR.

Genetic and Environmental Influences in AUD

The modern era of genetic studies regarding alcohol and other drug-related problems was built upon many years of observations that these problems cluster in families. Thus, children of parents with AUD have a three to four times higher risk of having AUD themselves than children of parents without AUD.[1,2] However, the presence of a familial influence does not by itself demonstrate whether this familial link relates to shared genes, a shared environment, or their combination. Those distinctions were subsequently addressed in part through twin studies demonstrating that twins of people with AUD were at significantly higher risk to have AUD themselves if they were identical twins, who shared 100% of their genes, than if they were fraternal twins, who shared only 50% of their genes. An identical twin of someone with AUD has about a 60% risk of AUD compared to about a 40% risk for fraternal twins. Therefore, even in identical twins, the risk that the second twin also developed AUD was not 100%, indicating the involvement of additional factors.[3-5]

Additional studies examined if the enhanced risk for alcohol problems observed in children of parents with AUD remained even if the offspring had been separated from that parent early in life. In 1972, analyses of half-siblings from AUD families and control families found that adverse alcohol outcomes in offspring related more closely to presence of an AUD in a biological parent than to alcohol problems in a non-biological parent who raised the child.[6] These data were consistent with subsequent larger and better controlled investigations of adoptees in Scandinavia.[2,7] Overall, these studies supported the conclusion that genes and gene-environment interactions explained between 40% and 60% of the AUD risk.[8-10]

The research also indicated that genetic variants (i.e., mutations) that affect AUD risk operate in complex ways that do not fit into either dominant or recessive models of inheritance. Rather, like diabetes and hypertension, AUD can be considered a complex genetically influenced condition to which numerous genes contribute. In other words, AUD reflects the impact of multiple characteristics that do not by themselves cause the problems with alcohol but contribute to overall risk. Subsequently, research identified several genetically influenced characteristics, or intermediate phenotypes, through which genes impacting AUD risk operate.

One such intermediate phenotype is an intense alcohol-related skin flushing reaction caused by several variants of alcohol-metabolizing enzymes, which were identified in the 1970s. This phenomenon, which has been observed for centuries in people of Japanese, Chinese, or Korean descent who consume alcohol, is associated with a decreased risk for AUD but is unrelated to other types of substance use disorder (SUD).[11] The second intermediate phenotype, which enhances risk for both AUD and other types of SUD, is the long-known association between substance-related problems and impulsive-like or externalizing behaviors.[12,13] The underlying characteristics include elevated levels of sensation seeking and behavioral/physiological disinhibition. These behaviors contribute to what has been referred to as type 2 and type B subtypes of AUD that are associated with an early onset of alcohol and other drug problems and a severe clinical course.[14] A third intermediate group of phenotypes that also is related to increased risks for both AUD and other types of SUD operates through the presence of several additional major psychiatric conditions, such as schizophrenia and bipolar disorders.[15,16] Finally, this abbreviated list of genetically influenced characteristics related to the risk for AUD includes a phenotype characterized by low LR to alcohol, as described in the next section.

Each step of these studies of genetic influences for AUD also demonstrates the importance of the environment as well as gene-environment relationships. One example of data supporting the influence of environment is the finding that identical twins of individuals with AUD have only about a 60% risk for this disorder, not the 100% rate one would expect if genes explained the entire

risk. Thus, it is important to study both genes and environment when looking for characteristics that might be helpful in early identification of the risk for repetitive alcohol problems or might reveal clues of ways to mitigate that risk.

Low LR to Alcohol and Risk of Alcohol Problems

A low LR to alcohol is a genetically influenced characteristic that increases AUD risk but does not significantly impact vulnerability toward other forms of SUD or other psychiatric conditions. This low LR phenotype is most prominent at peak and falling blood alcohol concentrations (BACs).[17,18] The rationale for linking a low LR with heavier drinking relates to a Social Information Processing Model which posits that individuals are likely to consume as many drinks as are needed to achieve the desired effects.[19] According to this model, which is presented in Figure 1, young people begin drinking to achieve an effect, such as intoxication. If they need to consume more alcohol to achieve this effect—for example, because of a low LR—they will increase consumption. The resulting heavier drinking becomes associated with other outcomes, especially in individuals with a family history of AUD (FHalc), such as choosing friends who also drink heavily (Peer) or starting to expect that heavy drinking is the best way to have fun (Expect). As heavy drinking begins to increase life problems and stress, alcohol is increasingly used as a means to cope with the stress (Cope). Thus, the major impact of the low LR is on drinking quantity which then increases the risk for alcohol problems (↑HD & Probs). However, low LR has a less robust relationship with drinking frequency.[20]

The low LR is not the only response-related phenotype linked to adverse alcohol outcomes. Another phenotype is greater stimulation from alcohol, which is observed most prominently at rapidly rising BACs in some research paradigms.[21,22] However, prospective work with low LR beginning in the mid-1970s forms the basis for follow-ups in the ongoing prospective study described below. Therefore, the data presented here focus on the low LR.[23]

The first documentation of the relationship between a low LR and several AUD risk factors, such as a family history of AUD, came from alcohol challenges carried out with alcohol-consuming young adults who did not have AUD but were at higher or lower AUD risk.[24] The study compared participants at a higher risk of AUD because of a positive family history with participants at lower risk because of a negative family history who were closely matched on sex, race, percent body water, and recent drinking histories. The study found that both groups had almost identical BACs during the challenge. However, the family-history–positive group demonstrated lower intensities of response to alcohol than the family-history–negative group as measured by a range of effects, including subjective feelings of intoxication, standing steadiness (body sway), changes in hormones, and/or several electrophysiological measures.[24-27]

Because these alcohol challenge analyses were cost- and labor-intensive, researchers subsequently developed a less expensive and less time-consuming measure of LR that could be used in large numbers of subjects, including younger drinkers. The Self-Report of the Effects of Alcohol (SRE) questionnaire—a simple 12-item retrospective self-report—records a person's perception of the number of standard drinks (10 to 12 grams of ethanol) required to experience up to four subjective effects (to first feel any effect, dizzy or slurred speech, unsteady gait, and unwanted falling asleep) during a typical drinking session.[28] This instrument gathers

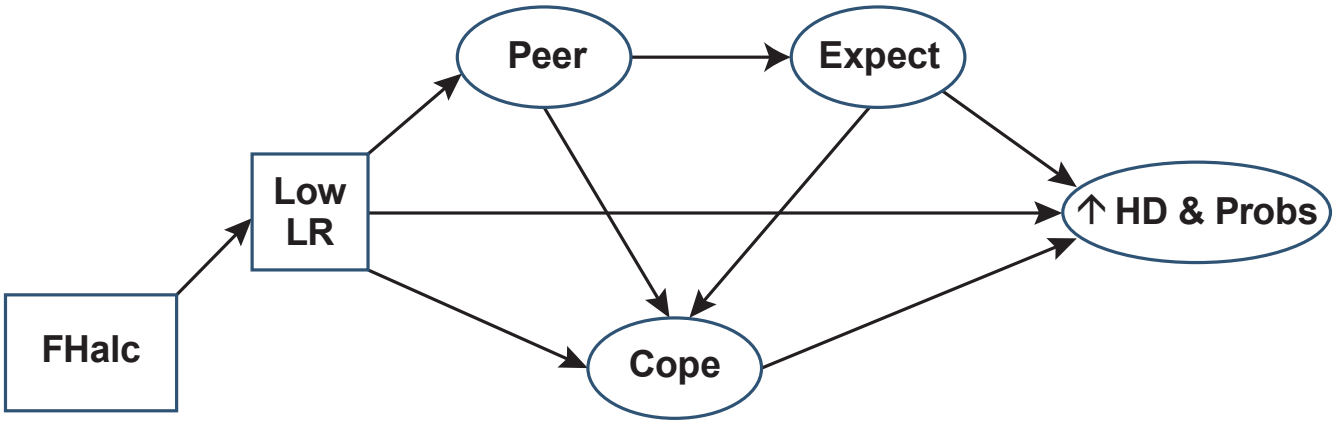

Figure 1. The level of response (LR) model. A low LR to alcohol, which is often associated with a family history of alcohol use disorder (FHalc), increases the risk for heavy drinking and alcohol problems (HD & Probs) both directly and indirectly, through association with heavier-drinking peers (Peer), expectations that heavy drinking is desirable (Expect), and use of alcohol to cope with stress (Cope).[31,37,42] *Source:* Adapted from Schuckit et al. (2004).[19] Reprinted with permission.

data for three timeframes, including the approximate first five times of consuming a full drink (SRE-5), the most recent 3 months of drinking (SRE-3), and the period of heaviest drinking (SRE-H). The score for each timeframe is generated by adding the number of drinks needed for effects that the respondent has experienced and dividing that sum by the number of effects the respondent reported; this calculation yields the average number of drinks needed to achieve effects for that period. SRE values have retest reliabilities and predictive validities regarding drinking quantities and alcohol-related problems of .7 or higher.[28,29] Moreover, multiple studies have documented significant positive correlations between SRE scores (i.e., needing on average higher numbers of drinks for effects or a lower LR per drink) and future heavier alcohol intake and alcohol problems.[30-32]

The retrospective LR measure is not identical to the alcohol challenge in which specific changes in alcohol responses are observed at rising, peak, and falling alcohol blood levels.[18,23] However, laboratory measures of subjective feelings gathered at about the same time as the self-report questionnaire correlated with the SRE at >.3, and SRE ratings overlapped about 60% with alcohol-challenge results in predicting drinking quantities.[28,33]

The SDPS: An Ongoing Prospective Protocol

The study comparing young adult sons of individuals who had a parent with AUD and family history controls described above progressed into the 40-year San Diego Prospective Study (SDPS), each stage of which was approved by the University of California, San Diego (UCSD), Human Research Protections Committee. The study began in 1978 with the recruitment of 453 young men (the original subjects, or probands; average age, 22 years) who were recruited through questionnaires randomly distributed to UCSD students. The participants were 18- to 25-year-old men who consumed alcohol but had never met criteria for AUD.[24] Individuals with lifetime histories of schizophrenia, bipolar disorder, or multiple problems with alcohol or illicit drugs were also excluded.

When entering the study, probands were evaluated for low LR using oral alcohol challenges that resulted in average BACs of 60 mg/dL at 60 minutes.[24,34] Probands then were followed over the next 40 years with personal interviews about every 5 years regarding changes in demography, substance use and problems, as well as major psychiatric disorders. These interviews used questions derived from the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) instrument, which has validity, retest reliabilities, and cross-interviewer reliabilities of .7 to .8.[35,36] Over the years, as probands themselves became parents, information about their children's early development was gathered from the probands and the offspring's mothers, and the same interviews used for the probands were also used with their children when they reached age 18 and older.

During the follow-up evaluations, probands and their children gave information on their LR to alcohol using the SRE instrument described above. Beginning with the 15-year follow-up of SDPS families, the investigators also began to record environmental and attitudinal characteristics that might partially mediate the impact of low LR on heavy drinking and alcohol problems.[31,37,38] These mediators included:

- Perception of the maximum number of standard drinks consumed by close peers as assessed using a short version of the Important People and Activities Scale, which is scored from 0 (abstainer) to 4 (> 10 drinks) with retest reliabilities >.85 (noted in Figure 1 as Peer);[39]
- The usual effects a person expects to experience from alcohol as measured by the Social Behavior (e.g., alcohol makes parties more fun) and Increased Arousal (e.g., alcohol helps people stand up to others) subscales of the Alcohol Expectancy Questionnaires (AEQ) that are graded on a 5-point scale with an internal consistency (Cronbach's alphas) of .72 to .92 (noted in Figure 1 as Expect);[40]
- Whether a person uses alcohol to cope with psychological problems as assessed by the Drinking to Cope scale that records how often respondents use alcohol to decrease negative emotions or boredom or to feel more confident; scores range from 1 (almost never) to 4 (almost always), and Cronbach's alpha is .79 (noted in Figure 1 as Cope).[41]

Testing has supported the hypothetical model in Figure 1 regarding how a low LR, which occurs more frequently in individuals with a family history of AUD, increases the risk for heavy drinking and alcohol problems both directly and indirectly through these potential mediators.[31,37,42] The findings suggested that as much as half of the impact of low LR on adverse alcohol outcomes occurs indirectly, through associating with heavier-drinking peers, expectations that getting drunk is rewarding and desirable, and using alcohol to cope with stress. These findings raised the possibility that for individuals with low LR, interventions that decrease the impact of these three mediators on heavier drinking might reduce the risk for higher maximum drinks and alcohol problems later.

Decreasing Risk of Adverse Outcomes in People With Low LR

The findings of the SDPS served as the basis for a subsequent new study in a different population that assessed an intervention to reduce the risk of heavy drinking and alcohol problems in individuals with a low LR. To recruit participants, a questionnaire was distributed to 18-year-old students entering UCSD as freshmen to review their demography, alcohol and drug use, and

related diagnoses.[43] Potential participants also filled out the SRE to measure LR. After excluding nondrinkers and those who had been diagnosed with alcohol or drug problems, schizophrenia, bipolar disorder, or antisocial personality disorder, the researchers used a median split on the SRE to identify individuals with low and high LR, with the two groups matched on sex, ethnicity/race, and recent alcohol consumption quantities and frequencies. More than 80% of eligible students agreed to participate, and the process continued until 250 pairs of high LR and low LR respondents (500 individuals) were enrolled.

These pairs were randomly assigned to one of three conditions: One group watched four 45-minute internet-based videos that taught general ways to avoid heavy drinking and emphasized the importance of low LR (LR-based group), one group watched similar videos with information about how to limit drinking but without an emphasis on LR (state-of-the-art group), and a control group who were followed over the same 55 weeks as the first two groups but who watched no education videos. The education-group participants received $25 for viewing each of the four 45-minute lectures, one each during the first 4 weeks of the study. Students in all three groups were also paid $25 for filling out each of seven 20-minute internet-based questionnaires over the 55 weeks of the study regarding their recent drinking patterns and problems. More than 90% of participants fully participated in the protocol.

The analyses focused mainly on the pattern of drinking quantities (i.e., usual drinks per occasion and maximum drinks per occasion) and alcohol-related problems (i.e., alcohol-related blackouts) over the 55 weeks for the three groups and the differences between the participants with low LR and high LR. Figure 2 illustrates the findings for the average maximum number of drinks; the results for usual drinks per occasion and the number of alcohol-related blackouts were similar. The left side of Figure 2, panel A, gives the average maximum drinks at each of seven timepoints over the 55 weeks for the participants with SRE scores above the median (i.e., had a lower response per drink, or a lower LR). These data are demonstrated separately for controls (in black), for the state-of-the-art group (in orange), and for the LR-based group (in blue). The right side of Figure 2, panel B, gives the results for individuals who had lower SRE scores (i.e., had higher responses per drink, or higher LRs).

The study found that among the participants with low LR, the average maximum number of drinks per occasion increased steadily over the school year, peaking during the period when the university hosted a spring celebration where heavier drinking was more common than usual. Overall, participants in the control

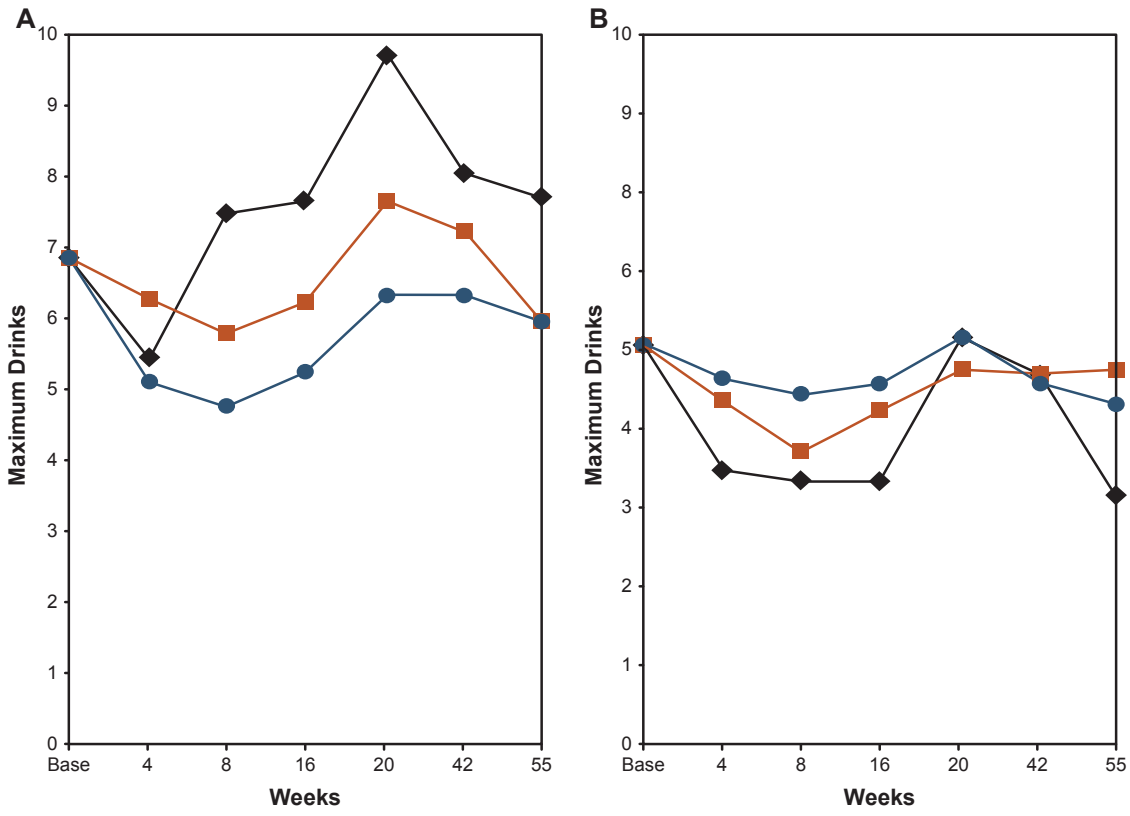

Figure 2. Maximum number of drinks consumed per occasion by students with low (panel A) or high (panel B) level of response (LR) to alcohol over 55 weeks in the San Diego Prevention Study. Blue lines and circle symbols represent students who had watched four videos with LR-based information, orange lines and square symbols represent students who had watched four videos with general alcohol education, and black lines and diamond symbols represent control students who had watched no videos. *Source:* Adapted from Schuckit et al. (2016).[43] Reprinted with permission.

group had the highest maximum number of drinks; the group receiving the standard-of-care intervention had significantly lower maximum numbers of drinks per occasion over the 55-week study period. The greatest reduction in maximum number of drinks, however, was found in the group who had received the LR-based intervention. Among the students who had high LR (i.e., were more sensitive to alcohol's effects), in contrast, there were no significant changes in the maximum number of drinks over time. Moreover, no significant differences existed between the control group, the group receiving the standard-of-care intervention, and the group receiving the LR-based intervention.[43]

This study joins several others[44,45] that underscore the potential importance of targeting a person's specific preexisting vulnerability toward heavy drinking. Imparting knowledge about the genetically influenced risk factor and the mediators that amplify the impact of that risk factor can modify drinking behaviors for extended periods of time.

Conclusions

Long-term prospective studies such as SDPS with its follow-up component provide an opportunity to evaluate problems from a unique perspective compared to other investigations.[31,43,46,47] Such studies are challenging to carry out when funding requires renewal every 3 to 5 years, and they require great effort to ensure consistent participation over time. Thus, such investigations are costly and the number of subjects in the protocol are often limited to several hundred individuals or less, but the data that can be produced by these efforts are unique.

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Alcohol Screening, Brief Intervention, and Referral to Treatment (SBIRT) for Girls and Women

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Females ages 12 and older are the fastest growing segment of alcohol consumers in the United States, with the past decade showing a 16% increase in alcohol use per 12-month period and a 58% increase in high-risk drinking (i.e., > 3 drinks in a day and/or > 7 drinks in a week) per 12-month period. The increase in alcohol use and risk drinking poses unique and serious consequences for women. Women have a more rapid progression to alcohol-related problems and alcohol use disorders (AUD) than men, and if pregnant, women can potentially expose the fetus to alcohol. Screening, brief intervention, and referral to treatment (SBIRT) is an evidence-based, integrated public health approach used to identify and address risky alcohol use among women in a variety of health and social service settings. This article presents the current status of SBIRT among girls ages 12 and older, women of childbearing age, and older women. Screening instruments, brief interventions, and implementation issues specific to women of all ages are described. Through this review of the current literature, care providers can determine best practices for the prevention and treatment of risk drinking in women of all ages presenting in health care settings.

KEY WORDS: brief intervention; risk; alcohol; SBIRT; screening; women; female adolescents

INTRODUCTION

Alcohol is the most commonly consumed substance among Americans ages 12 and older, and women are the fastest growing segment of alcohol consumers in the United States.[1,2] Female alcohol consumption that meets criteria for risk drinking, defined as more than three drinks in a single day or more than seven drinks per week, has the potential to negatively affect the health and well-being of women across their life spans.[3] Evidence indicates converging patterns of alcohol consumption between men and women resulting from recent increases in female alcohol

use behaviors.[2,4,5] For instance, data collected in the past decade reveal that among U.S. women, alcohol use increased by 16% per 12-month period, high-risk drinking increased by 58% per 12-month period, and diagnoses of alcohol use disorder (AUD)—as defined in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders*—increased by 84% per 12-month period.[2] These increases have unique and serious consequences for women given that they experience a more rapid progression—at lower consumption levels—to alcohol-related problems and AUD than men.[6,7]

This recent increase in female alcohol consumption underlines a need for additional research and clinical efforts to address alcohol use among girls and women.[2,4] Because risky drinking poses unique and detrimental consequences to all women, age and life circumstances should not preclude any subset of girls or women from research or clinical efforts to address this growing public health concern. Indeed, risky alcohol use is prevalent among young girls;[8,9] pregnant and postpartum women;[10,11] victims of child abuse,[12] sexual trauma,[13] and intimate partner violence;[14] female veterans;[15] incarcerated girls and women;[16] sexual-minority women;[17] and older women.[5] Due to alcohol's nondiscriminatory nature towards varying groups of women, universal screening, brief intervention, and referral to treatment (SBIRT) appears to be an appropriate, evidence-based public health approach capable of identifying and addressing risky alcohol use among females in a variety of health and social service settings.[18] This article presents a review of the literature regarding the role of SBIRT in addressing risky alcohol consumption among girls (ages 12 to 18), women of childbearing age (i.e., ages 18 to 44), and older women (i.e., ages 65 and older). There is a general lack of currently available research data specific to women ages 45 to 64, but other than risk of pregnancy associated with women ages 18 to 44, the role of SBIRT is similar for women ages 45 to 64 to that for younger women. Databases used for this review include PubMed, Cochrane Library, Google Scholar, and Academic Search Complete. The reference lists of selected articles and texts were also explored.

SBIRT

The current SBIRT model is based on a recommendation from the National Academy of Medicine (previously called the Institute of Medicine) to develop integrated service systems that bridge the gap between primary prevention and treatment services for individuals with problematic alcohol and/or illicit drug use.[19] In 2003, the Substance Abuse and Mental Health Services Administration (SAMHSA) established an initial SBIRT grant program, with the intent of integrating behavioral health services into settings where individuals who engaged in risky substance use behaviors could be identified and offered an appropriate level of intervention and care.[20] Findings from this initiative suggest that SBIRT is associated with improvements in alcohol use outcomes.[20,21]

The U.S. Preventive Services Task Force (USPSTF), an independent entity consisting of experts in preventive medicine, recently updated its recommendation for care providers. This update recommends that care providers screen all adults ages 18 and older, including pregnant women, for risky alcohol use and provide brief behavioral counseling interventions, when appropriate, to reduce unhealthy alcohol use.[22] Screening adolescents younger than age 18 was not included in the updated recommendation; the USPSTF concluded that there is insufficient evidence to properly assess the benefits versus risks for alcohol screening and brief interventions (BI).[22] The American Academy of Pediatrics (AAP), however, has recommended the practice of screening and providing BI to adolescent alcohol users, citing low cost, minimal potential for harm, and emerging evidence of the benefit that SBIRT may have among adolescent alcohol users.[23]

SBIRT is intended to identify, reduce, and prevent problematic alcohol use behaviors and is made up of three key components: screening, brief intervention, and referral to treatment. Ideally, the first step of the SBIRT process is to administer a validated prescreen

instrument to all presenting individuals in a practice setting, as part of the routine intake procedure, to identify those who are drinking at or above risky levels.[24,25,26] When prescreen instruments detect consumption at risk levels, measured by standard drinks (14 grams or 0.6 fluid ounces of pure alcohol) consumed, a more comprehensive assessment can be conducted to gauge the severity of alcohol use and inform BI and/or treatment options.[3] For example, the National Council for Behavioral Health recommends that a symptom checklist or other validated assessment be used to obtain alcohol-related symptoms from individuals whose prescreen indicates risky consumption.[26] If it is determined that an individual is consuming alcohol at moderate risk levels (i.e., above NIAAA threshold for low-risk consumption but not at a level indicative of AUD), then the second step in the SBIRT process is to complete a BI protocol. BIs are often based on principles of motivational interviewing (MI) and aim to increase awareness of alcohol-related risks and consequences and to encourage motivation for change. If an individual is identified to be drinking at levels that are suggestive of AUD, then referral to specialized treatment for further assessment and care is recommended.[27]

SCREENING

SBIRT begins with universal screening, the goal of which is to identify individuals who have, or are at risk of developing, alcohol-related problems.[27] Universal screening that is adherent to SBIRT standards, and described in multiple SBIRT practice guides, involves the administration of a validated prescreen instrument that has been limited to a few questions needing only simple responses.[24,26,28,29] Ideal screening instruments have high sensitivity and specificity ratings, with cutoff scores designed to maximize both ratings in order to minimize false positives and false negatives.[30] However, for prescreen instruments that are intended to be universally administered, priority is often given to sensitivity over specificity so that individuals in large clinical populations (e.g., women in primary or reproductive care settings who consume alcohol while pregnant) are appropriately identified for further assessment.[30,31]

This article classifies screening instruments into prescreen and screen categories. The purpose of prescreening is to assess an individual's frequency and quantity of alcohol use to determine whether the person is drinking at age-specific risk levels, whereas the purpose of screening is to elicit alcohol-related symptoms from those that have been identified as drinking at risk levels. Prescreens and screens should work in succession, and because many instruments are capable of serving both screening purposes, this dual process is sometimes consolidated into a single step within clinical practice settings.

Universal prescreening and screening efforts must be conducted using valid, age-appropriate instruments with cutoff scores that are tailored to a population's sex and age (see Table 1).[32] Following is an overview of screening practices and instruments that have been validated for use within specified age groups of girls and women.

Adolescents

NIAAA, SAMHSA, and AAP recommend that care providers screen all adolescents and young adults ages 12 to 21 for alcohol and substance use behaviors using validated screening instruments on a yearly basis and, as needed, during acute care visits.[33] There are currently three prescreen options that are applicable to adolescents: the two age-specific questions found in NIAAA's *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide*;[29] the first three questions of the Screening to Brief Intervention (S2BI); and the three-item Alcohol Use Disorders Identification Test–Concise (AUDIT-C).[33] The two age-specific questions found within NIAAA's guide ask about an adolescent's personal alcohol use as well as that of their friends and is appropriate for children and adolescents between the ages of 9 and 18. This AAP-endorsed guide includes elementary, middle, and high school age-appropriate variations of these two questions, which allow for accurate correlation of patient responses to current or potential risky alcohol consumption.[29] The S2BI instrument screens

for alcohol, tobacco, marijuana, and illicit drug use by asking a single frequency-of-use question per substance. This screener is highly sensitive and specific at discerning among various risk categories, from no use to severe substance use disorder (SUD). Although not a formal diagnostic instrument, the S2BI has been shown to closely correspond with the likelihood of current SUD.[34] The AUDIT-C, validated for use with young people ages 12 to 19, has three questions to identify the quantity and frequency of alcohol consumption.[32,35,36]

When adolescents score positive on a prescreen instrument, indicating some level of risky alcohol consumption, they are asked to respond to additional, more specific screening questions to determine whether a BI or referral to treatment is appropriate. Screening instruments that have been validated for use with adolescents and can be used to inform next steps include the 10-item Alcohol Use Disorders Identification Test (AUDIT); the Brief Screener for Tobacco, Alcohol, and Other Drugs (BSTAD); and the Car, Relax, Alone, Forget, Friends, Trouble (CRAFFT) screening instrument.[23,32,37] The AUDIT is the most widely tested alcohol screening instrument and is commonly used to assist in the early identification of individuals engaging in risky drinking behaviors.[22] Furthermore, the AUDIT has been validated for use among young people,and evidence suggests a lack of gender bias between female and male adolescents.[32,35] The BSTAD, an adaptation of the questions found within NIAAA's guide includes questions on alcohol, tobacco, and drugs, and has been shown to be highly sensitive and specific at identifying risky past-year alcohol use among adolescents ages 12 to 17.[38] Recommended by both NIAAA and AAP, the CRAFFT has been validated across pediatric settings to identify risky substance use behaviors among adolescents.[18,39] Interestingly, the CRAFFT was able to detect preconception substance use in a small cohort of pregnant adolescents and young women between ages 17 and 25.[33,40] The CRAFFT has many advantages, including a short administration time and high sensitivity and specificity.[33] It also shows no evidence of gender bias.[36]

Screening adolescents for risky alcohol use can be incorporated into psychosocial approaches. For example, the home environment, education and employment, eating, peer-related activities, drugs, sexuality, suicide/depression, and safety from injury and violence (HEEADSSS) and the strengths, school, home, activities, drugs/substance use, emotions/depression, sexuality, safety (SSHADESS) tools are interview frameworks specifically designed for use with adolescents in health care settings.[23,33] The HEEADSSS interview is a practical, complementary strategy that establishes rapport by asking less threatening questions at the beginning of the encounter before transitioning to more personal or potentially intrusive topics such as substance use.[33] The SSHADESS interview covers the same life areas as the HEEADSSS, but it also underscores adolescents' resiliency by identifying their perceived and realized strengths before asking questions related to environmental context or risky behaviors.[23]

A caveat is that an assurance of confidentiality is needed to improve the accuracy of adolescent screening responses. Because most adolescents are not comfortable discussing topics like alcohol use and sexual activity in the presence of a parent or guardian, clinicians are encouraged to create scripts or other procedures to excuse the accompanying adult from a portion of the health exam.[33] For example, asking the adult to leave the room during the physical exam portion validates the adolescent's developmental need for privacy and creates space for a confidential discussion concerning alcohol and other potentially risky behaviors.[33] Federal and state privacy laws entitle adolescents to privacy regarding substance use treatment, so adolescents may further benefit from a script ensuring that what is disclosed to the provider will not be shared with their caregiver unless an immediate risk of injury to oneself or another is divulged.[33]

Women of Childbearing Age

For women of childbearing age, the USPSTF supports the use of brief prescreening instruments for alcohol with 1 to 3 items—such as the

AUDIT-C or the NIAAA-recommended Single Alcohol Screening Question (SASQ), also referred to as the "single binge drinking question"—to quickly identify women who may be at risk.[22,41,42] The use of a single binge drinking question has also been recommended as a first step to effectively and efficiently identify women who are likely to be at risk of an alcohol-exposed pregnancy (AEP).[43] For example, a single binge drinking question was found to correctly identify 99% of women, from two countries and cultures, who had been identified as at risk of an AEP.[43] The Quick Drinking Screen (QDS) is another brief instrument that is efficacious at initially identifying women at risk of an AEP.[44] Items from the QDS were measured against data collected from a 90-day timeline followback (TLFB) assessment among a sample of women already determined to be at risk of an AEP. The results found that the women's answers to QDS items were highly similar to their 90-day TLFB responses.[43]

Once a brief prescreening measure identifies a woman who is likely to be at risk for alcohol misuse and/or an AEP, it is recommended that a more comprehensive instrument be administered.[22,43] For example, the 10-item AUDIT is an efficacious measure that has been validated for use with this population.[45] There are also several assessments designed specifically for women of childbearing age, including pregnant women and women at risk of an AEP. It is recommended that universal prescreening among women of childbearing age be used to identify and assess women at risk of an AEP.[45,46] Screening this population provides the opportunity for early intervention among women who may have consumed alcohol prior to becoming aware of their pregnancy. Screening also alerts care providers of consumption levels indicative of AUD so that they can refer these women for specialized treatment.

The Tolerance, Annoyed, Cut Down, Eye-Opener (T-ACE) questionnaire was the first validated screening instrument developed to identify drinking among pregnant women. It is often used in reproductive settings, including maternity care and gynecological clinics.[25,31] In comparison to the AUDIT, the four-item T-ACE has shown slightly higher sensitivity at detecting current alcohol consumption among pregnant women.[31] In addition, the T-ACE accurately identifies varying levels of alcohol consumption and is acceptable for use among culturally diverse obstetric populations.[31] The five-item Tolerance, Worried, Eye-Opener, Amnesia, K/Cut Down (TWEAK) screening instrument is another validated questionnaire for identifying drinking among women, including those who are pregnant and those at risk of an AEP.[25,31,45] Although the TWEAK questionnaire appears to be highly sensitive at identifying heavy patterns of alcohol consumption, primarily among white women, it is less sensitive at detecting lower levels of drinking that could still be considered at risk.[25,47]

In addition to the T-ACE and TWEAK, the USPSTF also recommends the Normal Drinker, Eye-Opener, Tolerance (NET), and the Parents, Partner, Past, Present Pregnancy (4P's Plus) as screening measures capable of assessing alcohol use among pregnant women.[22,47,48] Nonetheless, the T-ACE and TWEAK reportedly perform best among pregnant women and do not appear to have a significant advantage over one another, because both are well-validated screening measures that can be quickly administered in a variety of women's health settings.[18]

Older Women

Older women are often missed by screening efforts because their alcohol-related symptoms are often mistaken for signs of aging.[49] For this reason, systems must be put into place to ensure universal screening on a recurring basis in settings that care for older women.[50] Alcohol screening should take place any time new mental or physical health symptoms arise, before prescribing a new medication, in response to major life changes (e.g., retirement, death of a spouse), and on a yearly basis as part of routine physical and mental health services.[50,51] Providers should be aware that a history of risky alcohol use among older adults often predicts future increases in drinking.[50] Prescreening questions like "During your lifetime,

have you ever used alcohol?" followed by "During the past year, have you had four or more drinks on a single occasion?" help to determine whether more comprehensive assessments are warranted.[51,52] The AUDIT-C and the two-item Substance Use Brief Screen (SUBS) are also prescreen options available for use with this population.[53-55]

Several screening instruments have been validated for use with older adults. Measures like the AUDIT include screening questions on lifetime problems to assess current alcohol-related risk.[54,56] Other screening tools include the Cut Down, Annoyed, Guilty, Eye-Opener (CAGE), the Michigan Alcoholism Screening Test—Geriatric Version (MAST-G), the Short MAST-G, and the Comorbidity Alcohol Risk Evaluation Tool (CARET).[54,57] All of these instruments gather information about the level of consumption and offer decision support for care providers.[50,54] In general, alcohol screening and assessment instruments among older women should contain questions about the frequency and quantity of alcohol use, experiences with drinking-related consequences, medication use, and feelings of depression.[50]

SCREENING RECOMMENDATIONS

There are very few studies on alcohol screening specific to adolescent females and older adult females beyond childbearing age, with a majority of information coming from mixed-gender studies. The largest body of evidence on screening women is for those of childbearing age, likely due to the added risks and harms associated with prenatal alcohol exposure. Nonetheless, universal screening should begin in early adolescence and be repeated at regular intervals across settings that provide health care and social services to girls and women. However, although alcohol screening instruments elicit important information about an individual's level of risk and alcohol-related symptoms, these tools are not a replacement for a complete substance use assessment. Because these instruments are brief and, in many cases, can be self-administered, it is often recommended that care providers use them as decision support aids to guide additional steps based on the preliminary level of risk indicated by these alcohol screening instruments.

The successful implementation of a screening protocol depends on the setting in which it is delivered. For example, settings with access to interdisciplinary professionals may find that longer, more thorough assessment instruments are practical, whereas settings with fewer resources are likely to benefit from utilizing brief instruments like the AUDIT, which has been validated for use across age groups.[32,35,56] Additionally, questions or measures may be added to assessment protocols to identify other factors known to be associated with female alcohol use behaviors (e.g., age of onset, depression and anxiety, childhood and/or intimate partner abuse, co-occurring substance use behaviors) to better inform BI and referral to treatment practices.[13,16,58,59] Moreover, care providers need to remain mindful regarding the language they use to describe alcohol-related concerns so as not to further stigmatize female populations.[60] For example, some women may be sensitive to language such as "alcoholic," "addict," or "abuser"; the use of such language may dissuade women from providing relevant information pertaining to their alcohol use behaviors. Therefore, care providers are advised to use medically accurate terms throughout their discussions regarding alcohol and substance use behaviors.[55,60]

BRIEF INTERVENTIONS

BIs are evidence-based practices that are short, targeted conversations between women and clinicians that follow screening results indicative of risky alcohol consumption. The overall goal of BIs is to help adolescent girls and women who are at risk of alcohol-related consequences by increasing their awareness about the ways alcohol use may put them at risk and encouraging their self-motivation for change.[27,61] Common components of BIs include conversations on standard drink sizes, low- versus high-risk drinking limits, and potential health effects and

social consequences of drinking.[3,62] Another common element of BIs is providing personalized normative feedback, with evidence supporting the use of gender-specific feedback for women.[63,64,65] BIs can be delivered by professionals with different backgrounds and expertise, and they can take place in face-to-face settings, over the phone, or through electronic means.[61,66] How effective BIs are can depend on the number of sessions and length of time allotted for each session. For example, systematic reviews and meta-analyses have found that very brief (i.e., ≤ 5 min) and brief single-contact interventions (i.e., 6 to 15 min) tend to be less effective than brief multicontact interventions (i.e., each contact ≤ 15 min), which evidence shows is the most effective across populations and outcomes.[18,63,67] Additionally, one meta-analysis found that extended BIs (defined by the author as BIs that required several visits, or multicontact interventions) resulted in significant change in alcohol consumption for women but not men.[68]

BIs for risky alcohol use are often based on the principles of MI. Using this collaborative, client-centered approach, providers help females explore and resolve their ambivalence toward changing unhealthy behaviors (e.g., alcohol consumption at risk levels).[69] A core tenet of MI is the use of nonconfrontational techniques to allow individuals to guide themselves toward change without feeling the need to defend their choices.[69]

Adolescents

AAP recommends basing the degree of intervention delivery for youth on the level of risk identified at the time of screening. When no alcohol use is reported, clinicians are encouraged to provide positive verbal reinforcements to motivate continued abstinence. Evidence suggests that even a few positive words from a health care provider may delay alcohol use initiation, and thus extend time for adolescent brain maturation.[23] These positive reinforcements may be critical for female adolescents to receive, especially girls at risk of early alcohol initiation,[7,58] because of the detrimental effects of alcohol on the female developing brain.[70] When infrequent alcohol use is endorsed by female adolescents, such as when an S2BI result indicates alcohol use of one to two times the previous year, it is recommended that care providers advise adolescents to abstain. This advice may combine information on negative health consequences with recognition of personal strengths and positive attributes.[23]

BIs are recommended when an adolescent screens positive for drinking at risky levels. Evidence from a recent meta-analysis of 185 studies examining the effects of alcohol-related BIs for adolescents and young adults found that the interventions effectively reduced drinking and alcohol-related consequences, with effects lasting up to 1 year and showing no demographic variance.[65]

BIs that utilize MI have been found to be effective with substance-using adolescent populations. Much of the research supporting this view falls into the harm-reduction continuum: that is, adolescents do not move directly into abstinence but rather gradually decrease their risky behavior.[71,72] In addition to the effectiveness of MI techniques within this population, a systematic review and meta-analysis conducted by Carney and Myers also found that adolescents showed a preference for individualized interventions (i.e., compared with a group format) conducted over multiple sessions (i.e., compared with a single event).[67]

In alignment with the USPSTF finding of there being insufficient evidence to evaluate the utility of BIs among alcohol-using adolescent populations, evidence specific to adolescent females who receive brief alcohol interventions is also lacking and warrants future investigation. In a recent systematic review and meta-analysis of the literature on brief alcohol interventions for adolescents and young adults, Tanner-Smith and Lipsey found a limited number of studies with boy-only or girl-only samples that reported little to no evidence of differential effectiveness based on gender.[65] There is some evidence, however, suggesting that BIs for alcohol use may be particularly effective for adolescent girls, especially when the provider is also female and the information is delivered in the context of an ongoing provider–patient relationship.[73]

Women of Childbearing Age

There is strong evidence supporting the use of BIs among pregnant and nonpregnant women of childbearing age as a means of reducing levels of alcohol consumption and risks associated with AEPs.[18,62,74] For example, in one large multisite trial, approximately 69% of women who, at intake, were drinking at risky levels and not using effective contraceptive methods reduced their risk of an AEP at the 9-month follow-up after receiving an intervention incorporating MI. The women in this study achieved risk reduction by abstaining from alcohol or drinking below risky levels, by using effective contraceptive methods every time they had vaginal intercourse with a fertile male, or both.[75] A number of randomized controlled trials with pregnant women have also reported significant reductions in alcohol use and improved newborn outcomes following the facilitation of BIs.[62]

In addition to previously mentioned common components of BIs (e.g., personalized normative feedback), interventions with women of childbearing age often also include feedback on the potential effects of alcohol on fetal and child development.[25,64] It is recommended that postpartum women receive information on infant exposure to alcohol through breastmilk and that contraceptive use should be incorporated into BIs with nonpregnant women who are at risk of an AEP.[25,64]

Efficacious prevention and intervention programs have been developed for use with women of childbearing age. One example is the CHOICES program and its adaptations: BALANCE, EARLY, and CHOICES Plus.[76,77,78] CHOICES is an established AEP prevention program based on the principles of MI and designed to provide nonpregnant women of childbearing age with information to help them make informed choices on ways to avoid an AEP.[43] The CHOICES protocol has been widely disseminated across health and social service settings (e.g., primary care facilities, jails, sexually transmitted disease clinics).[75,78,79] Also, as a result of meeting rigorous peer-review criteria, the CHOICES program was included in SAMHSA's Evidence-Based Practices Resource Center (https://www.cdc.gov/ncbddd/fasd/choices-importance-preventing-alcohol-exposed-pregnancies.html).

Older Women

Although limited, studies on BIs with older adults suggest that BIs are effective at reducing risky alcohol consumption, with sustained reductions ranging from 2 to 18 months.[80,81,82] The content and format of most BIs are similar, as are the recommendations, whether delivered to younger or older cohorts. For example, providers are advised to use nonstigmatizing and nonjudgmental language when discussing screening results and any potential alcohol-related health consequences with women.[55] Regarding older women, some experts suggest that providers may find that incorporating the women's family and friends into various parts of the BI process may prove successful.[51]

Other BIs

Multiple BI models have been created to aid in the facilitation of BI conversations.[25,27] A systematic review of BIs for risky drinking in primary care settings reported that a majority are arranged according to the SAMHSA-endorsed Feedback, Responsibility, Advice, Menu of strategies, Empathy, Self-efficacy (FRAMES) model.[33,64] Other BI models that are endorsed by SAMHSA include the Feedback, Listen, Options (FLO) model, the Brief Negotiated Interview (BNI) Steps, and the BNI and Active Referral to Treatment: Provider Training Algorithms.[27] All of these models serve as useful guides for delivering BIs and are presumed to be equally efficacious regardless of age or gender. Practitioners should choose the model that best suits their work setting.

In summary, BIs are valuable tools for reducing alcohol consumption and its associated risks (e.g., AEPs). It is vital to consider that despite a number of randomized controlled trials suggesting similar efficacy for brief alcohol interventions among women and men,[83,84] women have been less likely to receive BIs in practice. As such, lending attention to this issue is critical considering that the prevalence rates for alcohol use among women are rising.[85]

REFERRAL TO TREATMENT

Referral to treatment is a process designed to assist women with accessing specialized treatment, selecting facilities, and navigating barriers that may prevent treatment engagement.[27] Treatment options for women with AUD may include residential treatment, outpatient psychological therapy (e.g., family, group, conjoint, individual), medication-assisted treatment, self-help or support group programs (e.g., 12-step programs such as Alcoholics Anonymous), harm reduction approaches, use of a recovery coach, or any combination of these. There are also treatment options that cater exclusively to women, such as the Women for Sobriety program and women-only Alcoholics Anonymous groups. Specialized alcohol treatment should be personalized to the woman, taking into account her medical, social, and cultural needs. Providers should be aware of local treatment options in order to conduct warm handoffs—referrals facilitated in the presence of the patient to encourage communication and partnership between the patient and treatment team—when needed. Providers should also pay special attention to the treatment selection for pregnant and postpartum women to ensure that appropriate medical care and social support options are available.[25] Providers may also choose to access SAMHSA's online resource guide, which includes samples of scripts, procedures, and links to treatment locator websites.[27] Other referral resources include NIAAA's online Alcohol Treatment Navigator tool (https://alcoholtreatment.niaaa.nih.gov) and NIAAA's publicly available resource guides, with information specific to referrals: *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide*[29] and *Helping Patients Who Drink Too Much: A Clinician's Guide*.[28]

Referral to treatment is a critical, yet often overlooked, component of SBIRT. Although some studies have found it effective to link individuals to specialty treatments,[86,87] evidence from many others suggests that it is often difficult to link individuals in need of alcohol-related specialized care to substance use treatment services. For example, a meta-analysis of nine studies found no evidence that brief alcohol interventions were efficacious for increasing the use of alcohol-related services.[88] Referral to treatment is further compounded by gender-specific barriers to treatment that impact women's ability to engage in services. In general, women are less likely than men to initiate alcohol treatment services, and when they do, research suggests that women often contend with stigma, negative staff attitudes, lack of affordable or safe childcare options, and concerns over child custody.[89] When they do access treatment services, more women than men present with histories of trauma and abuse, psychological distress and mental health concerns, interpersonal and family-related issues, and financial constraints.[90] Barriers on a systemic level include lack of treatment options because of geographic isolation and lack of awareness among care providers regarding local treatment options that are capable of addressing the unique needs of adolescent girls and women in treatment settings.[89]

BARRIERS AND FACILITATORS TO SBIRT IMPLEMENTATION

A number of health and social service providers (e.g., physicians, nurses, social workers, psychologists, midwives) are qualified to effectively implement SBIRT across a variety of patient and client settings. However, studies of SBIRT implementation reveal that few providers feel comfortable doing so, with the lowest screening and counseling rates seen among young adult and women's reproductive care providers.[18] For example, one study found that one-third of women who endorsed alcohol consumption in women's health clinics were not asked how much they drank and that a majority of women drinking at risk levels did not receive advice on low-risk limits.[91] Another study concluded that approximately half of women at risk of an AEP did not receive information pertaining to this risk from their health care providers.[91] These findings corroborate national survey data of family planning clinicians, which found that of these clinicians,

approximately one-third used a validated screening measure and one-fifth provided a referral that consisted of more than a list of treatment options.[92]

Qualitative analyses conducted among health care providers have revealed several common barriers to implementing SBIRT, including time constraints, competing priorities, cost, and privacy and confidentiality concerns.[93-96] Barriers that pediatric providers cited include concerns regarding the willingness of adolescents to return for follow-up, limited access to and knowledge of adolescent treatment programs or local expertise, and confidentiality concerns.[94] Additional SBIRT barriers that prenatal care providers identified included lack of rapport between providers and women presenting for an initial prenatal consultation; providers' misperception that there is a low prevalence of alcohol use by pregnant women; providers' lack of skills, training, and follow-up protocol; women's underreporting or false disclosure of alcohol consumption; and providers' concerns over creating guilt and anxiety among pregnant women.[95,96]

Many of these provider-identified barriers should be considered in combination with, and resulting from, U.S. state policies mandating that health care providers report perinatal substance use to child welfare agencies.[97,98] For instance, in 2017, Jarlenski and colleagues conducted a systematic content analysis that identified 24 states with statutes around reporting perinatal substance use by health care providers. Twenty of the states identified had mandatory reporting statutes, while 11 states specified a penalty capable of resulting in a misdemeanor charge for health care providers who failed to report known perinatal substance use.[98] Furthermore, some state statutes allow for involuntary commitment and custody loss solely as a result of prenatal substance use, thus creating an ethical and moral dilemma for prenatal care providers because this violates the principles of patient autonomy and beneficence.[99] This issue was further complicated for prenatal care providers by updated recommendations from the American College of Obstetricians and Gynecologists and the Centers for Disease Control and Prevention, which advise providers to conduct universal screening at initial prenatal appointments.[46,98]

In addition to the barriers faced by prenatal care providers, pregnant women engaged in substance use behaviors often face their own barriers to receiving care, such as fear of stigmatization and legal consequences. This may result in a lack of engagement in prenatal care altogether, thus eliminating the potential for SBIRT implementation and posing significant risks to the health of both mother and child.[60]

Older women also face unique barriers to alcohol intervention and treatment efforts. These include financial limitations and lack of mobility and transportation. Older women also report higher rates of stigma, shame, and guilt than younger women, which may lead to an increased prevalence of isolation, anxiety, and depression.[51]

Approaches to Facilitating SBIRT Implementation

In response to the many recognized barriers, research has begun to identify approaches that facilitate successful SBIRT implementation. So far, evidence suggests that having a practice champion, utilizing an interprofessional team, communicating the details of each SBIRT step, developing relationships with referral partners, instituting ongoing SBIRT training for sustainability, aligning SBIRT practices with the organization's flow, and integrating SBIRT into electronic health records are all ways to facilitate ongoing SBIRT efforts.[24] Additionally, a study of ongoing SBIRT facilitation compared usual care and two adolescent SBIRT delivery modalities (pediatrician-only and pediatrician with an embedded behavioral clinician) and found that although substance use outcomes did not differ between pediatrician-only and embedded behavioral clinician groups, adolescents in the embedded group reported fewer depression symptoms at follow-up.[100] The inclusion of a

behavioral clinician in pediatric settings may be especially beneficial to adolescent girls in light of recent evidence that higher levels of depression severity among girls ages 13 to 16 predicted alcohol use in the following year.[59]

Technology

The use of technology is an additional option for overcoming SBIRT barriers in clinical settings that lack available staff and time resources for ongoing face-to-face implementation.[101] Technology is increasingly being used to facilitate various SBIRT components, with preliminary evidence observed among adolescent girls and women looking promising.[74,102,103] A recent systematic review of women's experiences with technology-based screening found that the perception of anonymity made it easier to divulge potentially stigmatizing information compared to in-person, face-to-face screening methods. Therefore, technology-based screening has the potential to increase disclosure rates and intervention receipt.[104] Studies also suggest that women feel less embarrassed and less afraid of judgment when they participate in technology-based interventions, and the flexibility offered by some technology-based treatments may also be appealing to women who are not willing or able to participate in more formal treatment programs because of family and societal roles.[104]

Nevertheless, whether electronic SBIRT can be effective as a stand-alone entity has yet to be established. One recent study demonstrated successful implementation of a technology-based alcohol intervention (i.e., sans personnel) among women of childbearing age;[66] however, interaction findings from other studies suggest that various female groups may have other intervention needs.[105] For example, Choo and colleagues reported that although female victims of intimate partner violence were receptive to electronic screening and advice, they also desired empathy and compassion from human interaction provided during intervention delivery.[105] Still, evidence has suggested that electronically delivered SBIRT components are mutually beneficial to both women and providers.[103,106] In the future, the use of electronic approaches could also assist in the translation of research findings into routine care settings by standardizing intervention delivery methods while maintaining wide applicability across health and social service settings.[107]

FUTURE DIRECTIONS

More research is needed to evaluate the effectiveness, efficacy, and feasibility of SBIRT practices among females, primarily those in younger and older cohorts, and those at risk of AEPs.[4,10,59,64] Recent reports showed increases in alcohol use among adolescent girls, with evidence suggesting a reversal from traditional male excess to slight female excess in 8th grade, and by 12th grade, 35% of girls reported past-month alcohol use, corresponding to a 250% increase from 8th grade.[9,102] Age of alcohol use initiation is particularly worrisome among adolescent females, given that early initiating females drink more than all male adolescents from ages 12 to 17.[8] Additionally, the association between depression severity and alcohol use appears to be more salient for early adolescent girls than for boys of the same age, with observations suggesting that alcohol use both predicts and is a consequence of depression.[59] Research is also needed to address alcohol use among older women due to population increases. Given the aging of the baby-boom generation, population projections estimate that by 2040, the proportion of women to men ages 65 or older will be 127 to 100.[51,108]

SBIRT is essential for the ongoing identification and intervention of risky alcohol use behaviors among adolescent girls and women. As the prevalence rate of female alcohol use increases, so too should the implementation of SBIRT. These prevention and intervention efforts can help promote lifelong health and well-being among women, with special attention paid to younger and older cohorts, and those at risk of an AEP.

Table 1 Alcohol Screening Instruments

Instrument	No. of Items in Instrument	Approx. Time to Administer (min)	Applicable Population	Scoring That Indicates Risk and Statistical Performance (Sensitivity; Specificity)	Copyright, Source(s), and Cost‡‡	Link(s)
NIAAA *Alcohol Screening and Brief Intervention for Youth: A Practitioner's Guide*[29]	2 to 3 depending on severity	~2	Adolescents ages 9 to 18	Elementary or middle school adolescents (≤ 15 years old) reporting any alcohol use (0.89; 0.91)[33] High school adolescents (≥ 16 years old) reporting ≥ 6 days of past-year alcohol use (0.88; 0.81)[33]	Copyright: N/A Source: N/A Cost: Free online	Publicly available NIAAA guide containing screening questions (page 8): https://www.niaaa.nih.gov/sites/default/files/publications/YouthGuide.pdf
Screening to Brief Intervention (S2BI)[34*]	3 (additional 4 if past-year use indicated)	~2	Adolescents ages 12 to 17	Adolescents reporting alcohol use *once or twice* in the past year (0.96; 0.92) Adolescents reporting alcohol use *monthly* in the past year (0.79; 0.96) Adolescents reporting alcohol use *weekly or more* in the past year (1.00; 0.88)	Copyright: N/A Source: N/A Cost: Free online	Publicly available NIDA link to online version with options for patient or clinician administration: https://www.drugabuse.gov/ast/s2bi/#/
Brief Screener for Tobacco, Alcohol, and Other Drugs (BSTAD)[38*]	6 (additional 3 to 11 if past-year use indicated)	~2	Adolescents ages 12 to 17	≥ 2 days of past-year alcohol use (0.96; 0.85)	Copyright: N/A Source: N/A Cost: Free online	Publicly available NIDA link to web-based instrument with options for patient or clinician administration: https://www.drugabuse.gov/ast/bstad/#/
Alcohol Use Disorders Identification Test (AUDIT)	10	~2 to 3	Adolescent girls ages 12 to 19, adults,§ pregnant women, older adults	Positive score indicating risk: Adolescent girls: ≥ 5 (0.95; 0.77)[32] Adults: ≥ 8 (0.38–0.73; 0.89–0.97)[18]** Pregnant women: > 0[18] Older adults: ≥ 5 (0.86; 0.87)[54]	Copyright: 1989, Thomas Babor and the World Health Organization Sources: World Health Organization, Division of Mental Health & Prevention of Substance Abuse, 1211 Geneva 27, Switzerland Email: Publications@who.int Thomas F. Babor, Alcohol Research Center, University of Connecticut, Farmington, CT Cost: Core questionnaire can be reproduced without permission; test and manual are free; training module costs $75	Publicly available link to self-report instrument: https://cde.drugabuse.gov/sites/nida_cde/files/AUDIT-SelfReport_v1.0_2014May20.pdf

Instrument	No. of Items in Instrument	Approx. Time to Administer (min)	Applicable Population	Scoring That Indicates Risk and Statistical Performance (Sensitivity; Specificity)	Copyright, Source(s), and Cost‡‡	Link(s)
Alcohol Use Disorders Identification Test-Concise (AUDIT-C)	3	~1	Adolescent girls ages 12 to 19, adult women,† pregnant women, older adults	Adolescent girls: ≥ 3 (0.96; 0.65)[32] Adult women: ≥ 3 (0.73–0.97; 0.34–0.89)[18] Pregnant women: > 0 (NR‡)[18] Older adults: ≥ 4 (0.94; 0.80)[54]	Copyright: N/A Source: N/A Cost: Free online	Publicly available SAMHSA link: https://www.integration.samhsa.gov/images/res/tool_auditc.pdf
Car, Relax, Alone, Forget, Friends, Trouble (CRAFFT)[37]*	4 (additional 5 if past-year use indicated)	~2 to 3	Adolescents ages 12 to 21	≥ 1 (0.94; 0.74)[30,39] Optimal cutoff score indicating heightened risk for SUD: ≥ 2 (0.79; 0.97)[39]	Copyright: 2001, Boston Children's Hospital Source: The Center for Adolescent Substance Abuse Research, Children's Hospital, 300 Longwood Ave., Boston, MA 02115 Phone: 617-355-5433 Email: crafft@childrens.harvard.edu Cost: N/A	Publicly available SAMHSA link which states that the CRAFFT may be reproduced in [this] exact form for use in clinical settings courtesy of the Center for Adolescent Substance Abuse Research at the Boston Children's Hospital: https://www.integration.samhsa.gov/clinical-practice/sbirt/CRAFFT_Screening_interview.pdf Link from Boston Children's Hospital with additional information: http://crafft.org/
NIAAA Single Item Alcohol Screening Questionnaire (SASQ)[52]	1	~1	Adults	≥ 1 (0.82; 0.79)[18]	Copyright: N/A Source: N/A Cost: N/A	Publicly available SAMHSA link to NIAAA's *Helping Patients Who Drink Too Much: A Clinician's Guide,* which includes NIAAA SASQ (page 4): https://www.integration.samhsa.gov/clinical-practice/Helping_Patients_Who_Drink_Too_Much.pdf Publicly available USPSTF Final Recommendation Statement: *Unhealthy Alcohol Use in Adolescents and Adults: Screening and Behavioral Counseling Interventions,* includes NIAAA SASQ question: https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/unhealthy-alcohol-use-in-adolescents-and-adults-screening-and-behavioral-counseling-interventions

Instrument	No. of Items in Instrument	Approx. Time to Administer (min)	Applicable Population	Scoring That Indicates Risk and Statistical Performance (Sensitivity; Specificity)	Copyright, Source(s), and Cost‡‡	Link(s)
Quick Drinking Screen (QDS)[44,109]	3	~1	Adults	Scoring based on presence of NIAAA defined at-risk drinking (i.e., more than 3 drinks on any day or 7 drinks per week for adult women) in past 90 days[43††]	Copyright: 2003, Sobell & Sobell Source: Linda C. Sobell, PhD, ABPP, Center for Psychological Studies, Nova Southeastern University, 3301 College Ave., Fort Lauderdale, FL 33314 Email: sobelll@nova.edu Cost: Free	Publicly available link that states that this screener can be freely used as it is in the public domain: https://www.nova.edu/gsc/forms/quick_drinking_screen.pdf
Tolerance, Annoyed, Cut Down, Eye Opener (T-ACE)[31]	4	~1	Women of childbearing age	≥ 2 (0.69–0.88; 0.71–0.89)[25]	Copyright: 1989, Harcourt Health Sciences; permission needed to publish Sources: S. Martier, Ob/Gyn, 4707 Saint Antoine, Detroit, MI 48201 Permissions Department, Mosby, Inc. (a division of Elsevier), 6277 Sea Harbor Dr., Orlando, FL Phone: 407-345-3994 http://www.us.elsevierhealth.com/ Cost: N/A	Publicly available NIAAA link containing copyright information: https://pubs.niaaa.nih.gov/publications/t_ace.htm Publicly available NIAAA link containing T-ACE questions: https://pubs.niaaa.nih.gov/publications/arh28-2/78-79.htm
Tolerance, Worried, Eye Opener, Amnesia, K-Cut Down (TWEAK)[31]	5	~2	Pregnant women	≥ 2 (0.71–0.91; 0.73–0.83)[25]	Copyright: None Source: Marcia Russell Prevention Research Center, 1995 University Avenue, Suite 450, Berkeley, CA 94704 Phone: 510-883-5703 Email: russell@prev.org Cost: Free	Publicly available NIAAA link with more information: https://pubs.niaaa.nih.gov/publications/assessingalcohol/instrumentpdfs/74_tweak.pdf
Normal Drinker, Eye-Opener, Tolerance (NET)[47]	3	~1	Pregnant women	≥ 2 (0.61; 0.87)[47]	Copyright: 1989, Lippincott Williams & Wilkins Source: Lippincott Williams & Wilkins Permissions Department, 351 West Camden St., Baltimore, MD 21201 Phone: 410-528-4050 Email: permissions@lww.com http://www.lww.com/permissions/index.htm Cost: N/A	Not publicly available
Parents, Partner, Past, Present Pregnancy (4P's Plus)[48]*	5	~1	Pregnant women	≥ 1 (0.87; 0.76)[48]	Copyright: The National Training Institute/NTI Upstream Source: NTI Upstream, 180 N. Michigan Ave., Suite 700, Chicago, IL 60601 Cost: Licensing fees may apply	Publicly available link with more information: https://www.ntiupstream.com/4psabout

Instrument	No. of Items in Instrument	Approx. Time to Administer (min)	Applicable Population	Scoring That Indicates Risk and Statistical Performance (Sensitivity; Specificity)	Copyright, Source(s), and Cost‡‡	Link(s)
Substance Use Brief Screen (SUBS)[53*]	4	~1	Adults	Any response other than "never" on alcohol binge question: (0.85; 0.77)	Copyright: N/A Source: N/A Cost: N/A	Publicly available NIH publication with more information: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4475501/
Cut Down, Annoyed, Guilty, Eye-Opener (CAGE)[57]	4	~1	Adults	≥ 2 (0.14–0.39; 0.97)	Copyright: None Source: N/A Cost: Freely available as it is in the public domain and no permission is necessary unless used in a profit-making endeavor	Publicly available SAMHSA link: https://www.integration.samhsa.gov/clinical-practice/sbirt/CAGE_questionaire.pdf
Michigan Alcohol Screening Test–Geriatric Version (MAST-G)[57]	24	~5 to 10	Older adults	≥ 5 (0.70–0.91; 0.81–0.85)	Copyright: 1991, The Regents of the University of Michigan Source: Frederick C. Blow, PhD, University of Michigan Alcohol Research Center, 400 E. Eisenhower Parkway, Suite A, Ann Arbor, MI 48104 Phone: 313-998-7952 Cost: Free online	Publicly available NIH link to SAMHSA's *Substance Abuse Among Older Adults: Treatment Improvement Protocol No. 26* (page 55): https://www.ncbi.nlm.nih.gov/books/NBK64419/pdf/Bookshelf_NBK64419.pdf
Short Michigan Alcohol Screening Test–Geriatric Version (SMAST-G)[57]	10	Not reported	Older adults	≥ 2 (0.52; 0.96)	Copyright: 1991, The Regents of the University of Michigan Source: N/A Cost: N/A	Publicly available link provided by The Hartford Institute for Geriatric Nursing, New York University, Rory Meyers College of Nursing: https://consultgeri.org/try-this/general-assessment/issue-17.pdf
Comorbidity Alcohol Risk Evaluation Tool (CARET)	10	~2 to 5	Older adults	A positive response in any of the seven risk categories (0.92; 0.51)[54]	Copyright: N/A Source: N/A Cost: N/A	Not publicly available

NIAAA = National Institute on Alcohol Abuse and Alcoholism; NIDA = National Institute on Drug Abuse; NIH = National Institutes of Health; SAMHSA = Substance Abuse and Mental Health Services Administration.

* Instrument screens for alcohol and other substances.

† Recommended AUDIT-C cutoff score is different for adult women (≥ 3) and men (≥ 4).[18]

‡ Not reported.

§ Recommended AUDIT cutoff score is the same for adult women and men (≥ 8).[18]

** Several U.S.-based studies show more optimal balances of sensitivity and specificity at lower AUDIT cutoffs (e.g., 3, 4, 5); preliminary findings from the USPSTF 2018 updated evidence report and systematic review indicates that lower cutoffs may be preferred.[18]

†† Sensitivity and specificity are not reported for this instrument.

‡‡ N/A, information was not available or retrievable. None, the instrument explicitly states that no copyright is held. Cost: N/A, no information was found regarding cost. Free/free online, the information pertaining to the instrument explicitly states that it is available to the public.

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Development, Prevention, and Treatment of Alcohol-Induced Organ Injury

The Role of Nutrition

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Alcohol and nutrition have the potential to interact at multiple levels. For example, heavy alcohol consumption can interfere with normal nutrition, resulting in overall malnutrition or in deficiencies of important micronutrients, such as zinc, by reducing their absorption or increasing their loss. Interactions between alcohol consumption and nutrition also can affect epigenetic regulation of gene expression by influencing multiple regulatory mechanisms, including methylation and acetylation of histone proteins and DNA. These effects may contribute to alcohol-related organ or tissue injury. The impact of alcohol–nutrition interactions has been assessed for several organs and tissues, including the intestine, where heavy alcohol use can increase intestinal permeability, and the liver, where the degree of malnutrition can be associated with the severity of liver injury and liver disease. Alcohol–nutrition interactions also play a role in alcohol-related lung injury, brain injury, and immune dysfunction. Therefore, treatment involving nutrient supplementation (e.g., with zinc or S-adenosylmethionine) may help prevent or attenuate some types of alcohol-induced organ damage.

Key words: Alcohol consumption; alcohol use, abuse, and disorder; heavy alcohol consumption; alcohol–nutrition interactions; organ injury; tissue injury; intestine; nutrition; nutrients

The effect of alcohol on organ health and injury is complex and influenced by a host of different factors, such as dose of alcohol consumed; duration and pattern of drinking (e.g., binge drinking); and, as reviewed in this article, potential interactions with nutrition. The *2015–2020 Dietary Guidelines for Americans* (U.S. Department of Health and Human Services and U.S. Department of Agriculture 2015) highlight the concept of the standard drink and the fact that if alcohol is consumed, it should be in moderation (i.e., up to 1 drink per day for women and 2 drinks per day for men in adults of legal drinking age). It is becoming increasingly accepted that this moderate form of drinking may have health benefits that seem to lessen many types of organ injury. This concept was popularized in 1991, when Morley Safer presented information on the television show *60 Minutes* related to the "French paradox"—that is, the observation that the French seemed to have lower rates of heart attacks despite higher fat consumption. This outcome was postulated as possibly resulting from the beneficial effects of wine consumption by the French. Subsequent studies have shown that all forms of alcohol, when consumed in moderation, seem to lower the risk of coronary artery disease (Yang et al. 2016). The beneficial effect can be represented by a J-shaped curve, in which low alcohol consumption has protective effects compared with abstention, whereas excessive alcohol consumption is harmful. Moderate drinking also may have

beneficial effects on several other organs and organ systems, including the following:

- Decreased risk of ischemic stroke (Sacco et al. 1999);
- Protection against type 2 diabetes (Conigrave et al. 2001);
- Decrease in rheumatoid arthritis (Di Giuseppe et al. 2012);
- Improved cognition (Anstey et al. 2009);
- Decreased progression of liver disease to fibrosis in obese individuals (Thomson et al. 2012); and
- Improved renal function (Koning et al. 2015).

Indeed, moderate alcohol consumption may be associated with an overall modest survival benefit (Ford et al. 2011).

Moderate alcohol consumption also has been shown to decrease biomarkers of inflammation, such as C-reactive protein, and reduced inflammation could be one unifying mechanism underlying alcohol's protective effects (Imhof et al. 2004). On the other hand, long-term heavy alcohol abuse can cause organ injury, which may, at least in part, result from alcohol–nutrient interactions and alcohol-related nutrient deficiencies. As described in this article, people who abuse alcohol frequently consume large amounts of alcohol, which may contribute to the displacement of needed nutrients (see figure 1). Indeed, recent analyses of nutritional status and alcohol consumption in people with alcohol use disorder (AUD) who were admitted to a rehabilitation program demonstrated that the participants generally had a normal body mass index, were not overtly malnourished, and did not have clinical evidence of alcohol-induced organ injury. However, these people were consuming, on average, 14 drinks per day, which would amount to about 2,000 calories per day or more consumed as alcohol (Vatsalya et al. 2016). Considering that the participants had a normal body mass index, this suggests that they replaced normal nutrients with alcoholic beverages, resulting in potential nutrient deficiencies. Nutritional supplementation may either help ameliorate such deficiencies or have pharmacologic effects.

Alcohol and nutrition can interact at multiple levels. For example, alcohol metabolism can result in the generation of reactive oxygen species, which can deplete endogenous nutritional antioxidant stores and contribute to oxidative stress. Heavy alcohol consumption also can cause poor intestinal absorption of certain nutrients (e.g., zinc) or increase nutrient losses (e.g., by

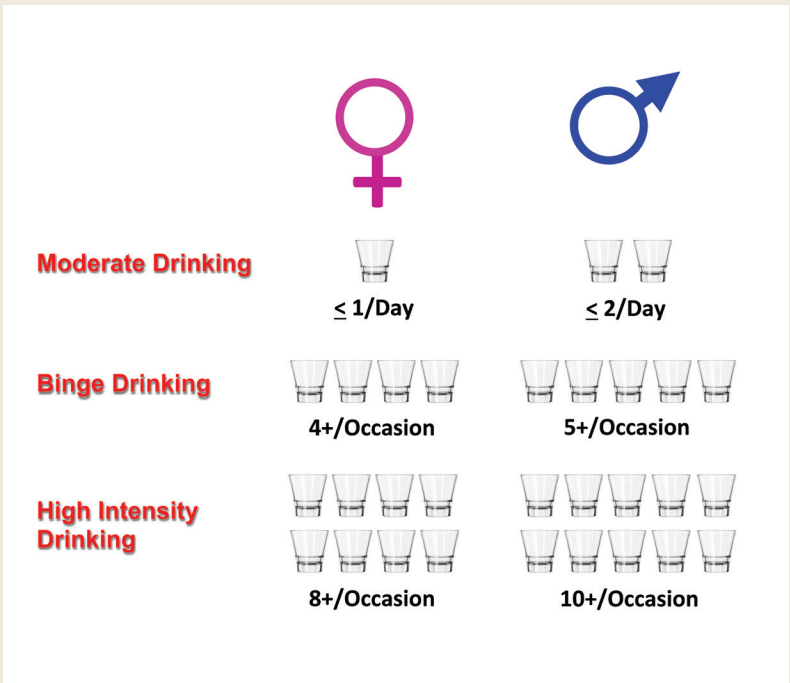

Figure 1 Drinking levels and their consequences. In the United States, drinking levels are expressed in terms of standard drinks consumed—that is, the number of alcoholic beverages drunk, each containing about 0.6 fluid ounce or 14 grams of pure alcohol. The *Dietary Guidelines for Americans 2015–2020* defines moderate drinking as consuming up to 2 drinks/day for men and up to 1 drink/day for women. The Substance Abuse and Mental Health Services Administration defines binge drinking as consuming 5 or more (for men) or 4 or more (for women) alcoholic drinks on the same occasion on at least 1 day in the past 30 days (National Institute on Alcohol Abuse and Alcoholism 2016). High-intensity drinking refers to drinking at levels far beyond the binge threshold, resulting in high peak blood alcohol concentrations. Some studies define high-intensity drinking as two or more times the gender-specific binge drinking thresholds (Patrick et al. 2016); others use a higher threshold (Johnston et al. 2016). Some individuals drink considerably more than this. For example, one study found that patients admitted to a National Institutes of Health treatment facility with a diagnosis of alcohol use disorder consumed the equivalent of 13 drinks per day (Vatsalaya et al. 2016). In these drinkers, the metabolic effects of alcohol and altered nutrient intake may set the stage for alcohol–nutrient interactions and organ injury.

increasing zinc and magnesium excretion in the urine). Moreover, nutrition can have a far-reaching impact through altering epigenetic mechanisms, such as methylation and acetylation of DNA and associated proteins. Finally, the degree of alcohol-related malnutrition can be associated with the severity of organ injury (e.g., alcoholic hepatitis). This article reviews how nutritional alterations may predispose to alcohol-induced organ injury and how nutritional supplementation may prevent and/or treat alcohol-induced organ injury. The article specifically highlights the effects of certain alcohol–nutrient interactions, with a focus on zinc and linoleic acid, and their impact on epigenetics and selected organ injury.

Nutrition and Nutritional Alterations Following Alcohol Use/Abuse

Alcohol: Nutrition Overview

From a nutrition perspective, alcohol is a significant source of calories, but these can be considered "empty" calories—that is, they contain few micronutrients, such as vitamins and minerals, normally found in most food sources (Antonow and McClain 1985). The main site of beverage alcohol (i.e., ethanol) metabolism is the liver, where ethanol is converted to carbon dioxide and water, with an energy yield of 7 kcal/g of alcohol. Regular alcohol intake can be a major source of calories, because beer has approximately 150 kcal per 12-ounce can and bourbon or scotch with a mixer has approximately 125 kcal per drink. Thus, a person can easily consume 200 to 500 calories or more per day by consuming 2 to 3 drinks. For people attempting weight reduction, alcohol consumption therefore can be considered a source of unwanted and empty calories. Moreover, when alcohol intake is combined with fructose-containing sugared drinks, the intake of empty calories increases even further, enhancing the opportunity for alcohol-induced organ injury. Finally, alcohol can be an expensive source of calories compared with traditional foods, and this may become a major problem for people with limited incomes.

The issue of alcohol as a nutrient becomes more prominent when dealing with people with AUD and those with alcohol-induced organ injury. Analyses of the nutritional status of people with AUD admitted to treatment programs found that these individuals often consumed 35 to 50 percent of their total calories as alcohol, and some exhibited inadequate micronutrient intake and micronutrient serum levels (Antonow and McClain 1985). However, most had little or no evidence of protein-calorie malnutrition and loss of muscle mass. In contrast, patients admitted to hospitals for severe alcoholic hepatitis who also consumed 50 percent of their total calories as alcohol not only regularly showed depletion of certain micronutrients but also loss of muscle mass (Mendenhall et al. 1995*a*). The following sections focus on the micronutrient zinc, which may be deficient or have altered metabolism with heavy alcohol consumption, and a macronutrient (i.e., dietary fat) that may play a role in alcohol-induced organ injury. Some of the other micronutrients for which heavy alcohol intake may cause deficiency states or altered metabolism are listed in the table.

Zinc

Zinc is an essential trace element required for normal cell growth, development, and differentiation, including such processes as DNA synthesis, RNA transcription, and cell division and activation. It is a critical component of many proteins/enzymes, including zinc-dependent transcription factors. Zinc deficiency or altered zinc metabolism is frequently observed in heavy alcohol drinkers and may result from decreased dietary intake, increased urinary excretion, abnormal activation of certain zinc transporters, and induction of hepatic metallothionein (Mohammad et al. 2012). Zinc deficiency may manifest itself in many ways in alcoholics, ranging from raised, crusting skin lesions around the eyes, nose, and mouth (figure 2) to impaired wound healing or liver regeneration, altered mental status, or altered immune function (Mohammad et al. 2012). Importantly, oxidative stress (e.g., resulting from ethanol metabolism) may cause release of zinc from critical zinc-finger proteins and cause loss of DNA-binding activity. Specifically, oxidative stress causes modification of certain amino acids (i.e., cysteine residues) that hold the zinc in place in zinc-finger proteins such as hepatocyte nuclear factor 4 (HNF4), a transcription factor that is essential for liver development.

Zinc supplementation has been documented to block or attenuate experimental organ injury and dysfunction in the gut, liver, lung, and brain through multiple pathways. Thus, zinc may

Figure 2 Chronic alcohol user who had been consuming large amounts of beer before admission. Note classical skin lesions of zinc deficiency around the eyes, nose, and mouth.

strengthen the integrity of the intestinal wall by stabilizing tight junctions, reduce transfer of toxic bacterial molecules (e.g., endotoxin) into the blood, lower the levels of metabolic toxins such as ammonia in the blood, decrease production of inflammation-promoting (i.e., proinflammatory) cytokines, reduce oxidative stress, and attenuate apoptotic cell death (Zhong et al. 2010, 2015) (figure 3). The dose of zinc used for treatment of alcohol-induced organ injury such as liver disease usually is 50 mg of elemental zinc taken with a meal to decrease the potential side effect of nausea. Intake of greater than 50 mg of elemental zinc per day can cause dose-related side effects, such as copper deficiency resulting from reduced copper absorption.

Table Types of Nutrient Deficiency Caused by Heavy Drinking and the Associated Signs and Symptoms

Selected Nutrient Deficiency	Signs/Symptoms
Magnesium	Insulin resistance, muscle cramps
Selenium	Myopathy, cardiomyopathy
Vitamin B1/Thiamine	Wernicke-Korsakoff syndrome, neurologic symptoms
Vitamin B2/Riboflavin	Glossitis, cheilitis, and lingual papillae atrophy
Vitamin A/Retinol	Abnormal dark adaptation, rough skin
Vitamin C	Scurvy with purpura and petechiae
Vitamin D	Altered bone metabolism, altered gut barrier/immune function
Vitamin E	Oxidative stress
Niacin	Skin photosensitivity, confusion, pellagra
Folate, S-Adenosylmethionine	Anemia, altered methylation, epigenetic effects

Dietary Fats

The critical role for specific types of dietary fat (i.e., saturated versus unsaturated fats) in intestinal and liver injury has been demonstrated and extensively studied in preclinical animal models of alcohol feeding using various sources of dietary lipids. Experimental evidence has shown that dietary saturated fats (SFs) attenuated, and unsaturated fats (USFs) enhanced, alcohol-induced liver damage (Nanji and French 1989). Thus, in contrast to the general assumption that SFs are less healthy than USFs, in this situation SFs had a protective effect and USFs had a harmful effect.

Further analyses focused on the role of different types of dietary polyunsaturated fatty acids (PUFAs) in alcohol-induced gut and liver injury. There are two major families of dietary PUFAs—omega-6 [ω-6] and omega-3 [ω-3] PUFAs—each of which includes numerous related metabolites. It has been demonstrated that linoleic acid, an ω-6 PUFA [18:2ω-6], is required for the development of experimental alcohol-induced intestinal and liver injury and that the severity of alcoholic liver disease (ALD) is correlated with the amount of linoleic acid in the diet (Nanji and French 1989; Ronis et al. 2004). Conversely, fish oil (a rich source for ω-3 PUFAs) or purified ω-3 PUFAs (e.g., eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA], which are known to be important in brain development) may be beneficial in ALD. For example, in mice, prior ingestion of fish oil, specifically tuna fish oil, in amounts that provided 30 percent of the total caloric intake, resulted in reduced hepatic fat accumulation caused by a single dose of ethanol administration. This effect was mediated, at least in part, through marked reductions in the expression of the hepatic enzyme stearoyl-CoA desaturase-1 and in the activity of the transcription factor sterol regulatory element–binding protein (Wada et al. 2008). Mice supplemented with highly purified DHA also had significantly decreased alcohol-induced liver steatosis, inflammation, and injury (Huang et al. 2013). The beneficial role of ω-3 PUFAs in experimental ALD also has been supported by the observation that when rhesus monkeys who had free access to an ethanol solution were fed a diet that was generally nutritionally adequate (including the linoleic acid amount), but with a low ω-3 PUFA content (i.e., a very low concentration of α-linolenic acid), the animals developed hepatic steatosis and fibrosis (Pawlosky and Salem 2004). The ω-3 PUFAs also are precursors to factors that resolve injury and inflammation, such as resolvins (e.g., E- and D-series resolvins generated from EPA and DHA, respectively), and a high dietary ω-6/ω-3 PUFA ratio may be disadvantageous to resolving inflammation (Serhan and Petasis 2011). Thus, emerging evidence suggests that dietary fats can play a role in both initiation and treatment of alcohol-induced organ injury in the gut and liver as well as in the brain (which will be discussed later in this article).

Nutrition–Alcohol Interactions and Epigenetics

In virtually every cell type, epigenetic mechanisms—that is, modifications to the genetic material that do not alter the DNA sequence—play a critical role in both the physiologic and pathologic regulation of gene expression. These mechanisms, which involve chromatin remodeling initiated by posttranslational modifications of

histones and changes in DNA methylation status, can activate or deactivate gene transcription. The proteins that are involved in posttranslational histone modifications and DNA methylation changes require a variety of cofactors, including acetyl coenzyme A, S-adenosylmethionine (SAM), nicotinamide adenine dinucleotide, and zinc (Moghe et al. 2011). A person's nutritional status can significantly influence the availability of these cofactors and, consequently, epigenetic mechanisms, gene expression, and disease pathogenesis. Chronic alcohol consumption is known to affect nutritional status at many levels, including nutrient intake, absorption, utilization, and excretion, causing nutritional disturbances and deficiencies in these cofactors. Research has determined that alcohol-induced nutrient fluctuations can impact transcriptional activity and expression of genes by modulating epigenetic parameters, including histone modifications and DNA methylation (Moghe et al. 2011; Zakhari 2013). Hence, in people with AUD, the combined effects of alcohol metabolism and compromised nutrition are likely to influence epigenetic mechanisms, gene expression, and disease pathogenesis involving intestinal barrier dysfunction, immune suppression, and organ injury.

Alcohol's Effects on Histone Acetylation and Methylation

It is becoming increasingly evident that histone-associated epigenetic modifications, such as histone acetylation and methylation, play a significant role in the regulation of gene expression and development of alcohol-induced organ pathology, such as liver disease and immune dysfunction (Moghe et al. 2011). In particular, histone acetylation in promoter regions is a key regulator of gene expression and is associated with enhanced transcriptional activity, whereas deacetylation typically is associated with transcriptional repression. Steady-state levels of acetylation result from the balance between the opposing activities of two groups of enzymes—histone acetyltransferases and histone deacetylases. The expression and activities of both types of enzymes can be influenced by alcohol and cofactors, such as nicotinamide adenine dinucleotide and zinc (Ghare et al. 2014; Moghe et al. 2011). Taken together, epigenetic histone modifications provide a likely link between alcohol-mediated nutrient alterations in gene expression and disease pathogenesis.

Alcohol's Effects on DNA Methylation

Investigation of the dietary influences on epigenetic processes has revealed a direct link between SAM, which serves as the primary biological methyl donor, and DNA methylation changes that epigenetically influence gene expression (McCabe and Caudill 2005). In general, DNA hypermethylation at DNA sequences called CpG islands in gene promoters leads to transcriptional silencing, whereas DNA hypomethylation allows for transcription to occur.

Excessive alcohol consumption can decrease SAM levels via multiple mechanisms, such as reduced folate levels and inhibition of key enzymes in one-carbon metabolism. The reduced SAM levels lead to aberrant DNA methylation patterns and pathogenic alterations in gene expression (Varela-Rey et al. 2013). Importantly, alcohol-induced perturbations in global and regional DNA methylation have been linked with diverse pathological conditions, including ALD, carcinogenesis in various organs, alcohol dependence, and fetal alcohol spectrum disorders

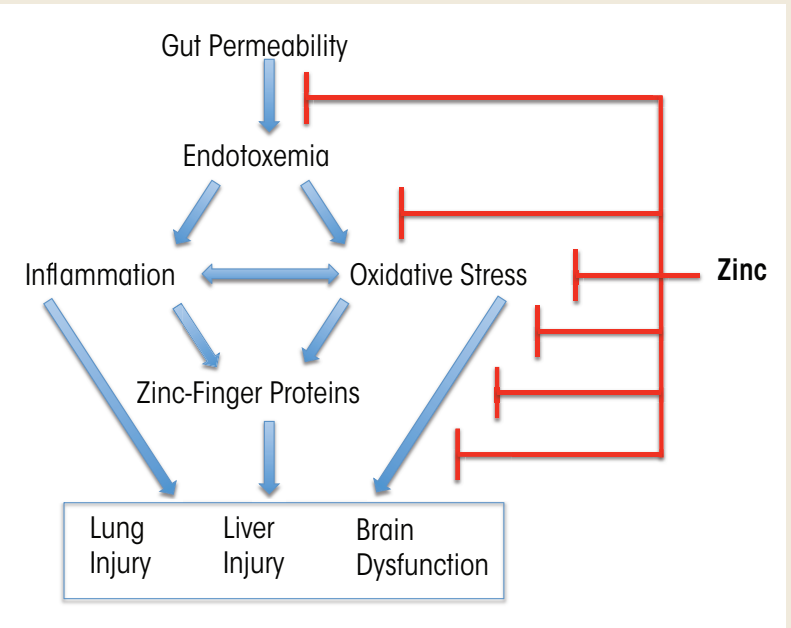

Figure 3 Zinc therapy positively affects multiple mechanisms of alcohol-induced organ injury. Thus, zinc enhances the gut barrier and tight junctions, thereby reducing gut permeability and the risk of transfer of bacterial endotoxin into the blood (i.e., endotoxemia). In addition, zinc decreases proinflammatory cytokine production and oxidative stress and ensures proper functioning of important zinc-dependent regulatory proteins (e.g., zinc-finger proteins). Through these and other mechanisms, zinc supplementation can improve liver injury and may attenuate lung and brain dysfunction.

(FASD), to name only a few. Clearly, further research is needed to detail the alcohol–nutrient interactions that influence epigenetic mechanisms underlying pathogenic changes in gene expression and disease progression, with the goal of developing nutrient-based therapies.

Examples of Nutrition–Alcohol Interactions in Alcohol-Induced Organ/Tissue Injury

Intestine

The intestinal mucosa plays a critical role in preventing passage of toxins from the intestine into the bloodstream, as well as in immune function, detoxification, and metabolism. The importance of the gut in alcohol-mediated multiorgan pathology is becoming increasingly recognized. Clinical and experimental data have demonstrated that the gut-derived bacterial product, lipopolysaccharide, also referred to as endotoxin, plays a crucial role in the development and progression of alcohol-induced organ injuries, including ALD. Significantly increased endotoxin levels in the blood (i.e., endotoxemia) have been found in patients with different stages of ALD, including fatty liver, hepatitis, and cirrhosis (Parlesak et al. 2000).

Multiple mechanisms contribute to alcohol-associated endotoxemia, including alcohol-mediated alterations in the composition of the bacterial population of the gut (i.e., gut microbiome) (Mutlu et al. 2009) and increased lipopolysaccharide translocation as a result of disruption of intestinal barrier integrity. Recent studies in mice have demonstrated that the type of dietary fat consumed can influence alcohol-induced changes in the gut microbiome composition (and, therefore, function), intestinal injury/inflammation, and intestinal barrier function (figures 4 and 5). Specifically, when comparing animals that were fed either dietary USFs or SFs plus ethanol (EtOH),[1] the studies found the following:

[1] The diet containing USFs was rich in corn oil, whereas the diet containing SFs was rich in medium-chain triglycerides.

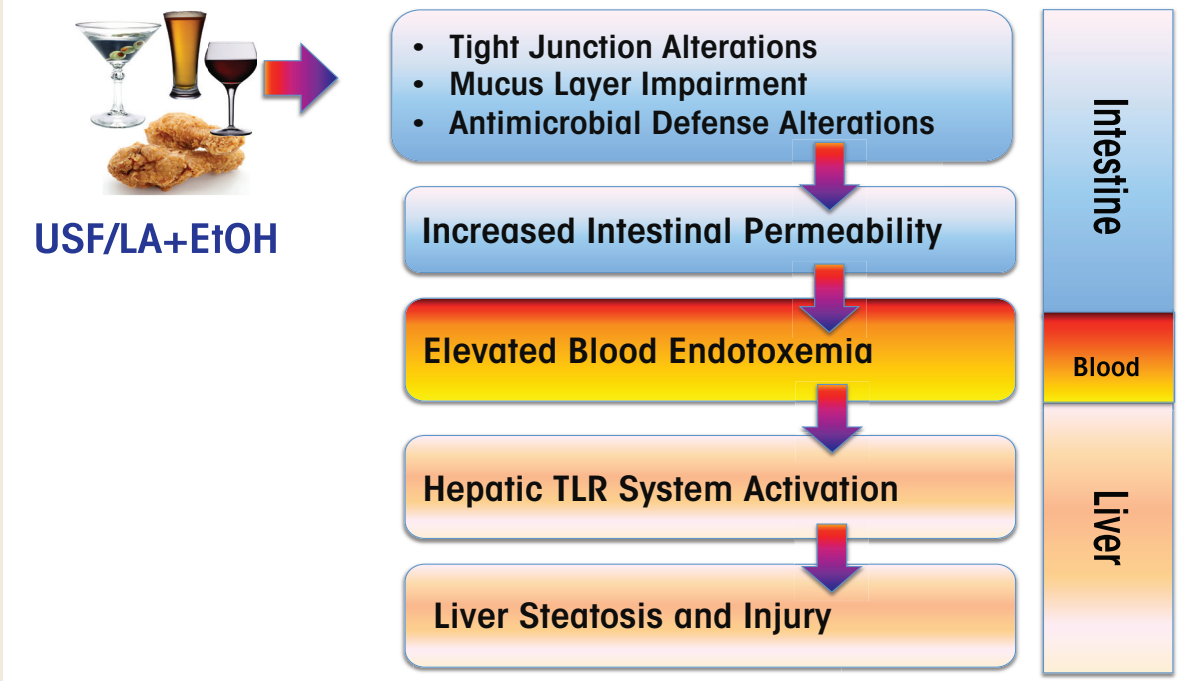

Figure 4 Alcohol (EtOH) consumption combined with dietary intake of unsaturated fatty acids (USFs) (e.g., linoleic acid [LA]) can have numerous deleterious effects on the intestine, blood, and liver. In the intestine, this combination changes the bacterial composition (microbiome) and interferes with various aspects of the body's defense systems, thereby increasing intestinal permeability. This leads to endotoxemia and liver injury.

NOTE: TLR = toll-like receptor.

- The animals that received EtOH+USF showed increased gut permeability and elevated endotoxemia compared with those that received EtOH+SF (Kirpich et al. 2012) (figure 5A).

- Compared with EtOH+SF, a chronic EtOH+USF diet triggered an intestinal proinflammatory response characterized by increased levels of several cytokines, including tumor necrosis factor-α and monocyte chemoattractant protein-1. In addition, the intestinal mucus layer and antimicrobial defenses were altered (Kirpich et al. 2013).

- Intestinal inflammation was positively correlated with the EtOH+USF-triggered disruption of the intestinal tight junctions (figure 5B). Even in the absence of alcohol, a USF diet resulted in downregulation of intestinal expression of tight-junction protein mRNA compared with an SF diet. Alcohol further suppressed tight-junction proteins in animals receiving EtOH+USF, but did not affect intestinal tight junctions in the EtOH+SF group (Kirpich et al. 2013) (figure 5B).

- Unlike EtOH+SF, dietary EtOH+USF caused alterations in gut microbiota (Bull-Otterson et al. 2012; Kirpich et al. 2016) (figure 5C).[2] The observed microbiota and intestinal barrier changes were associated with significant liver steatosis, inflammation, and injury in EtOH+USF-fed mice (figure 5D). These adverse effects of ethanol on the liver were markedly attenuated by a SF diet containing medium-chain triglycerides.

[2] The EtOH+USF-induced changes in gut microbiota were characterized by the decrease of certain bacteria (i.e., the *Bacteriodetes* phylum) with a proportional increase in others (i.e., gram-negative *Proteobacteria* and gram-positive *Actinobacteria* phyla). The bacterial genera that showed the biggest expansion were the gram-negative, alkaline-tolerant *Alcaligenes* and gram-positive *Corynebacterium* (Bull-Otterson et al. 2013).

Thus, it is clear that the interactions of dietary fat and alcohol are important in mediating alcohol-induced intestinal and liver injury.

Similarly, in mice, zinc deficiency associated with chronic alcohol intake led to markedly decreased tight-junction proteins and increased endotoxemia. Zinc supplementation corrected these effects through multiple mechanisms, including zinc-finger function and epigenetic mechanisms (Zhong et al. 2015). In summary, an important component of alcohol-induced organ inflammation/injury arises in the gut and may be modified by nutrition.

Liver Injury

Patients with severe alcoholic hepatitis almost invariably demonstrate some form of malnutrition. Probably the most detailed information concerning malnutrition in ALD comes from two large studies from the Veterans Health Administration (VA) Cooperative Studies Program in patients with alcoholic hepatitis (Mendenhall et al. 1984, 1986, 1995*a,b*). In these studies, almost 50 percent of the patients' energy intake was derived from alcohol. Although they frequently showed no inadequate calorie intake, the patients often exhibited insufficient intake of protein and critical micronutrients. The severity of liver disease generally correlated with the severity of malnutrition. During treatment, the patients received a balanced 2,500-kcal hospital diet (monitored by a dietitian) that they were encouraged to consume. Investigators found that voluntary oral food intake correlated in a stepwise fashion with 6-month mortality data. Thus, patients who voluntarily consumed more than 3,000 kcal per day had virtually no mortality, whereas those who consumed less than 1,000 kcal per day had a 6-month mortality of more than 80 percent (Mendenhall et al. 1995*a*). Moreover, the degree of malnutrition correlated with the development of serious complications, such as encephalopathy, ascites, and hepatorenal syndrome (Mendenhall et al. 1995*a*).

Initial interest in nutrition therapy for ALD was stimulated by Patek and colleagues (1948) who demonstrated that a "nutritious diet" improved the 5-year outcome of patients with alcoholic cirrhosis compared with historic control subjects. Subsequently, nutritional supplementation through a feeding tube was shown to significantly improve liver function in inpatients with ALD compared with inpatients who ate a hospital diet (Kearns et al. 1992). Probably the most important data supporting nutrition therapy came from a multicenter study by Cabré and colleagues (2000), who randomly assigned patients with severe alcoholic hepatitis to receive either the glucocorticoid prednisone (40 mg daily) or a liver-specific formula containing 2,000 calories per day through a feeding tube.[3] The 1-month mortality was the same in both groups, but the 1-year mortality was significantly lower in the enteral-nutrition group than in the glucocorticoid group, mainly because they experienced fewer infectious complications. This study clearly documented the importance of enteral nutrition in severe alcoholic hepatitis. Oral/enteral nutrition is preferable over parenteral nutrition because of lower costs, risk of sepsis from the parenteral nutrition line, preservation of the integrity of the gut mucosa, and prevention of bacterial translocation and multiple-organ failure.

Enteral nutrition supplements also have been shown to improve nutritional status and immune function in outpatients with alcoholic cirrhosis as well as to reduce hospitalization. The concept of an outpatient late-evening snack (prior to bedtime) was established after studies demonstrated altered energy metabolism in people with liver cirrhosis. These patients exhibit depleted hepatic glycogen stores, which force the body to depend on fat and protein stores, leading to catabolism during an overnight fast.

[3] This polymeric enteral solution was enriched in branched-chain amino acids, energy dense (1.3 kcal/ml), and low in fat and sodium.

A randomized controlled trial demonstrated that provision of a late-evening nutritional supplement (compared with daytime supplements) over a 12-month period could improve body protein stores in patients with cirrhosis. The nighttime snack resulted in body protein accrual equivalent to about 2 kg of lean tissue sustained over 12 months, whereas this benefit was not observed with daytime snacks. Thus, late-evening snacks are valuable nutritional interventions in outpatients with alcoholic cirrhosis (Plank et al. 2008).

Many types of nutritional supplements have yielded positive effects in animal models of ALD, especially antioxidants. However, human studies using specific nutrients or combination therapy are limited and generally have shown equivocal or negative results. Larger, well-designed studies are required.

Lung Injury

Chronic alcohol abuse alters the phenotype of the lung and makes it more susceptible to subsequent challenges, such as bacterial infection and acute lung injury. One of the mechanisms that contribute to increased susceptibility to infection and injury is alcohol-induced oxidative stress. Oxidative

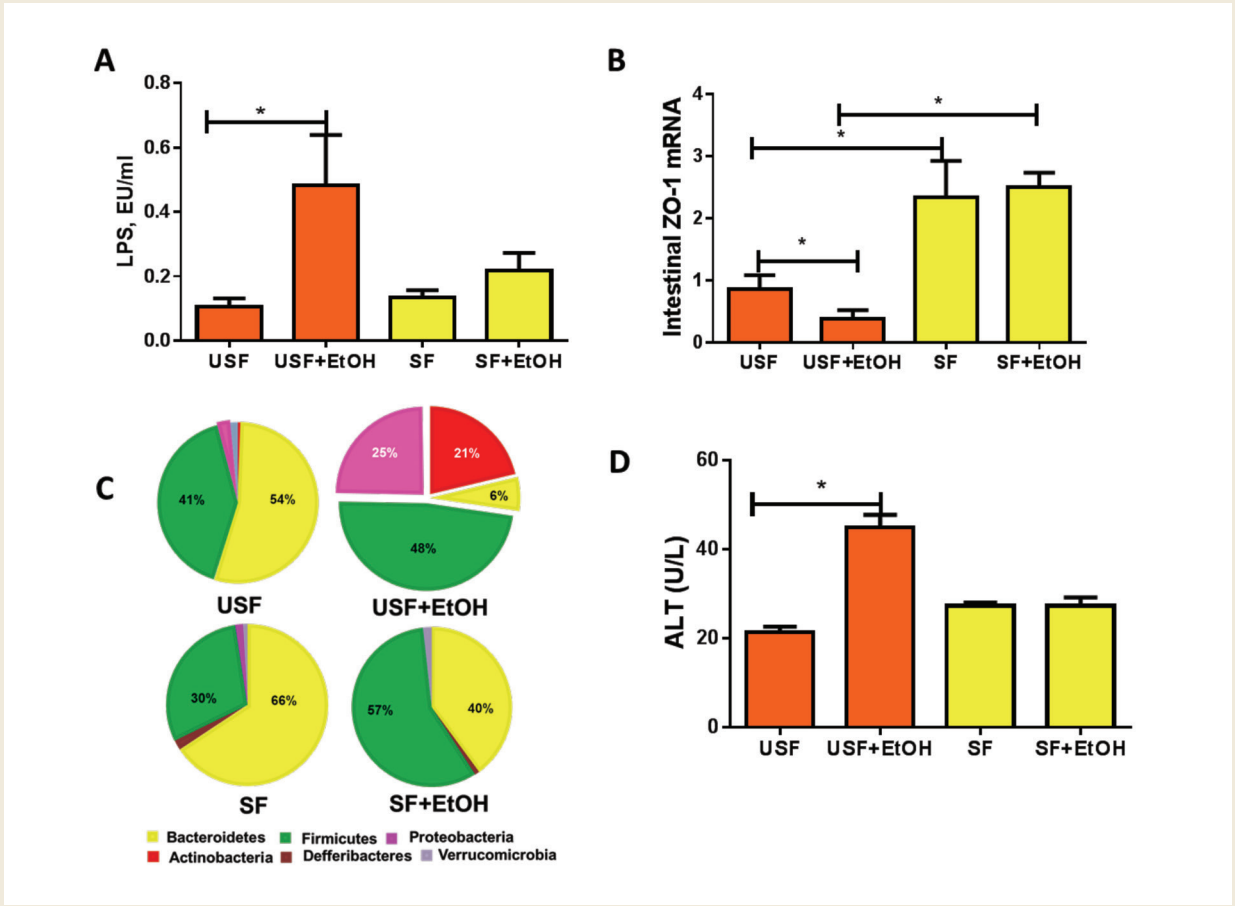

Figure 5 Effects of saturated fat (SF) and unsaturated fat (USF) diets on endotoxemia, intestinal tight junctions, gut microbiome, and liver injury in response to chronic alcohol (EtOH) feeding. **(A)** Plasma endotoxin levels assessed by plasma lipopolysaccharide (LPS) measurement. Alcohol feeding significantly increases LPS levels in the plasma when combined with a USF diet. **(B)** Levels of the mRNA for the tight-junction protein zonula occuldens-1 (ZO-1) in the intestine. Animals receiving a USF diet showed greater disruption of tight junctions (i.e., lower ZO-1 levels) than animals receiving a SF diet; this effect was exacerbated with alcohol feeding. **(C)** Comparative analysis of the relative abundance of different phyla of gut bacteria in mice fed ethanol and different types of dietary lipids. The phyla abundance is indicated by the color bars. **(D)** Liver injury was evaluated by plasma alanine aminotransferase (ALT) activity. In animals receiving a USF diet, but not in those receiving a SF diet, alcohol feeding caused significant liver injury.

NOTE: Horizontal bars indicate statistically significant differences.

stress is defined as an imbalance between oxidants and antioxidants, and the way cells sense and respond to such an imbalance is a key determinant of disease initiation/progression or resolution. Oxidant-sensing and -signaling pathways rely primarily on proteins with reactive thiol-containing cysteine residues. The reactivity of a given protein thiol can be fine tuned by its local redox environment—that is, by the ratio of reduced versus oxidized molecules in the cell. This redox environment largely is controlled by two low-molecular-weight thiol-disulfide redox couples: one composed of the amino acid cysteine (Cys), which is the reduced partner of the pair, and its disulfide cystine (CySS), which serves as the oxidized partner. The other redox pair comprises glutathione (GSH) as the reduced partner and its disulfide GSSG as the oxidized partner. The two pairs are related but have different roles. Cys is one of the three component amino acids making up GSH, so it is not surprising that they share similar chemical properties. However, these redox control systems are compartmentalized; GSH/GSSG provides control mechanisms within cells and in the lung-lining fluid, whereas Cys/CySS predominates in the extracellular fluids of plasma and interstitium. The extracellular Cys/CySS redox state has been shown to have a direct effect on the production of two important proinflammatory cytokines, namely production of transforming growth factor β by lung fibroblasts (Ramirez et al. 2007) and interleukin-1 β by monocytes (Iyer et al. 2009).

Accumulating evidence suggests that the Cys/CySS and GSH/GSSG redox couples can be controlled by the diet. Dietary supplementation with the cysteine precursors N-acetylcysteine or procysteine has been used extensively to counteract the effects of oxidative stress. Although the effects of these cysteine precursors usually are attributed to enhanced GSH synthesis, they also are effective even when given in combination with a GSH-synthesis inhibitor (e.g., buthionine sulfoximine) (Lailey et al. 1991). Recent studies showed that supplementing the diet with a combination of cysteine and methionine could prevent oxidation of the plasma Cys/CySS redox couple and decrease circulating levels of proinflammatory interleukin-1 β in endotoxin-challenged mice (Iyer at al 2009). Similar diets also can alter the plasma Cys/CySS redox state in humans (Jones et al. 2011). It will be interesting to determine whether this type of dietary intervention can protect against lung injury in chronic alcoholics.

Zinc deficiency, particularly within immune cells in the lungs (i.e., alveolar macrophages), also contributes to increased susceptibility to bacterial infection in chronic alcoholics (Mehta et al. 2011). Studies in rats showed that chronic alcohol feeding decreased bacterial clearance from lung and oxidized Cys/CySS in the alveolar space. Dietary zinc supplementation blocked both of these effects (Mehta et al. 2011).

Brain Injury

Prenatal alcohol exposure can result in a range of detrimental effects, including damage to the developing brain, that are collectively known as FASD. Early autopsy studies, as well as more recent magnetic resonance imaging studies in both animal models and humans have revealed a variety of brain abnormalities, including reduced brain size (i.e., microcephaly) and anomalies of specific brain structures (e.g., the cerebrum, cerebellum, hippocampus, basal ganglia, and corpus callosum) after prenatal alcohol exposure (Lebel et al. 2011; Lipinski et al. 2012). These ethanol-induced brain insults contribute to the learning deficits, impairment in memory, difficulties with motor planning, and problems in regulating emotions and behavior observed in children with FASD.

Alcohol can damage the developing embryo through multiple mechanisms. Oxidative stress seems to play an important role in ethanol-induced programmed cell death (i.e., apoptosis) and morphological abnormalities (Chen et al. 2013). In addition, accumulating evidence suggests that changes in epigenetic regulation are involved in the pathogenesis of FASD. For example, in animal studies, prenatal alcohol exposure increased the proportion of offspring with an unusual coat color by inducing hypermethylation of a specific gene, *Avylocus (*Kaminen-Ahola et al. 2010). Moreover, recent studies demonstrated that microRNA 125b can prevent ethanol-induced apoptosis of certain embryonal cells (i.e., neural crest cells) by targeting two specific genes called *Bak1* and *PUMA* (Chen et al. 2015).

It also is well known that nutritional deficiencies contribute to the pathogenesis of FASD and to ethanol-induced damage to the developing brain. Heavy maternal alcohol consumption results in deficiency in nutrients that are critical for fetal development and maternal health, including vitamins A and D, thiamin, folate, and zinc (Dreosti 1993). Moreover, as in adult brains, DHA deficiency occurred in the developing brain of animals prenatally exposed to ethanol. Finally, studies have shown that diets low in nutrients exacerbate alcohol-induced brain damage in the offspring (Nacach et al. 2009).

Maternal nutrient supplementation may decrease the risk of FASD and serve as a potential intervention for FASD. Some nutritional interventions target oxidative stress. For example, antioxidant supplements, such as vitamins C and E, can reduce oxidative stress, cell death, and behavioral impairments in animals prenatally exposed to ethanol. Studies in the adult brain have demonstrated that ethanol-induced neuro-inflammation and degeneration can be countered by dietary DHA. Similarly, an ω-3-enriched diet that contains 24.6 percent DHA has been shown to reduce ethanol-induced oxidative stress in the developing brain (Patten et al. 2011), consistent with the relationship between dietary fat and organ injury discussed earlier. Other nutritional

Glossary

Ascites: Accumulation of fluids in the abdominal cavity.

Cardiomyopathy: A condition of the heart muscle wherein it becomes enlarged, thick, or rigid. In rare cases, the muscle tissue in the heart is replaced with scar tissue.

Cell-Mediated Immunity: Part of the immune response that involves the activation of phagocytes, antigen-specific cytotoxic T-lymphocytes, and the release of various *cytokines* in response to a foreign molecule (i.e., antigen).

Cheilitis: Inflammation affecting the lips; this inflammation may include the skin around the mouth (i.e., perioral skin), the vermilion border, and/or the labial mucosa.

CpG Islands: Short DNA sequences that contain high levels of the normally rare cytosine–guanine sequence among the nucleotide sequence; they are targets of *DNA methylation* and are involved in the regulation of gene transcription.

Cytokines: A broad and loose category of small proteins (~5–20 kDa) that are important in cell signaling. Their release has an effect on the behavior of cells around them. They can be either proinflammatory or anti-inflammatory in their effects.

DNA Methylation: Epigenetic mechanism of regulation of gene expression, in which a strand of DNA is modified by addition of a methyl group (CH_3) to any cytosine located directly before a guanine.

Encephalopathy: A syndrome of overall brain dysfunction that can have many different organic and inorganic causes.

Enteral Nutrition: Delivery of nutrients in liquid form directly into the stomach or intestine.

Epigenetic: Heritable or nonheritable changes in phenotype or gene expression caused by mechanisms other than changes in the underlying DNA sequence; epigenetic changes can alter the appearance and structure of the DNA or the histone proteins around which the DNA is wound (e.g., *DNA methylation, histone acetylation*), thereby influencing gene expression.

Glossitis: Inflammation of the tongue.

Glycogen: Large, branched carbohydrate molecule consisting of glucose residues; constitutes the major carbohydrate reserve of animals and is stored primarily in liver and muscle.

Hepatorenal Syndrome: Functional kidney failure, but without pathological changes to the kidneys that is associated with cirrhosis and *ascites*.

Histones: Protein structures around which DNA strands are wrapped.

Histone Acetylation: *Epigenetic* modification of *histones* that involves the addition of an acetyl group.

Humoral Immunity: Immunity mediated by proteins called antibodies.

Interstitium: The space between cells in a tissue or organ.

Metallothionein: Cysteine-rich proteins that can bind to heavy metals (e.g., zinc) through the *thiol* groups of their cysteine components. They participate in the uptake, transport, and regulation of zinc and can help control *oxidative stress*.

Methionine: An essential amino acid that can supply methyl groups for various metabolic reactions.

Micronutrient: Any essential dietary element required only in small quantities (e.g., trace minerals).

Myopathy: Muscular disease in which the muscle fibers do not function for any one of many reasons, resulting in muscular weakness.

Oxidative Stress: An imbalance between oxidants (e.g., free radicals) and antioxidants that can lead to excessive oxidation and cell damage.

Parenteral Nutrition: Intravenous administration of nutrients.

Pellagra: A clinical niacin deficiency syndrome characterized by dermatitis, inflammation of the mucous membranes, diarrhea, and psychic disturbances (e.g., depression, irritability, anxiety, disorientation, or hallucinations).

Glossary *(continued)*

Petechiae: Small, nonraised, perfectly round, purplish red spots caused by bleeding in the skin layer or beneath the mucous membranes.

Purpura: Any of a group of conditions characterized by small hemorrhages in the skin, mucous membranes, or serous membranes.

Redox Environment: The balance between oxidants and antioxidants in a cell or organ; often used to describe the balance of oxidized and reduced nicotinamide adenosine dinucleotide (NAD and NADH) in a biological system such as a cell or organ.

S-adenosylmethionine (SAM): Common co-substrate involved in methyl group transfers, transsulfuration, and aminopropylation. Although these anabolic reactions occur throughout the body, most SAM is produced and consumed in the liver.

Scurvy: Condition caused by vitamin C deficiency and characterized by weakness, anemia, spongy gums, and bleeding from the mucous membranes.

Steatosis: Abnormal accumulation of lipids in the functional cells of various tissues (e.g., in the liver).

Thiol: Any organic compound containing a thiol (-SH, or sulfhydryl) group; often have strong odors resembling garlic or rotten eggs.

Tight Junction: An intercellular junction between epithelial cells, at which the adjacent cell membranes are joined tightly together, forming a belt-like seal; these junctions limit the passage of small molecules and ions between cells.

Zinc-Finger Protein: A protein containing a small structural motif that is characterized by the coordination of one or more zinc ions in order to stabilize the fold.

interventions may work through epigenetic modulations. Supplementation with nutrients that act as methyl donors, including folic acid and choline, may modulate epigenetic profiles and alter the expression of genes important for neurodevelopment. Thus, prenatal folic acid supplementation attenuated ethanol-induced malformations, growth retardation, and neuronal loss (Wang et al. 2009), whereas prenatal and postnatal supplementation with choline reduced ethanol-induced malformations and behavioral impairment (Thomas et al. 2010). Furthermore, recent studies have shown that sulforaphane, a chemical that is abundant in broccoli sprouts and which can inhibit enzymes involved in epigenetic modifications (i.e., DNA methyltransferase and histone deacetylases), can diminish ethanol-induced apoptosis in neural crest cells through induction of nuclear factor (erythroid-derived 2)-like 2 (Nrf2) (Chen et al. 2013). These findings highlight the potential of nutrient supplementation in preventing or attenuating brain damage associated with FASD, improving cognitive function in children with FASD, and attenuating brain damage in adults.

Immune Dysfunction

Excessive alcohol consumption has deleterious effects on the immune system. Several clinical and experimental studies have suggested that long-term alcohol use can lead to the dysregulation of both cell-mediated and humoral immunity (Barve et al. 2002). Epidemiologic studies have documented that alcohol-induced impairment of the immune system leads to increased susceptibility to opportunistic infections and development of certain tumors (Barve et al. 2002). Although many types of immune cells are affected by alcohol, including neutrophils, natural killer cells, and monocytes/macrophages, several observations suggest that the major effect of ethanol involves the impairment of thymus-derived lymphocytes (T lymphocytes or T cells). Because a subgroup of T-lymphocytes (i.e., CD4+ T cells) are the central regulators of the immune system, including cell-mediated and humoral immunity, loss of their survival and function constitutes a critical part of alcohol-induced immune dysfunction.

A number of experimental animal models of ethanol abuse have established that chronic alcohol administration decreases the absolute numbers of CD4+ T cells in the thymus, spleen, lymph nodes, and periphery, as well as the immune function of these cells (Barve et al. 2002). Similarly, patients with AUD exhibit significantly reduced numbers of CD4+ T cells (Barve et al. 2002). Although other clinical complications in alcoholic patients can negatively influence the immune system, recovery of the CD4+ T-cell count was noted after alcohol withdrawal in several studies, suggesting that ethanol can directly affect CD4+ T-cell survival (Barve et al. 2002). Moreover, experimental and clinical studies have documented that alcohol intake can cause depletion of CD4+T cells, and the mechanisms underlying this effect are only beginning to be understood. Research has indicated that ethanol

can potentially act as a cofactor and exacerbate clinical conditions that cause CD4+ T-cell depletion by enhancing activation-induced, fatty acid synthase–mediated apoptosis (Ghare et al. 2014). In addition to affecting CD4+ T-cell numbers, ethanol also has a major effect on T-cell function by decreasing the production of the cytokine, interleukin-2, which is critical for the clonal expansion of CD4+ T cells (Ghare et al. 2011).

In subjects with AUD, the combined effects of alcohol metabolism and compromised nutrition led to major nutrient disturbances, including deficiency of the critical nutrient metabolite, SAM. Studies found that levels of SAM as well as of methionine adenosyltransferase (MAT II), the enzyme that converts methionine to SAM, were markedly reduced in cultured CD4+ cells exposed to alcohol. This resulted in a significant upregulation of expression and activity of several enzymes involved in apoptosis, leading to increased apoptotic cell death (Hote et al. 2008). Moreover, restoration of intracellular SAM levels via SAM supplementation considerably attenuated this apoptotic death in T cells, implying a causal/protective role for SAM in T-cell survival (Hote et al. 2008).

Overall, these findings have begun to provide critical molecular insights into epigenetic mechanisms underlying the alcohol- and nutrient (SAM)-status–induced immunotoxicity in human CD4+ T cells. Because there currently is no Food and Drug Administration–approved therapy for the treatment of immune suppression associated with chronic alcohol abuse, these findings have the potential to facilitate the development of nutrient (SAM)-based therapy in alcoholic patients.

Conclusions

Alterations in nutrition and nutrient metabolism are common in chronic alcoholics and may contribute to alcohol-induced organ injury. Conversely, nutritional supplementation may prevent the development or attenuate the progression of alcohol-induced organ injury. Nutritional supplements may alleviate a nutrient deficiency or act as pharmacologic agents. Such nutrients also may have epigenetic effects. Nutritional supplementation as a therapy is especially attractive because there are currently no Food and Drug Administration–approved therapies for most forms of alcohol-induced organ injury and nutrient supplements are readily available.

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Advances in Substance Abuse Prevention and Treatment Interventions Among Racial, Ethnic, and Sexual Minority Populations

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Substance abuse research among racial, ethnic, and sexual minority populations historically has lagged behind that conducted with majority samples. However, interesting and potentially important advances in prevention, brief interventions, and treatment have been made in the last few years, at least among some minority populations, such as American Indian youth. New prevention efforts have focused on point-of-sale interventions for alcohol, as well as on family-unit interventions designed with subpopulation cultural values in mind. In addition, previously established evidence-based and culturally relevant interventions are being combined with computer technology. Empirical data support using brief interventions with patients of color in medical settings, capitalizing on teachable and reachable moments during a physical trauma or other health crisis. Finally, use of empirically supported treatment may be helpful, with a caveat that these interventions must appropriately match cultural traditions and respect the values of the clients. More research clearly is needed, especially among certain minority populations in the United States. A greater emphasis should be placed on developing novel, culturally grounded interventions in partnership with communities, in addition to adapting existing mainstream interventions for use by other cultures.

Key words: Alcohol use, abuse, and dependence; alcohol research; race; ethnicity; minorities; ethnic minorities; sexual minorities; prevention; intervention; treatment; point of sale intervention; family intervention; computer technology; cultural traditions; culturally grounded intervention

Historically, prevention and treatment intervention research rarely has been conducted with racial and ethnic or sexual minorities as its principal focus; this also holds true for the alcohol and other drug abuse field. The lack of credible research has been one source of the disparities in substance abuse and its consequences found among many of these groups. Fortunately, advances recently have been made in preventing, intervening in, and treating substance abuse among traditionally underserved racial, ethnic, and sexual minority subpopulations. This article reviews some of these advances, focusing on alcohol abuse but also including abuse of other drugs or substance abuse in general, as appropriate. The article also will suggest next steps for research in this area.

Challenges in Addressing Prevention and Treatment for Minority Populations

Many minority populations in the United States face well-documented challenges, such as higher-than-average rates of poverty, homelessness, and incarceration, which may contribute to increased rates of alcohol use disorder as well as other substance use disorders. A less concrete factor influencing prevention and treatment is that minorities often face stereotypes in the general population. Such stereotypes foster biased behavior toward minority groups, which may promote alcohol and other drug abuse and create greater levels of anxiety among group members themselves (Blume et al. 2012). Such factors also are likely to affect whether members of minority groups decide to seek treatment and how they experience treatment if they do (for a review of access to treatment studies, see Schmidt in this issue).

Cultural background also figures into how minority populations respond to treatment and prevention efforts. Differences in worldviews, cultural traditions, and upbringing mean that not all groups may respond to an intervention that has demonstrated success in the general population (Taylor 2003). Certain groups also face specific challenges. For treatment to be effective, providers need to identify those challenges and offer appropriate interventions. For example, American Indian (AI) and Alaska Native (AN) populations face high rates of alcohol abuse among youth (SAMHSA 2014), and relatively easy access to alcohol may be one of the contributing factors. Thus, in one study (Lynne-Landsman et al. 2015) about 75 percent of all outlets tested sold alcohol to young-appearing AI buyers at least once. Other research confirmed that underage AI youth may obtain alcoholic beverages from stores both on and near reservations either directly through illegal sales to minors or indirectly through purchases by adult friends (Lee et al. 2015). Prevention efforts aimed at lowering sales of alcohol to minors therefore could be effective for these groups. For example, Moore and colleagues (2013) demonstrated that a reward-and-reminder underage drinking prevention program in convenience stores could reduce alcohol sales to minors near rural reservations.

Recent research focused on prevention and treatment efforts for minorities has suggested that feeling safe in the environment both inside and outside of treatment centers plays a pivotal role in the success of interventions. As is discussed below, when a group's basic needs are met, group members are more likely to cut back on drinking (Larimer et al. 2009). Furthermore, when they feel secure—that is, understood culturally and not threatened—they express deeper satisfaction with treatment or prevention programs and may be more likely to continue participating (Guerrero 2013). In some cases, adapting empirically proven treatment methods is sufficient in helping clients feel safe; but in others, novel, culturally centered approaches may prove useful.

Advances in Understanding the Treatment Environment

Various studies have highlighted the importance of a safe environment for positive treatment outcomes among clients from racial, ethnic, and sexual minority groups. The groundbreaking Housing First study demonstrated that a safe housing environment alone was sufficient to improve substance-use outcomes and reduce public health costs in people with severe alcohol problems, including many homeless people of color (Larimer et al. 2009). A more recent data analysis found that motivation to change predicted improved alcohol-use outcomes 2 years after the Housing First intervention, whereas attending abstinence-based treatment did not (Collins et al. 2012).

The prevention and treatment environment also affect substance abuse treatment outcomes through the therapeutic working alliance—that is, the working relationship that clients believe they have with their therapists. Positive working alliances have been found to predict successful treatment engagement and completion (Meier et al. 2005). Davis and Ancis (2012) pointed out that most studies investigating the working alliance in treatment have been conducted with predominately White patient samples. However, they did identify three important factors that affect the working alliance among clients of color. First, culturally responsive treatment has been positively associated with improvements in

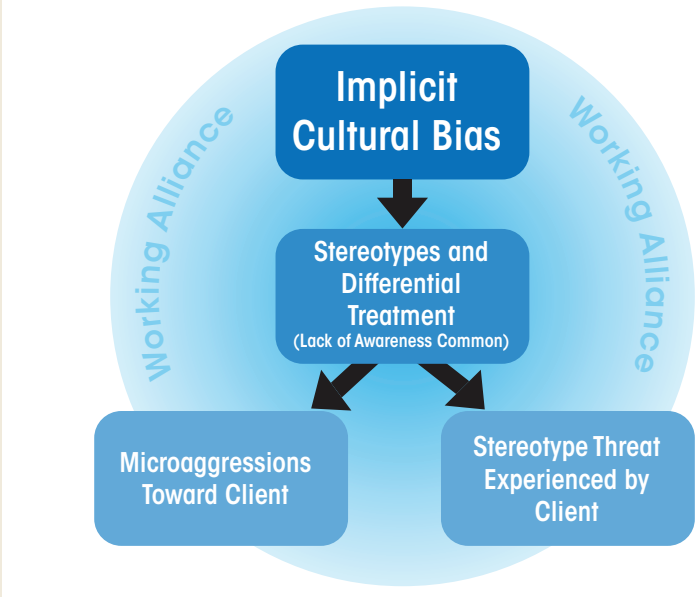

Figure 1 Implicit bias and its threat to working alliance. All people, including treatment professionals, are affected by implicit biases transmitted within our culture that may escape our personal awareness. Implicit bias makes the commission of microaggressions by staff and the experience of stereotype threat by minority clients more likely. This potentially harms the working alliance and undermines treatment outcomes.

the working alliance. Second, in their interactions with both counselors and other treatment staff, clients of color encounter biased beliefs and attitudes, which often are the result of stereotyping. Third, poor working alliances frequently are a function of how often a client in therapy experiences microaggressions—commonly experienced insults, put-downs, or messages of exclusion stemming from stereotypes associated with minority-group membership—and of a client's perceptions of a therapist's low cultural competence.

Microaggressions correlate with alcohol abuse and greater anxiety (Blume et al. 2012). Thus, they may foster an environment conducive to alcohol problems and also may undermine the treatment environment and the working alliance. Microaggressions occur in the context of culturally implicit bias—that is, cultural biases ingrained in the social order that perpetuate stereotypes and prejudices often expressed automatically and without awareness by members of the social order (figure 1). Mental health professionals may direct microaggressions toward their clients automatically and unwittingly. Microaggressions also may result from programmatic or institutional cultural insensitivity toward clients (Sue et al. 2007). Interestingly, clients of color interpret the common lack of discussion in treatment concerning bias and prejudice and their links to substance-use behavior as a microaggression (Burris 2012).

Stereotyping also may influence substance-use and treatment outcomes by increasing the risk of stereotype-threat situations, in which minority members find themselves at risk for fulfilling a commonly held group-based stereotype (e.g., African Americans in academic situations where they are expected to perform poorly) (Steele and Aronson 1995). These situations place significant stress on minority-group members that can affect both physiological responses (e.g., blood pressure) (Blascovich et al. 2001) and cognitive function, including in substance abusers (Cole et al. 2006; Looby and Earleywine 2010). As an example, AI/AN clients often are stereotyped by the firewater myth, a belief that Native Americans cannot tolerate or regulate the ingestion of alcohol and will lose behavioral control if they drink any alcohol. AI/AN clients could experience stereotype- threat situations that may adversely affect treatment outcomes when treatment programs or professionals (perhaps unwittingly) communicate an understanding of addiction that aligns with the assumptions of the firewater myth.

The therapist is only one source of stereotyping and microaggression. The working alliance transcends the client–therapist relationship and includes the positive or negative impacts of institutional climate on clients. Indeed, discussions concerning prejudice and homophobia and their links to substance abuse have largely been ignored until very recently.

Research also has demonstrated that the cultural climate of treatment is a critical factor influencing treatment outcomes. Thus, increased cultural competence among treatment-center staff has been shown to contribute to higher rates of treatment retention (Guerrero 2013). Similarly, improved cultural sensitivity among treatment-program managers has been positively associated with higher rates of retention and less time on waitlists before treatment admission (Guerrero and Andrews 2011). Increasing the cultural competence of treatment administrators, counselors, and treatment-center staff who interact with clients seems to be one method for improving treatment outcomes, perhaps by making it less likely that clients will experience microaggressions and stereotype-threat situations.

Matching and Molding Prevention and Treatment Interventions

In addition to evaluating the impact of the treatment environment, investigators have focused on determining which alcohol-related interventions facilitate success for minority clients. Recent studies in both prevention and treatment show that some mainstream interventions may be effective when matched with certain population subgroups in culturally appropriate ways. Moreover, their success often improves when adapted for use in different cultures.

Moving beyond such adaptations, some research suggests that creating new prevention and treatment methods with the participation of minority-group members can foster the success of interventions even more (Bermúdez Parsai et al. 2011; De las Nueces et al. 2012; Stacciarini et al. 2011; Tapp et al. 2013). Community-based participatory research (CBPR) methods, a research model that respects minority-community authority, needs, and values in the conduct of research, makes community stakeholders equal partners with scientists during all phases of project development, implementation, and dissemination. CBPR can be used to create novel interventions specifically tailored for racial and ethnic minority communities. The following sections focusing on prevention and treatment studies, respectively, demonstrate that all three approaches—matching existing methods in culturally relevant ways to the values and needs of the communities being served, adapting existing methods to different cultures, and creating new strategies with the participation of the target community—are demonstrating success in addressing alcohol problems among minority clients.

Advances in Prevention

Over the last few years, researchers have begun developing and sometimes adapting prevention programs aimed at addressing problems specific to target populations and testing the programs empirically. One promising intervention targeted the availability of alcohol to underage purchasers near AI reservations in California. The reward-and-reminder program

enlisted young-looking confederates who attempted to purchase alcohol without showing proper identification. When convenience-store clerks requested identification, they were rewarded with gift cards; when they did not, they were sent reminder letters concerning State laws about liquor sales. After two cycles of rewards and reminders, stores were completely in compliance when assessed (Moore et al. 2012).

Culturally relevant prevention programs that focus on the family rather than on individuals have been successful, because they acknowledge beliefs held by many minority cultures concerning the importance of the family (rather than the individual) as the principal unit of function (figure 2). This family-oriented approach stresses the value of interdependence and the commonly held tenet that families work together to solve the problems of individual members. These interventions generally involve family members and parent–youth dyads working in unison on various family-building strategies (e.g., family communication) and substance-use prevention program components (e.g., parental monitoring). Other approaches include completing the more traditional individualized prevention components, such as parent training (for adults) or drink-refusal skills (for youth).

One family-oriented intervention, for example, targeted mother–daughter dyads through a Web-based delivery system. The investigators found reduced substance use, improved child–parent relationships, and increased self-efficacy and refusal skills among female adolescent African Americans, Asian Americans, and Latinas (Fang et al. 2010; Schinke et al. 2011). Other examples include the Familias Unidas program with Latino youth in the juvenile justice system and their primary caretakers, which led to a drop in substance abuse as well as in high-risk sex (Prado et al. 2012). The Strong African American Families and Adults in the Making programs resulted in slower increases in alcohol consumption and intoxication (i.e., slower alcohol-use escalation) among African-American youth compared with control subjects (Brody et al. 2010, 2012).

Skill-based interventions that incorporate traditional practices to strengthen the bonds of youth to their communities and cultures also are under investigation. Komro and colleagues (2015) are conducting a promising screening, brief intervention, and referral to treatment (SBIRT) prevention trial that includes a culturally centered approach to intervention targeting the youth environment within the Cherokee Nation. A computer-based intervention that incorporates developmentally appropriate gaming and video clips to prevent substance use (Project HAWK) also is being tested among AI youth (Raghupathy and Go Forth 2012). Researchers have not yet evaluated the efficacy of these new methods. Think Smart, another school-based program that develops both traditional and mainstream cultural competence among AI participants in the later elementary school grades, was associated with lower student inhalant abuse but showed null results for other substance use (Johnson et al. 2009).

Both Project HAWK and the Think Smart program were derived from the evidence-based State-wide Indian Drug Prevention Program that features skills training to increase bicultural competence and resilience among at-risk AI youth (Schinke et al. 2000). Use of innovative skills-training interventions is a fruitful area for improving prevention programs for other groups as well. For example, the REAL skills groups that focus on various refusal skills and a group-based social-norms approach have improved outcomes in the culturally

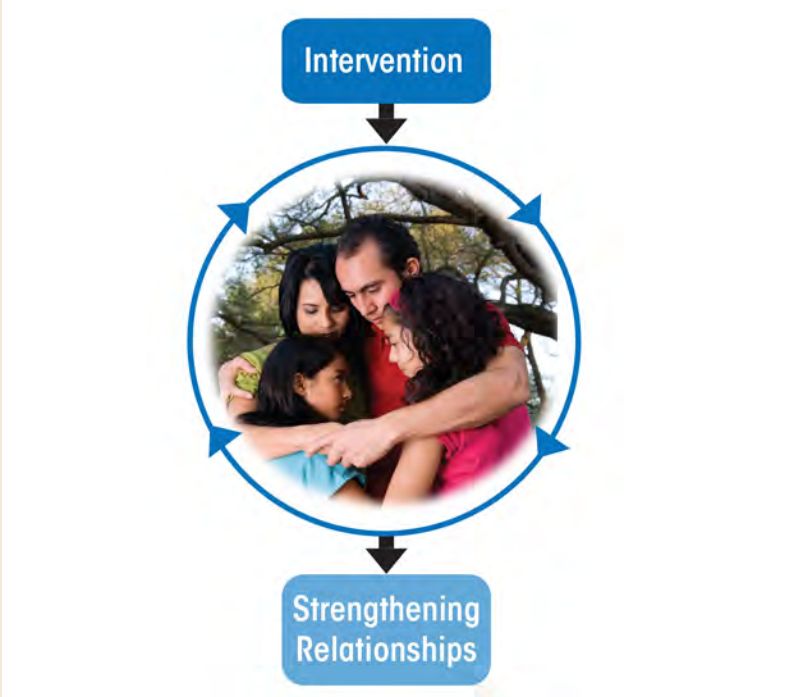

Figure 2 Family-oriented interventions. Recent advances in effective prevention programs among subpopulations have focused on family-level interventions consistent with the strong cultural values about the importance of family in collectively addressing the needs of a family member.

based prevention program for Latino youth called Keepin' It Real, especially when used with youth around the seventh grade (Marsiglia et al. 2012).

Beyond such adaptations of existing programs, other communities are experimenting with new methods developed in cooperation with minority groups themselves. For example, the Cherokee Talking Circle school-based intervention program, a uniquely Cherokee-centered strategy that includes the use of talking-circle groups as a culturally relevant approach to solving problems together, was associated with reduced substance use among AI youth. Those randomly assigned to the Cherokee Talking Circle intervention had significantly better outcomes with respect to total symptom severity, substance use, general life problems, and internal and external behavior at 3 months post-intervention than those assigned to a mainstream school-based substance abuse education program (Lowe et al. 2012).

Such CBPR among racial and ethnic minority populations has demonstrated the ethical and practical necessity of adaptive interventions that tend to evolve during the course of a research study. This can be done while preliminary outcomes are analyzed by researchers and community stakeholders and used to modify interventions (Henry et al. 2012). At the same time, some researchers have voiced concerns about overemphasizing the process of culturally adapting empirically validated mainstream interventions to the exclusion of other methods. One experienced AI research team (Whitbeck et al. 2012) urged a paradigm shift away from adapting Western best practices and toward development of novel evidence-based and culturally relevant interventions in partnership with Native communities. They suggested such a shift because interventions developed for Western populations sometimes do not align with Native worldviews and traditions. Moreover, many Native communities harbor a lingering deep distrust of Western-oriented practices because of historical abuses by researchers (Whitbeck et al. 2012).

Advances in SBIRT and Motivational Interventions

Although novel, culturally based treatments ultimately may be considered ideal, mainstream SBIRT has been used successfully in racial and ethnic populations. One report (Madras et al. 2009) pooled data from multiple medical care settings (including emergency departments, primary care, and other institutions) for a study funded by SAMHSA to evaluate SBIRT, with the majority of the participating patients being people of color. The investigators found that, across the sites, patients experienced improved outcomes for substance-use and functional status 6 months post-intervention. Unfortunately, the types of brief interventions were not consistent across sites and there were no control groups, although all participating sites seemed to foster the spirit of motivational interviewing.

Brief motivational interventions with African Americans and Latinos in trauma centers also have been associated with reductions in alcohol use at 6 and 12 months post-intervention (Field et al. 2010). Ethnic matches between Latino clients and interventionists seemed to improve outcomes (Field and Caetano 2010), potentially supporting other research on the importance of the working alliance. Positive outcomes also did not depend on whether the subject subsequently attended treatment (Field et al. 2013).

Research from the National Institute on Drug Abuse (NIDA) Clinical Trials Network found that motivational enhancement therapy was particularly effective among African-American participants with higher readiness-to-change scores (Burlew et al. 2013). In a multisite randomized controlled trial, motivational enhancement therapy also was effective with and personally appealing to Spanish-speaking Latino adults who primarily misused alcohol, but less effective for those who used other drugs (Carroll et al. 2009). In another pilot study, culturally adapted motivational interviewing was well received by Latino immigrant participants (Lee et al. 2011).

Other Advances in Treatment

Research studies have demonstrated empirical support for mindfulness-based relapse prevention as a substance-use intervention among women of color (Amaro et al. 2014; Witkiewitz et al. 2013; see sidebar "Religious Affiliation and Spiritual Practices: An Examination of the Role of Spirituality in Alcohol Use and Alcohol Use Disorder"). Although interest in using mindfulness as a substance-use intervention among racial and ethnic minorities has increased substantially, some researchers have raised questions about the cultural relevance of such interventions. For example, Hall and colleagues (2011) expressed concerns that mindfulness interventions may be highly Westernized. These strategies are not particularly helpful for certain racial and ethnic minority groups unless they are aligned with traditional cultural values and traditions.

Drink-refusal skills also have been identified as potentially helpful for African-American clients. In an examination of Project COMBINE data, African-American participants who completed drink-refusal skills training had significantly more positive treatment outcomes compared with those who did not complete the skills-training component. The positive outcomes were demonstrated up to 1 year post-intervention (Witkiewitz et al. 2011).

Communities also have collaborated with researchers using CBPR methods to create novel treatment interventions, just as they have done with prevention programs. One recent and promising example is the development of Drum-Assisted Recovery Therapy, which uses traditional Native American drumming and singing as well as talking circles to help AI/AN treatment

clients with recovery from substance abuse (Dickerson et al. 2012). Researchers used qualitative methods and key community stakeholder involvement to develop and refine the culturally grounded therapy protocol that bears little resemblance to traditional treatment methods or mainstream therapies.

Interventions for Sexual Minorities

Sexual minorities have been relatively overlooked in prevention and treatment intervention research, perhaps because of substance abuse stigma and homophobia. For sexual-minority clients of color, there also are the added dimensions of racial- and ethnic-based prejudice and bias. Sexual minorities experience elevated risk for substance abuse, but intervention research with this particular subpopulation is sorely lacking (Green and Feinstein 2012). However, researchers have found that in general, sexual-minority clients prefer to seek alternative rather than mainstream forms of treatment, especially if they do not closely identify with mainstream heterosexual beliefs (Dillworth et al. 2009).

Real Men Are Safe is a group-based program that emphasizes motivational enhancement, didactics, and skills training targeting high-risk sexual behavior among men in substance abuse treatment. It has been associated with modest improvements in safe-sex practices among sexual-minority men of color in substance abuse treatment. The program was culturally adapted by a qualitative examination of data collected from an expert panel of professionals who conducted research among ethnic sexual minorities that was then used to revise and enhance program content. Some evidence also suggests that the adapted Real Men Are Safe may have been more culturally relevant for African Americans and Latinos than for other groups (Calsyn et al. 2012, 2013). The results are promising and suggest that mainstream treatment can be culturally adapted for sexual-minority clients in ways that may reduce other risk behaviors.

Advances in Pharmacologic Treatment

Beyond advances in psychotherapy, pharmacological approaches have been investigated in minority populations as well. In one randomized placebo-controlled trial with a rather high dropout rate, naltrexone use was associated with fewer alcohol-related consequences and greater percentage of days abstinent among AN clients in isolated rural areas of Alaska (O'Malley et al. 2008; see also Greenfield and Venner 2012).

However, two other studies found null results for naltrexone's efficacy among African-American clients—one from Project COMBINE that examined alcohol-dependent participants (Ray and Oslin 2009) and another that investigated social drinkers under laboratory conditions (Plebani et al. 2011). Few pharmacotherapy studies have been conducted with minority population samples large enough to produce meaningful results. More investigation is needed to assess the efficacy of specific drugs, including naltrexone, among various subpopulations.

Conclusions and Future Directions

Exciting new programs for prevention, brief opportunistic intervention, and treatment have been successfully developed and tested with racial, ethnic, and sexual minority populations—groups often at risk for substance abuse and with well-documented disparities. Recent interventions have combined computer- or Web-based technologies with culturally relevant adaptations, including a focus on the family as the unit of intervention, as well as culturally grounded and informed measurement (see Allen and Mohatt 2014). In addition, empirically supported skills-based approaches seem helpful for certain subpopulations, with the caveat that the interventions may require appropriate cultural alignment of the intervention with the beliefs and traditions of the group being targeted. Recent studies continue to demonstrate that when appropriate CBPR methods are used, evidence-based interventions can be used in culturally appropriate ways to benefit some racial, ethnic, and sexual minority populations.

However, given the vast heterogeneity of some minority groups (e.g., AI/AN) (Etz et al. 2012), some minority communities likely will reject existing interventions as culturally insensitive or not reflecting their beliefs and values (Whitbeck et al. 2012). In addition, some studies using culturally adapted interventions based on empirical evidence have found null or inconsistent outcomes (e.g., Carroll et al. 2009), suggesting that other approaches are needed. Thus, although such interventions can be helpful for some minority groups, a prudent strategy would involve simultaneously developing novel and culturally specific interventions using rigorous CBPR strategies for communities where other interventions may not work well (Etz et al. 2012; Whitbeck et al. 2012).

Intervening at the level of the treatment environment to improve outcomes for racial, ethnic, and sexual minority clients also is an exciting new development that holds particular promise for improving the working alliance, a consistent predictor of treatment outcomes independent of intervention modality. Above all, more can be done to improve the climate of prevention and treatment programs. Such efforts could reduce the likelihood of microaggressions and risk of stereotyping and stereotype threats that may negatively affect client outcomes following interventions.

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Putting the Screen in Screening

Technology-Based Alcohol Screening and Brief Interventions in Medical Settings

Sion Kim Harris, Ph.D., and John R. Knight, M.D.

Alcohol is strongly linked to the leading causes of adolescent and adult mortality and health problems, making medical settings such as primary care and emergency departments important venues for addressing alcohol use. Extensive research evidence supports the effectiveness of alcohol screening and brief interventions (SBIs) in medical settings, but this valuable strategy remains underused, with medical staff citing lack of time and training as major implementation barriers. Technology-based tools may offer a way to improve efficiency and quality of SBI delivery in such settings. This review describes the latest research examining the feasibility and efficacy of computer- or other technology-based alcohol SBI tools in medical settings, as they relate to the following three patient populations: adults (18 years or older); pregnant women; and adolescents (17 years or younger). The small but growing evidence base generally shows strong feasibility and acceptability of technology-based SBI in medical settings. However, evidence for effectiveness in changing alcohol use is limited in this young field.

Key words: Alcohol use, abuse, and dependence; screening and brief intervention; medical setting; primary care; emergency room; adult; adolescent; pregnant women; technology; computer-based screening and brief intervention; literature review

Alcohol-related screening and brief interventions (SBIs) in medical settings have the potential to transform the treatment of alcohol misuse and prevent considerable alcohol-related harm (Babor and Higgins-Biddle 2001). Rapid screening and assessment tools allow health care providers to quickly assess the extent of patients' alcohol use, identify those with problematic use, provide them with an immediate brief intervention, and refer patients with more severe alcohol use disorders to a substance abuse specialist when available. SBIs have proven effective for detecting potential alcohol problems and reducing the severity of problems in a wide range of populations and settings (Kaner et al. 2009; O'Donnell et al. 2014)—so much so that agencies focused on preventing and treating alcohol use, including the U.S. Preventive Services Task Force (USPSTF), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the Substance Abuse and Mental Health Services Administration (SAMHSA), recommend that primary care and other medical settings expand their SBI use for patients ages 18 years and older (Moyer 2013; NIAAA 1995; SAMHSA 2011). Although the USPSTF cited insufficient evidence to recommend SBIs for adolescents (Moyer 2013), recognition of and evidence for the potential utility of SBIs for adolescents have been building in recent years (Harris et al. 2012; Mitchell and Gryczynski 2012; Pilowsky and Wu 2013), leading the American Academy of Pediatrics to recommend that all pediatricians use SBIs in their practices as part of routine care (American Academy of Pediatrics 2011).

Despite the push for using SBIs in medical settings, they remain underused. In a recent national survey of U.S. adults, only one in six (15.7 percent) respondents reported discussing alcohol use with a health professional in the past year, with State-specific estimates ranging from 8.7 percent to 25.5 percent (McKnight-Eily et al. 2014). The percentage was higher (34.9 percent), but still inadequate, among those with 10 or more binge-drinking episodes in the past month. An often-cited barrier to SBI implementation is lack of time (Van Hook et al. 2007; Wilson et al. 2011). Computer-facilitated SBI delivery may offer a solution for busy medical settings, allowing more widespread implementation. This article focuses on current- and emerging-technology–facilitated SBI tools that have been evaluated in primary care, pediatric, and emergency department (ED) settings. We review studies of technology-based SBI as they relate to adults (18 years or older), pregnant women, and adolescents (17 years or younger), the primary patient populations in which alcohol SBIs have been implemented.

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The studies reviewed here come from a systematic electronic literature search conducted between February 2014 and December 2014 using PubMed and PsycINFO, as well as the reference lists of published studies and review articles. We summarize the characteristics of the studies, including population, design, and results, in the table.

Value Added With Electronic SBIs

Technology-based SBIs could help increase the frequency and quality of SBI use in medical settings by enhancing efficiency and standardizing implementation. In terms of screening, touchscreen devices or standalone computers with Internet connections can allow patients to enter information in the waiting room prior to an appointment. Programs automatically score the screening results that staff can print or electronically transmit to practitioners. This reduces clinician time needed for administering and scoring a questionnaire during the visit. In addition, programs can be loaded with validated measures that improve the quality of screening and can automatically select appropriate questions according to the patient's age and previous responses. Patients also may be more willing to disclose sensitive information to a computer than to a person (Butler et al. 2009; Turner et al. 1998), and integration of computerized screening results with electronic health records may boost screening and documentation rates (Anand et al. 2012).

Similarly, computer-facilitated brief intervention delivery has the potential advantages of greater standardization, lower cost, and greater ease of implementation compared with face-to-face delivery. As with screening, programs can automatically tailor intervention content to individual patients. Interventions vary based on the program, but, as with face-to-face SBIs, computer-based SBI tools often follow screening with personalized feedback that includes a summary of patients' consumption patterns and risk status, a comparison of their consumption with recommended limits, estimated blood alcohol concentrations for their heaviest drinking occasion in the reported time frame, and a comparison between their consumption and consumption reported by others in their peer group. More extensive programs may incorporate intervention strategies based on principles of evidence-based face-to-face treatments, such as motivational interviewing (Miller and Rollnick 2012) and cognitive–behavioral therapy (Kadden et al. 1995).

Using technology for SBIs in medical settings may be especially valuable for reaching young people who are highly engaged with technology and nearly universal access to computers, cell phones, and the Internet (Madden et al. 2013; Marsch et al. 2007; Pew Research Center's Internet and American Life Project 2014). Indeed, using technology-facilitated alcohol SBIs in medical settings to reach adolescents may be a powerful mechanism to reduce medical costs and gain productive years of life, since alcohol use disorders are strongly linked to the leading causes of adolescent and adult mortality, including motor-vehicle crashes and suicide.

This high level of online engagement has fueled a surge of interest in the potential of standalone Web-based SBI programs to address problematic alcohol use, particularly among college students. These programs provide a means to inexpensively reach people less likely to access traditional health services. Detailed reviews of research on these standalone online alcohol SBIs are provided in articles by Carroll and Cronce in this issue and suggest that, at least among college students and adults, these programs tend to yield small to moderate effects, which are greatest at followups less than 3 months, gradually declining to little or no effect by 12 months (Donoghue et al. 2014). The lack of interpersonal contact with these programs may contribute to lower participation rates and adherence over time (Murray et al. 2013; Naimi and Cole 2014; Postel et al. 2011). In addition, alcohol use is strongly linked to many physical and mental health problems, such as cancer, cirrhosis, and depression (National Center on Addiction and Substance Abuse 2011). Therefore, standalone programs are unlikely to obviate the need for SBIs in medical settings, which is the focus of this review.

Medical Setting SBI for Adults

Twelve studies of varying design and stages of research (reported in 13 published papers) have examined computerized SBIs for adults in medical settings that include four studies in primary care (Bendtsen et al. 2011; Butler et al. 2003; Cucciare et al. 2013; Kypri et al. 2008), seven in EDs (Blow et al. 2006; Karlsson and Bendtsen 2005; Murphy et al. 2013; Neumann et al. 2006; Nilsen et al. 2009; Suffoletto et al. 2012; Trinks et al. 2010; Vaca et al. 2011), and one in a hospital outpatient department (Johnson et al. 2013) (see the table for study details). Half of the studies used a randomized design (Blow et al. 2006; Cucciare et al. 2013; Kypri et al. 2008; Neumann et al. 2006; Suffoletto et al. 2012; Trinks et al. 2010); one used a before-and-after design, with each clinic serving as its own control (Butler et al. 2003); and five are earlier-stage observational studies with small sample sizes (Bendtsen et al. 2011; Johnson et al. 2013; Karlsson and Bendtsen 2005; Murphy et al. 2013; Vaca et al. 2011). Generally, followup, where it existed, was short, with two studies following participants for 3 months, four for 6 months, and three for 12 months. The studies shared some common components.

SBI Delivery Method

All but one study by Suffoletto and colleagues (2012), tested screening and/or brief intervention delivery on a tablet or desktop computer located in the medical setting. Suffoletto and colleagues (2012) delivered their intervention through weekly mobile text messages following patient discharge from the ED.

Table 1 Characteristics of Computer-Assisted Alcohol Screening and Brief Intervention (SBI) Studies Conducted in Health Care Settings

Authors (Year)	Study Population	Setting	Screening and Other Measures	Study Design/ Treatment Conditions	Follow-up Period (% Completed)	Results
Adults (Age 18 or Older): Primary Care						
Butler et al. (2003)	English- or Spanish-speaking primary care patients (ages 18–99, *N* = 2,053 screened, 128 screened positive and completed followup, 68% female)	Primary care practices in Massachusetts, New York, and Florida	1) Alcohol Use Disorders Identification Test (AUDIT) 2) Stage-of-change measure	Before-and-after, each site own control: 1) Control phase (*N* = 66): Standard care with AUDIT after visit 2) Treatment phase (*N* = 62): 20-minute computerized SBI completed in medical office before visit, with tailored feedback and information to reduce risky drinking; clinician can be given printed report with suggested brief interventions	6 months (85%)	• Spanish version had lower AUDIT+ detection rates than English version; no such difference found with traditional AUDIT. • AUDIT-C scores declined for both groups during followup; no intervention effect; no difference between language groups.
Kypri et al. (2008)	University health service patients screening positive for at-risk drinking (ages 17–29; *N* = 975 screened, 429 screened positive, 52% female)	University health service in New Zealand	1) AUDIT 2) Past-2-weeks alcohol consumption 3) Alcohol Problems Scale	Randomized controlled trial (RCT) three groups: 1) Single-dose 10-minute Web-based SBI (*N* = 138): Assessment, personalized normative feedback, risk status, comparison of consumption with recommended limits 2) Multi-dose Web-based SBI (*N* = 145): same as above repeated at 1 and 6 months 3) Control (*N* = 146): Information pamphlet only	6 months (84%) 12 months (84%)	• Both intervention groups had lower alcohol consumption, AUDIT scores, and alcohol problems at 6 and 12 months compared with the control group. • Single-dose and multi-dose effects similar; provision of up to two additional sessions did not increase efficacy.
Bendtsen et al. (2011)	Primary care patients with risky drinking (ages 18 or older; *N* = 7,863 screened, 3,169 screened positive, 578 received e-SBI, 347 completed followup, 41% female)	Primary care clinics in one Swedish county	1) Average weekly use 2) Heavy episodic drinking (HED) occasions per month	Observational study of two cohorts: 1) "Self-referred" (*N* = 139): computerized SBI in clinic completed on own initiative 2) "Staff-referred": (*N* = 208) invited by clinician to complete computerized SBI after visit Behavioral intervention (BI) for both was printout of personalized written feedback	3 months (60%)	• No significant between-group differences at baseline and 3 months. • "Staff-referred" had reduction in weekly alcohol use but "self-referred" did not. • Significant reduction in HED for both. • Follow-up responders more likely to be older, have lower weekly alcohol use at baseline than non-responders; no difference in HED.

Table 1 Characteristics of Computer-Assisted Alcohol Screening and Brief Intervention (SBI) Studies Conducted in Health Care Settings *(continued)*

Authors (Year)	Study Population	Setting	Screening and Other Measures	Study Design/ Treatment Conditions	Follow-up Period (% Completed)	Results
Cucciare et al. (2013)	Military veterans screening positive for alcohol misuse (*N* = 167, 12% female)	Veterans Affairs primary care clinics in California	1) AUDIT-C 2) Timeline Follow-Back 3) Alcohol-related consequences	RCT two groups: 1) Intervention (*N* = 89): Standard care plus Web-based 10-minute SBI with assessment, personalized normative feedback, education, summary of alcohol-related consequences and risk factors, and self-reported motivation to change 2) Control (*N* = 78): Standard care only (brief counseling by PCP)	3 months (86%) 6 months (84%)	• Alcohol consumption and severity of alcohol-related problems declined for both groups. • No differences between groups.
Adults (Age 18 or Older): Emergency Department (ED)						
Karlsson and Bendtsen (2005)	ED patients (ages 18–70, *N* = 44, % female not available)	ED of university hospital in Sweden	1) Modified AUDIT-C 2) Patients' ratings of computerized screening and personalized feedback	Single-group acceptability study: Computerized screening and printout of personalized feedback and advice given to patient	N/A	• 95% rated computer easy to use. • 67% rated being screened positively. • 76% rated feedback and advice printout positively. • 74% preferred printout over nurse or doctor delivery. • 93% would read advice.
Blow et al. (2006)	Sub-critically injured ED patients screening positive for at-risk drinking (ages 19 or older, *N* = 4,476 screened, 577 screened positive and received BI, 29% female)	Midwestern level 1 trauma center in university hospital	1) Frequency of alcohol consumption and HED in past 3 months 2) Drinker Inventory of Consequence—Short Inventory of Problems	RCT four groups: Computerized screening plus computer generated: 1) Tailored message booklet with clinician-delivered brief advice (*N* = 129) 2) Tailored message booklet only (*N* = 121) 3) Generic message booklet with advice (*N* = 124) 4) Generic message booklet only (*N* = 120)	3 months (86%) 12 months (86%)	• All groups reduced mean drinks per week, HED, and alcohol-related consequences by 12 months. • No difference in outcomes between tailored vs. generic message conditions. • Brief advice had greater reductions than no advice, particularly among females and those aged 22 and older.

Table 1 Characteristics of Computer-Assisted Alcohol Screening and Brief Intervention (SBI) Studies Conducted in Health Care Settings *(continued)*

Authors (Year)	Study Population	Setting	Screening and Other Measures	Study Design/ Treatment Conditions	Follow-up Period (% Completed)	Results
Neumann et al. (2006)	Sub-critically injured ED patients screening positive for at-risk drinking (ages 18 or older, *N* = 1,139, 79% female)	ED in Germany	1) AUDIT 2) Readiness-to-Change questionnaire 3) Percent of patients with at-risk drinking (more than 30 g/d men; more than 20 g/d women)	RCT two groups: 1) Intervention: Standard care plus computerized SBI (*N* = 561): with customized normative feedback, advice, change strategies, and summary letter printed for patient before ED discharge 2) Control (*N* = 575): Standard care only	6 months (63%) 12 months (58%)	• Significant intervention effects at 6 and 12 months: intervention group had lower percent of patients reporting at-risk drinking, and greater decrease in alcohol intake, compared with control subjects.
Nilsen et al. (2009) Trinks et al. (2010)	ED patients screening positive for risky drinking (ages 18–69, *N* = 1,570 screened, 560 screened positive and received BI, 93 completed followup, 39% female)	County hospital ED in Sweden	1) AUDIT-C	RCT two groups: Computerized screening with printout given to patient of: 1) "Long-feedback" (*N* = 52): Traffic light graphic with risk level (hazardous, elevated, or no risk) and other tailored feedback about drinking pattern, and information to enhance motivation to change behavior 2) "Short-feedback" (*N* = 41): Traffic light graphic only	6 months (17%)	• 41% of those requested to do computer SBI did. • Both groups had reduced weekly alcohol consumption and HED frequency at 6 months. • No differences in change over time between groups. • 6-month respondents had lower HED frequency at baseline than non-respondents.
Vaca et al. (2011)	English- or Spanish-speaking ED patients (ages 18–65 or older, *N* = 4,375 screened, 742 screened positive and received BI, 385 consented to follow-up, 35% female)	University hospital ED in California	1) AUDIT 2) Drinks per week	Single-cohort observational study: Intervention: Computerized SBI involving brief negotiated interview, and personal alcohol reduction plans	6 months (57%)	• 47% of at-risk drinkers reduced drinking to below NIAAA-recommended limits. • Decreased frequency of driving while impaired. • Reductions greater among those with AUDIT scores higher than 8.

Table 1 Characteristics of Computer-Assisted Alcohol Screening and Brief Intervention (SBI) Studies Conducted in Health Care Settings *(continued)*

Authors (Year)	Study Population	Setting	Screening and Other Measures	Study Design/ Treatment Conditions	Follow-up Period (% Completed)	Results
Suffoletto et al. (2012)	ED patients (ages 18–24; *N* = 109, 52 screened positive, 45 consented to participate, 64% female)	Urban EDs in Pennsylvania	1) AUDIT 2) Timeline Follow-Back	RCT three groups: 1) Intervention (*N* = 15): Weekly text message (TM) feedback with goal setting 2) Assessment only (*N* = 15): Weekly TM-based assessments, no feedback 3) Control (*N* = 15): Weekly TM notifying number of weeks until 3-month followup	3 months (86%)	• 93% of intervention and assessment groups replied *one or more times* to weekly TM queries about drinking; 80% of intervention group replied to all 12 weeks of queries. • Intervention reduced heavy-drinking days and drinks per drinking day more than assessment-only.
Murphy et al. (2013)	ED patients (ages 21–85 years, *N* = 517, 63% female)	ED of urban academic medical center in New York	1) AUDIT 2) Patient acceptance and comprehension questionnaire 3) Research staff questionnaire	Single-group feasibility study: 15-minute Web-based SBI with assessment, tailored risk-level education, customized normative feedback, list of local alcohol treatment agencies	N/A	• 98% completed CASI program. • 89% liked program. • 93% found it easy to use. • 90% accurately reported alcohol risk level after program completion.
Adults (Age 18 or Older): Hospital Outpatient Clinics						
Johnson et al. (2013)	Hospital outpatients (ages 18 or older, *N* = 99 completed SBI, 69 invited for followup, 46% female)	Hospital ambulatory care center in Australia	1) AUDIT 2) Peak blood alcohol concentration (BAC) 3) Leeds Dependence Questionnaire 4) History of Trauma scale	Single-group feasibility study: Computerized SBI with normative feedback on screening results and peak BAC, comparison to recommended limits (not shown for low-risk drinkers), information about health and behavioral risks of different BACs, estimate of spending on alcohol per month, tips for reducing risk and local treatment options	Within few days of visit (75%)	• 93% of eligible consenting patients completed SBI. • 94% found it easy to complete. • 95% reported responding honestly. • 80% found feedback useful. • 96% had no concern about privacy.

Table 1 Characteristics of Computer-Assisted Alcohol Screening and Brief Intervention (SBI) Studies Conducted in Health Care Settings *(continued)*

Authors (Year)	Study Population	Setting	Screening and Other Measures	Study Design/ Treatment Conditions	Follow-up Period (% Completed)	Results
Pregnant Women						
Tzilos et al. (2011)	Pregnant women screening positive for problem alcohol use (ages 18–45, *N* = 50)	Urban prenatal care clinic in Michigan	1) T-ACE 2) Timeline Follow-Back 3) Readiness to Change 4) Acceptability of software 5) Birth outcome variables	RCT two groups: 1) Intervention (*N* = 27): 15- to 20-minute computerized SBI with educational content tailored to pregnant women, and to their current drinking status and motivation to change 2) Control (*N* = 23): Questionnaire on television show preferences and shown videos of popular shows	1 month (96%)	• High acceptability of computerized screening and BI. • Both groups showed significant decline in reported alcohol consumption during followup; no differences between groups. • Babies born to BI group had significantly higher birth weight compared with control subjects.
Pollick et al. (2013)	Pregnant African-American women who screened positive for problem drinking but quit during pregnancy (ages 18–29, *N* = 18)	Urban prenatal care clinic in Michigan	1) T-ACE 2) Alcohol use 3) Acceptability of software 4) Semistructured interview about user experience	Single-group pretesting study Computerized SBI: 20-minute interactive tailored program with content based on MI techniques with normed feedback, decisional balance exercise, menu of change (or relapse prevention) options, referral to local treatment options	N/A	• High ratings for software approval, ease of use, and perceived helpfulness. • Videos and graphs/ charts rated most useful components.
Adolescents (Age 17 or Younger)						
Gregor et al. (2003) Maio et al. (2005)	ED patients with minor injuries (ages 14–18 years, *N* = 655, 33% female)	ED of academic medical centers in Michigan	1) Alcohol Misuse Index of negative consequences of alcohol use 2) Binge-drinking episodes in past 3 months 3) Driving after drinking or riding with a driver that had been drinking	RCT two groups: 1) Intervention (*N* = 329): Computerized screening and single-session BI interactive educational program (virtual house party) to increase knowledge about risks, enhance refusal skills, decrease intention to use 2) Control (*N* = 326): Baseline survey with standard care only	3 months (93%) 12 months (89%)	Overall sample • 94% liked program, 74% reported it made them rethink their alcohol use, 5% needed assistance to use it. • No differences in alcohol outcomes between intervention and control: both decreased from baseline to 3 months, but returned to baseline levels by 12 months. Subgroup with baseline drinking and driving • Alcohol misuse and binge drinking lower at 12 months in intervention group.

Table 1 Characteristics of Computer-Assisted Alcohol Screening and Brief Intervention (SBI) Studies Conducted in Health Care Settings *(continued)*

Authors (Year)	Study Population	Setting	Screening and Other Measures	Study Design/ Treatment Conditions	Follow-up Period (% Completed)	Results
Cunningham et al. (2009, 2012) Walton et al. (2010)	ED patients with past-year violence and alcohol use (ages 14–18, *N* = 3,338 screened, 726 screened positive and consented to study, 56% females)	Urban ED in Michigan	1) AUDIT-C 2) POSIT 3) Conflict Tactic scale 4) Violence consequences	RCT three groups: 1) Computerized BI (*N* = 237) 2) Therapist-delivered BI (*N* = 254) • Both 35 minutes and based on motivational interviewing, with normative feedback and skills training 3) Control (*N* = 235): standard care with community resource brochure (also given to BI groups)	3 months (86%) 6 months (86%) 12 months (84%)	• 3 months: computer and therapist BI groups showed similar significant reductions in positive alcohol and violence attitudes, increases in refusal self-efficacy. • 6 months: Both BI groups less likely to report alcohol-related consequences than control group, but no effect on drinking frequency. • 12 months: significant therapist-BI effect on peer aggression and victimization; no BI effect (computer or therapist) on any alcohol variables.
Harris et al. (2012) Louis-Jacques et al. (2014)	Primary care patients (ages 12–18, *N* = 2,092 in United States [USA], 589 in Czech Republic [CZR]; USA/CZR 57%/47% females)	Primary care clinics in New England, and Prague, Czech Republic	1) CRAFFT screener 2) Timeline Follow-Back 3) Postvisit questionnaire 4) Personal Consequences Scale	Before-and-after, each site own control: 1) Control phase (USA/CZR *N* = 1,068/297): Treatment as usual (TAU) 2) Intervention phase (USA/CZR *N* = 1,028/292): 10-minute computer-assisted screening and provider brief advice (cSBA) with screening, risk-level feedback, educational pages, and provider report with screen results and prompts for 2 to 3 minutes of counseling	3 months (73%/88%) 12 months (73%/90%)	• 3 months: cSBA significantly reduced alcohol use rates compared with TAU in USA sample but not in CZR sample. Larger cSBA cessation effect found among drinking youth with peer risk (having friends who drank). • 12 months: cSBA effect attenuated but still significant among New England youth.

Table 1 Characteristics of Computer-Assisted Alcohol Screening and Brief Intervention (SBI) Studies Conducted in Health Care Settings *(continued)*

Authors (Year)	Study Population	Setting	Screening and Other Measures	Study Design/ Treatment Conditions	Follow-up Period (% Completed)	Results
Walton et al. (2014)	ED patients screening positive for risky drinking (ages 14–20, *N* = 4,389 screened, 1,053 screened positive, 836 consented to study, 48% female)	Urban ED in Michigan	1) AUDIT-C 2) Alcohol-related consequences (RAPI) 3) Psychological constructs related to behavior change: – Importance of cutting back – Likelihood to cut down in next 30 days – Readiness to stop – Desire for help to cut down	RCT three groups: 1) Computerized BI (*N* = 252): Offline "Facebook"-styled program 2) Therapist-delivered BI (*N* = 256) – Both BI had tailored normative feedback, based on motivational interviewing and cognitive–behavioral strategies 3) Control (*N* = 281): Standard care with community resource brochure (also given to BI groups)	Immediate posttest (99%)	• Increased importance of change in both BI groups compared with control groups. • Increased readiness to stop in Therapist BI group. • BI components positively related to changes in psychological constructs: *Computer BI* – Benefits of change – Alternate activities – Choosing goal to reduce or stop *Both* – Tools for reducing or stopping use – Personal strengths review

NOTES: Abbreviations:

AUDIT-C: Alcohol Use Disorders Identification Test—Consumption items (items 1–3)
CASI: Computerized alcohol screening and intervention
CRAFFT: Car, Relax, Alone, Forget, Family/Friends, Trouble
PCP: Primary care provider
POSIT: Problem Oriented Screening Instrument for Teenagers
RAPI: Rutgers Alcohol Problem Index
T-ACE: Mnemonic for 4-item screener for problem alcohol use (Tolerance, Annoyed, Cut down, Eye-opener)

Screening

All 12 studies used a self-administered computerized screener that assessed quantity and frequency of alcohol consumption and heavy episodic drinking (HED) episodes. Ten of the 12 studies (Butler et al. 2003; Cucciare et al. 2013; Johnson et al. 2013; Karlsson and Bendtsen 2005; Kypri et al. 2008; Murphy et al. 2013; Neumann et al. 2006; Suffoletto et al. 2012; Trinks et al. 2010; Vaca et al. 2011) used the Alcohol Use Disorders Identification Test (AUDIT) screening tool (Reinert and Allen 2002) or its shortened form, the AUDIT-C (Bush et al. 1998).

Brief Intervention Delivery

Seven of the studies (Blow et al. 2006; Cucciare et al. 2013; Kypri et al. 2008; Neumann et al. 2006; Suffoletto et al. 2012; Trinks et al. 2010; Vaca et al. 2011) only provided the brief intervention portion of the SBI to patients who screened positive for risky drinking, typically defined as AUDIT-C scores of 4 or higher for men and 3 or higher for women, or AUDIT scores of 8 or higher. The other five studies (Bendtsen et al. 2011; Butler et al. 2003; Karlsson and Bendtsen 2005; Murphy et al. 2013; Johnson et al. 2013) provided a brief intervention regardless of alcohol use level.

Brief Intervention Format

The brief interventions in 4 of the 12 studies (Bendtsen et al. 2011; Blow et al. 2006; Karlsson and Bendtsen 2005; Nilsen et al. 2009) were provided to patients using computer-generated printouts, whereas the rest were offline or Web-based computer programs. All but one computerized brief intervention consisted of a single session that lasted 10 to 20 minutes. The outlier examined both a single-dose Web-based brief intervention and a multi-dose version, where patients repeated the brief intervention at the 1- and 6-month followups (Kypri et al. 2008).

Brief Intervention Content

Nearly all of the brief interventions tested in these studies used at least some components of the FRAMES (Feedback, Responsibility, Advice, Menu of options, Empathy, Self-efficacy) model of brief intervention (Hester and Miller 1995). All the brief interventions in these studies provided feedback about the patient's risk level, drinking pattern relative to recommended limits, advice and information to enhance motivation to avoid use, and suggestions for behavior change strategies, if applicable. Capitalizing on a key feature of computerization, most of the brief interventions automatically tailored feedback and information to patients' screening results and other characteristics. That said, one of the randomized studies specifically examined the effect of tailored messages, compared with generic messages, either with or without clinician brief advice and found no significant effect of tailoring on alcohol consumption or related consequences after 12 months (Blow et al. 2006). Instead, patients who received brief advice from clinicians showed greater reductions in drinking than those who only received feedback from the computer SBI. Only one other study (Butler et al. 2003) included a printed report for the clinician with screening results and suggested brief intervention options. All other studies used technology-based self-guided brief intervention, with no explicit clinician involvement.

Findings

Among the seven experimental or quasi-experimental trials (Blow et al. 2006; Butler et al. 2003; Cucciare et al. 2013; Kypri et al. 2008; Neumann et al. 2006; Suffoletto et al. 2012; Trinks et al. 2010), findings were mixed, with several reporting differences between the intervention and comparison conditions in follow-up outcomes and others not. Overall, the 12 studies suggested that using technology-based SBIs in medical settings is feasible and acceptable to patients but were not able to clarify whether they are effective.

Primary Care

One controlled trial in a primary care setting (Kypri et al. 2008) found significant reductions in alcohol consumption scores and alcohol-related problems at both the 6- and 12-month followups among university health service patients in New Zealand who screened positive for alcohol problems and received a Web-based brief intervention, compared with patients who received a brochure. Two other trials (Butler et al. 2003; Cucciare et al. 2013) found reductions in alcohol consumption and related consequences out to 6 months, but the reductions were similar for both the standard care control and the computerized SBI groups. A fourth nonexperimental implementation study (Bendtsen et al. 2011) found that patients given access to a computerized SBI kiosk in a primary care clinic showed declines in heavy episodic drinking frequency at a 3-month followup. Patients referred to the SBI by a clinician, as opposed to those who self-initiated SBI use, showed a decline in weekly alcohol consumption. Without a control group, it is impossible to determine how much the decline is attributable to the SBI or some other confounder. That said, this study is unique in its examination of a computerized SBI system that routinely was offered at a primary care clinic, independent of a research study, showing that patients and clinicians are willing to use the system.

EDs

Only two of the ED studies used a nonintervention control group. One study (Neumann et al. 2006), a large German trial of 1,139 sub-critically injured ED patients with at-risk drinking, found significantly reduced prevalence of at-risk drinking and alcohol consumption at both the 6- and 12-month followups for patients receiving computerized

SBIs compared with those receiving standard care alone. Another, much smaller study (Suffoletto et al. 2012) conducted in three Pennsylvania EDs sent weekly text messages (TMs) to young-adult risky drinkers discharged from the EDs. The intervention group received TMs asking them to evaluate their drinking and providing them with information about setting alcohol consumption goals. Another group received TMs asking them to assess their drinking. A third group simply received TM notifications about the study's 3-month followup. Participants in the goal-setting intervention significantly reduced hazardous drinking behavior, compared with participants in the control groups (Suffoletto et al. 2012). However, this study found the greatest change among those with the highest baseline drinking levels, suggesting potential regression to the mean, which is a statistical phenomenon where more extreme values in data tend to move spontaneously towards the mean over time as a result of a certain amount of natural variation (Barnett et al. 2005). The other two ED studies did not use nonintervention control groups. Instead, they compared different active interventions. Both found that all the interventions tested reduced weekly alcohol consumption and HED frequency (Blow et al. 2006; Trinks et al. 2010), as well as alcohol-related consequences (Blow et al. 2006). All ED studies excluded patients that were intoxicated, had a high blood alcohol concentration at time of recruitment, were suicidal, or were otherwise being referred to psychiatry, which may have excluded patients with the most severe alcohol problems.

SBIs for Pregnant Women

Previous studies have shown the benefits of SBIs for addressing alcohol and drug use in pregnant women (Chang 2002; Ondersma et al. 2011). However, only one published randomized-controlled trial (Tzilos et al. 2011) has examined a computerized SBI for alcohol use during pregnancy. This early-stage randomized controlled trial in an urban prenatal care clinic included a convenience sample of 50 pregnant women that either screened positive on the T-ACE alcohol screening tool (Elliot and Hickam 1990; Sokol et al. 1989) or had drinking patterns before pregnancy that exceeded NIAAA drinking limits for women (NIAAA 2010). Participants randomly completed either the computerized SBI or an unrelated questionnaire. Those receiving the intervention gave it high marks for ease of use, likability, and respectfulness. Both intervention and control groups showed significant and equivalent reductions in drinking at the 1-month followup, although babies born to women in the intervention group had higher newborn birth weights.

More recently, Pollick and colleagues (2013) found high acceptability of, and user satisfaction with, a computerized brief intervention for alcohol use in pregnancy (C-BIAP) in a qualitative pilot study among 18 pregnant African-American women. Given the paucity of studies in this population, and that alcohol use in pregnant and parenting women additionally can cause secondary lifelong harm to the fetus or infant, more studies are critically needed to elucidate the utility of computerized strategies to enhance the efficient and effective implementation of alcohol SBIs in prenatal and antenatal clinics.

Targeting Adolescents

Numerous studies suggest that computerized screening of adolescent patients for alcohol use problems is acceptable, feasible, and effective in medical settings (Chisolm et al. 2008; Harris et al. 2012; Olson et al. 2009; Ozer et al. 2005; Stevens et al. 2008). Using computerized alcohol screening can increase adolescent satisfaction with the medical encounter (Gadomski et al. 2014; Harris et al. 2012) and efficiently boost physician recognition of substance use issues and patient–physician dialogue around substance-use topics (Harris et al. 2012; Olson et al. 2009; Stevens et al. 2008). These findings may help to bolster the case for increased adolescent screening for alcohol in medical settings, where screening rates remain suboptimal (Hingson et al. 2013).

Few studies have tested integrated computerized alcohol SBIs in adolescents. In fact, only four trials, yielding eight published papers (Cunningham et al. 2009, 2012; Gregor et al. 2003; Harris et al. 2012; Louis-Jacques et al. 2014; Maio et al. 2005; Walton et al. 2010, 2014), support computerized alcohol SBIs as feasible, acceptable, and, in some cases, effective for reducing drinking or alcohol-related problems among adolescents seen in medical settings.

Three of the four studies (Cunningham et al. 2012; Maio et al. 2005; Walton et al. 2014) were randomized controlled trials conducted among adolescent ED patients in the United States. These studies compared adolescents receiving standard care with adolescents receiving an integrated computerized SBI that screened patients and then delivered an approximately 30-minute single-session, highly interactive, tailored brief intervention that reflected principles of motivational interviewing (MI) and the social cognitive theory of behavior change (Bandura 1977). One trial (Maio et al. 2005) implemented a universal brief intervention aimed at both preventing and reducing use in adolescents with minor injuries. The other two only provided the brief intervention for adolescents who reported drinking in the past 12 months (Cunningham et al. 2012) or that screened positive for risky drinking on the AUDIT-C (Walton et al. 2014). The latter two trials additionally compared a single-session, computer-delivered brief intervention with a therapist-delivered version that was similar in content (Cunningham et al. 2012; Walton et al. 2014).

Overall, these ED-based studies found no significant differences in alcohol consumption outcomes between the intervention and standard-care control groups during followup, but some did find that the computer-based SBIs

influence other alcohol-related behaviors in certain populations:

- Maio and colleagues (2005) found in post hoc subgroup analysis a significant intervention effect on frequency of alcohol misuse and HED behaviors among adolescents admitting to having driven while impaired before entering the study. It may be that computerized brief interventions based on motivational enhancement approaches, like their face-to-face counterparts, tend to be more effective for individuals that have at least a certain level of substance use, or experience of negative consequences (Blow et al. 2009; Palfai et al. 2011; Spirito et al. 2004). Alternatively, those with greater use may be more subject to regression to the mean (Finney 2008).

- At a 6-month followup, Cunningham and colleagues (2009, 2012) found that their computerized and therapist-delivered brief interventions, which addressed peer violence and alcohol use (Walton et al. 2010) were associated with greater reductions in alcohol-related consequences, such as missing school because of alcohol use, compared with patients receiving the standard-care control. By the 12-month followup, patients receiving the therapist-delivered brief intervention maintained reductions in peer violence, but neither intervention continued to influence alcohol-related outcomes. The authors postulate that it may be difficult to address effectively more than one risk area with a brief intervention.

- Walton and colleagues (2014) examined the intermediate effects of a single-session, computerized or therapist-delivered brief intervention on psychological constructs hypothesized to be key moderators of behavior change. They were looking for the "active ingredients" that bring about change in adolescent risky drinkers. They found that, among 836 urban adolescent ED patients with risky drinking, those receiving either brief intervention significantly increased their perception that it was important to stop drinking, compared with adolescents receiving standard care. In addition, those receiving the therapist-delivered intervention increased their readiness to stop drinking. The analysis teased out two brief intervention components that had the strongest effect on these psychological outcomes, regardless of delivery mode: a review of personal strengths and suggested tools patients could use to reduce or stop drinking. Within the computer-delivered brief intervention, the components that most influenced outcomes were those that helped patients identify more benefits of behavior change, imagine sports activities that could be alternatives to alcohol use, and choose a goal to reduce or stop drinking. In contrast, the component of the therapist-delivered brief intervention that provided normative statistics/personalized feedback about current level of use was associated with negative effects on these cognitive outcomes. This study is ongoing and has yet to determine how these intermediate changes and brief intervention components connect to actual alcohol use and related consequences. However, it represents an important direction for future research into computerized SBI systems, such as the determination of the most effective ingredients, thus promoting the development of the most efficient and effective interventions possible.

The one adolescent trial of a computer-facilitated SBI conducted in a primary care setting involved several primary care clinics in the United States and the Czech Republic (Harris et al. 2012). The study utilized a before-and-after comparison design. Each clinic enrolled participants while providing standard care; then the clinic enrolled a comparison group of participants after implementing a computer-facilitated SBI system. The system consisted of three components:

- A pre-visit computerized screening using the CRAFFT behavioral health screening tool designed for children under age 21 (Knight et al. 2002);

- Immediate computer-delivered feedback to patients about their risk level, followed by several interactive pages of science-based and true-life information about substance-related health-risks and other harms; and

- Brief advice from a clinician during the primary care visit based on a printed provider report that suggested discussion points about substance use and related driving/riding risks tailored to each patient according to the screening results.

This multisite study found that U.S. adolescents, but not Czechs, had significantly reduced their alcohol use at the 3- and 6-month followups, although reductions at 12 months were less robust. In addition, the computer-facilitated SBI reduced both drinking initiation and cessation in the U.S. sample (Harris et al. 2012), and the short-term cessation effect actually was largest among drinking youth with friends who drink or approve of drinking (Louis-Jacques et al. 2014). This study also found a significant intervention effect in both countries at the 3-month followup on prevalence of driving after drinking or riding with a driver who had been drinking (Harris et al. 2011).

Because the computer system used in this study was designed to be integrated into a face-to-face primary care visit, these findings cannot disentangle the relative effects of the computerized versus the face-to-face components of the brief intervention. To this end, studies in adolescents are needed that use a factorial design (such as the study by Blow et al. 2006) to test the relative efficacy of clinician advice versus the computerized component.

With only four trials (Cunningham et al. 2009, 2012; Gregor et al. 2003; Harris et al. 2012; Louis-Jacques et al. 2014; Maio et al. 2005; Walton et al. 2010, 2014), the evidence currently is insufficient to recommend computerized

alcohol SBIs among adolescents in either EDs or primary care settings. More high-quality studies with randomized controlled designs and large sample sizes are needed, particularly in the primary care setting, which represents a key touch point with the health care system for adolescents where alcohol use can be detected early and where brief interventions are most likely to be effective. Alcohol and drug dependence are chronic, relapsing disorders with high treatment costs that most often begin during childhood. Given the relatively low risks and costs, and potential for benefit, of computerized prevention and early intervention, clinicians may wish to implement them as they become available.

Discussion and Future Directions

Research on technology-facilitated SBIs in medical settings is in its infancy. As such, there remain many questions and methodological issues that researchers should address when evaluating these interventions.

Special Populations

Although there is some evidence that the effectiveness of alcohol SBIs may be greater for people who have already experienced problems or negative consequences of drinking, it is unclear whether such programs are useful for patients with alcohol dependence (Saitz 2010). In addition, more studies should be conducted among pregnant women and adolescents, as well as in diverse racial and ethnic groups. Finally, studies should evaluate the effectiveness of Web-based alcohol SBI in high-risk, underserved, and remote populations, such as military personnel, American Indians, and Eskimo/Inuit, as such systems are particularly suited to access such hard-to-reach groups.

Screening Validity

Evidence to date suggests that responses to computerized screening are reliable and comparable to other screening modes (McNeely et al. 2014; Thomas and McCambridge 2008; Williams et al. 2000). However, other studies suggest differences between the two modalities that researchers may want to consider as they design their programs. For example, some studies find that people are more likely to report more sensitive or stigmatized behaviors, such as illicit drug use or higher levels of alcohol consumption, on computer self-administered questionnaires compared with face-to-face interview (e.g., Beck et al. 2014; Butler et al. 2009; Perlis et al. 2004) or even self-administered paper-and-pencil questionnaires (Wright et al. 1998). Additionally, adolescents seem to be particularly sensitive to mode and context effects when reporting sensitive behaviors (Gfroerer et al. 1997; Turner et al. 1998; Wright et al. 1998). In fact, a study of adolescent primary care patients found that their reactions to computerized screening was highly associated with their level of trust in the data being kept secure and private and used only for health care (Chisolm et al. 2008). Other studies suggest that factors such as language (Butler et al. 2003) and gender (Neumann et al. 2004) also may affect computerized screening performance.

Intervention Intensity

There is little evidence to date that the length of the intervention influences its effectiveness. No study in this review directly compared the effects of low-intensity to longer interventions, but there seemed to be no consistent pattern across trials indicating greater efficacy of longer interventions over shorter. A recent meta-analysis (Carey et al. 2012) of a computerized brief intervention targeting college students found that the effectiveness of the intervention was not affected by duration.

As for single-session versus multi-session interventions, the primary care study by Kypri and colleagues (2008) was the only trial reviewed here to compare the two directly. It found no increased benefit of additional brief intervention doses given at 1 and 6 months. This finding corroborates the conclusions of other reviews (Rooke et al. 2010; Donoghue et al. 2014; Kaner et al. 2007) that found no significant effect of the number of treatment sessions on the average effect size of computer-delivered and face-to-face SBIs (Kaner et al. 2007). A more recent 2012 review of face-to-face SBI studies did find larger effect sizes for brief (less than 15 minutes each) multi-contact interventions, compared with very brief (up to 5 minutes) or brief (5 to 15 minutes) single-contact interventions (Jonas et al. 2012). Compared with face-to-face delivery, technology-based delivery modes, including via the Internet or cell phones, offer the advantage of relative ease and low cost of delivering multiple doses. Therefore, further exploration of the question of optimal number of doses is clearly warranted.

Face-to-Face vs. Computerized Delivery

Another important question is whether self-guided computerized SBIs are as effective as face-to-face SBIs. Only four of the reviewed trials compared the two modalities. Two trials (Cunningham et al. 2012; Walton et al. 2014) directly compared a 35-minute therapist-delivered SBI and a self-guided computerized SBI provided to adolescent ED patients. Both modalities showed similar reductions in alcohol-related consequences and positive changes in psychological precursors to behavior change compared with a standard-care control (Cunningham et al. 2012; Walton et al. 2014). Other studies and reviews comparing face-to-face and technology-facilitated SBIs outside medical settings find an edge for face-to-face (Carey et al. 2012; Donoghue et al. 2014). It may be that combining face-to-face and technology-based SBI will be the most effective. Such a combination is easily accomplished in a medical setting where patients could complete a computerized portion of the alcohol SBI before a face-to-face encounter. This would

screen and "prime" the patient to discuss the topic when meeting with the clinician and could increase clinician fidelity of brief intervention implementation by using "prompts" to guide the clinician. Although computers have certain logistical advantages, they cannot convey empathy, regard, and complex reflections, which represent some of the most important ingredients of brief motivational interventions (Miller and Rollnick 2012). Also, patients may put less attention, thought, and effort into completing a computerized brief intervention compared with a face-to-face intervention (Walters and Neighbors 2011). Future research will benefit from examining a combination of face-to-face and computerized SBI delivery, as it may help to achieve larger and more enduring effects than self-guided computerized SBIs alone (White et al. 2010).

Outcome Measures

In terms of what intervention studies measure, more need to consider alcohol-related outcomes other than consumption, including negative consequences and problems related to alcohol use such as school problems for adolescents, driving while impaired, traffic violations, and crashes and injuries. Among the studies reviewed here, not all examined these outcomes, yet, in the face-to-face alcohol SBI literature, intervention effects on alcohol-related consequences or risks often have been larger than on alcohol consumption (Newton et al. 2013; Wachtel and Staniford 2010; Yuma-Guerrero et al. 2012). Therefore, failure to measure such outcomes, which have great public health import, may be a missed opportunity to identify some key intervention benefits.

Mediators and Moderators

There is a dearth of studies on mediators and moderators of the effects of computerized SBI in any setting and, in particular, within the small subset of studies examining these interventions within medical settings. Only one study (Walton et al. 2014) reviewed here attempted to elucidate the potential mechanisms and "active ingredients" underlying the effects of the computerized SBIs delivered to adolescents in an ED. Within the broader literature, the meta-analysis by Carey and colleagues (2012) found reduced computerized SBI effectiveness when the intervention included a decisional-balance or values-clarification exercise, identified high-risk situations, or included moderation strategies.

A few studies have found that certain patient characteristics, such as baseline stage-of-change or severity of alcohol involvement also may moderate the effectiveness of computerized SBIs. Among the studies reviewed here, Neumann and colleagues (2006) found greater intervention impact among patients who were contemplating changes in their drinking habits when they entered the study, and Vaca and colleagues (2011) found their SBIs to be more effective among patients reporting recent drinking and driving. The finding that an intervention may be more effective among individuals with more risky drinking behavior matches findings from a recent review of face-to-face alcohol/drug SBIs for adolescents seen in medical settings (Mitchell et al. 2013) and a study of a computerized SBI for college students (Carey et al. 2012).

Assessment Reactivity

One of the major methodological issues facing SBI research in general is the degree to which simply being part of a study that assesses alcohol use may affect study results (Elbourne 2014; Finney 2008; McCambridge and Kypri 2011; McCambridge et al. 2014). Indeed, studies find that simply evaluating people's drinking—as would happen in the screening part of an SBI—has a robust effect on drinking behavior over time (Dearing et al. 2013; Epstein et al. 2005). This "assessment reactivity" may underlie the similar changes in both the intervention and control groups seen among many of the studies reviewed here. To reduce the potential for assessment reactivity, future randomized controlled studies could include an additional minimal-assessment control arm that only measures outcomes at the final followup.

Summary

There is robust evidence that in-person alcohol SBIs are effective when delivered to patients by staff in medical settings (Moyer 2013; Newton et al. 2013; O'Donnell et al. 2014). However, the implementation rates of these face-to-face SBIs remain suboptimal (Hingson et al. 2013; McKnight-Eily et al. 2014). Technology-based solutions, such as computerized SBI systems, may help to address this problem, but evidence for their effectiveness is less clear. This review found a burgeoning, but still small, research field with only 23 published papers representing 18 different trials evaluating the use of technology-based alcohol SBIs among adults, pregnant women, and adolescents in medical settings. The studies all found that technology-based alcohol SBIs are feasible for delivery in the medical setting and acceptable among patients, but most had methodological limitations. Only 13 of the 18 were controlled trials, and the majority were conducted in adult populations, with just four conducted among adolescents and only two among pregnant women. More than half of the studies took place in EDs, which offers a prime "teachable" moment, particularly for injured patients. However, more studies are needed in primary care and other ambulatory medical care settings, where patients may have periodic and ongoing contact with their health care providers. Such longitudinal patient–clinician relationships would allow for continued support and followup regarding recommended behavior changes. New studies also will benefit from bigger sample sizes to increase the power of their findings, more comprehensive participant recruitment, higher retention rates, and longer follow-up periods.

Finally, a promising new direction for the field would be to evaluate the potential of mobile technologies that can be used in medical settings. Suffoletto and colleagues (2012) demonstrated that mobile devices offer the potential to act as "clinician-extenders," allowing clinicians to support and interact with patients after a visit and potentially boost the effect of a computerized brief intervention delivered in the medical setting. A review by Heron and Smyth (2010) of studies examining the use of ecological momentary interventions delivered through mobile technology, such as cell phones and tablet computers, found them to be feasible and acceptable and show efficacy for addressing a variety of psychosocial and other health behaviors, including alcohol use. Research also may begin to emerge on the use of smartphone apps and social-networking sites like Facebook for underage drinking prevention and intervention.

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Electronic Feedback in College Student Drinking Prevention and Intervention

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Alcohol consumption is prevalent among college students and can be associated with serious negative consequences. Several efficacious programs using one-on-one brief intervention techniques have been developed to target high-risk drinking by individual students, such as the Brief Alcohol Screening and Intervention for College Students (BASICS) (Dimeff et al. 1999). To reach a larger population (e.g., the incoming freshman class), researchers have adapted these interventions so that students can access them via the Internet or in some other electronic format. The purpose of this review is to discuss specific alcohol intervention programs that were (1) designed to be delivered remotely (e.g., via the Web or on an electronic device) without interaction with a provider and (2) were tested among college students using a randomized controlled trial design. Specific studies were drawn from earlier reviews as well as a comprehensive literature search. Although many programs have limited research support, and some findings are mixed, components that were directly translated from in-person BASICS to remote-delivery mediums (i.e., personalized feedback interventions [PFIs], personalized normative feedback [PNF] interventions), and broader programs that incorporate PFI/PNF, show promise in reducing alcohol use and/or negative consequences. However, more research is needed and suggestions for how the field can move these interventions forward are discussed.

Key words: Alcohol use, abuse, and dependence; alcohol consumption; alcohol use associated effects and consequences; problematic alcohol use; risky drinking; intervention; prevention; college students; undergraduate student; college freshman year; technology; electronic health technology; Internet; World Wide Web; brief intervention; personalized feedback intervention (PFI); personalized normative feedback (PNF); randomized controlled trial; literature search

Compared with young adults not in college, college students exhibit higher rates of both regular alcohol consumption (67.7 percent vs. 53.9 percent) and heavy episodic consumption[1] (37.4 percent vs. 29.5 percent) (Johnston et al. 2013) and are therefore at elevated risk for the myriad, and often costly, consequences related to alcohol misuse (Hingson et al. 2009; Perkins 2002). A variety of approaches to curtail high-risk drinking have been implemented over the years, including interventions aimed at the drinking behavior of individual students.

There has been a notable progression in individual-focused prevention efforts from purely educational programs, which typically emphasized potential life-altering consequences (e.g., grave injury, death) toward those that use alcohol-focused education to support alcohol skill use (e.g., refusal skills, protective behavioral strategies), placing primary focus on enhancing motivation and self-efficacy to act responsibly with respect to alcohol. The prototype for this latter approach is the Brief Alcohol Screening and Intervention for College Students (BASICS) (Dimeff et al. 1999), a brief motivational intervention (BMI) led by a facilitator trained in motivational interviewing (MI) (Miller and Rollnick 2013). In BASICS, each student participates in a one-on-one session to discuss personalized feedback related to alcohol use (i.e., the facilitator guides a discussion of the student's alcohol use and consequences, their normative perceptions of other students' drinking, their expectations about alcohol's effects, etc., which were assessed prior to the session and are summarized for the student on a printed feedback sheet), coupled with education and skills training. Although the shift toward programs such as BASICS predates the 2002 report from the National Institute on Alcohol Abuse and Alcoholism's (NIAAA's) Task Force on College Drinking (NIAAA 2002), the compelling evidence for skills-based, motivational enhancement approaches highlighted in the Task Force report spurred the field to generate new interventions based on components of

[1] Wechsler and colleagues (1995) define an occasion of heavy episodic consumption as five or more drinks for men and four or more drinks for women in a row. This definition was used most frequently across the studies reviewed here; although, the statistics from the Monitoring the Future study (Johnston et al. 2013) do not differentiate by gender, and only indicate the percentage of young adults and college students (both men and women) who consumed five or more drinks on a single occasion.

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efficacious in-person programs, such as BASICS, that could reach a larger segment of the student body.

The first step toward bringing a BASICS-style BMI to a larger population was to test the effects of written personalized feedback delivered on its own, without a facilitator trained in MI (i.e., participants would receive feedback via U.S. mail) (e.g., Agostinelli et al. 1995; Larimer et al., 2007). With this approach, the written feedback was expanded to incorporate narrative explanations and supplemental material to replicate the information previously provided verbally by a trained facilitator. The approach has since been adapted for delivery via the Web, which has lower environmental and financial costs than the U.S. mail (i.e., no paper/envelopes, postage) and has become yet more attractive as technology (e.g., smartphones, tablets) evolved into the primary means by which young adults engage with the world and receive information.

Electronic alcohol feedback prevention programs (i.e., those designed to be delivered remotely, using some form of technology, typically the Web) include personalized feedback interventions (PFIs) that deliver most or all of the components included in the original BASICS feedback as well as personalized normative feedback (PNF) interventions that only deliver the normative re-education component of the BASICS feedback (i.e., educating participants about drinking norms and commonly held misperceptions about alcohol use among their peers). These programs are now common and include commercial and noncommercial branded interventions and interventions that are not branded, per se; the specifics of which may be unique to a single or small series of outcome studies. Some of these programs originally were designed to be focused on education but have since been modified (e.g., increasing focus on personalized feedback). Additional programs include some level of personalized feedback but do not rise to the level of what would constitute a PFI or PNF intervention. Given the range of available programs, this article will review the extant outcome literature for alcohol-specific, individual-focused, intervention programs designed for electronic delivery that include some level of personalized feedback, most of which may be considered a PFI or PNF intervention, that have been the subject of peer-reviewed, randomized controlled trials (RCTs) among college student populations.

The articles reviewed below were drawn from prior comprehensive qualitative reviews conducted by Cronce and colleagues (Cronce and Larimer 2011; Larimer and Cronce 2002, 2007), covering the span from 1984 to 2010, supplemented by a literature search of PsycInfo and Medline using comparable search terms with the stipulation that interventions be electronic (Web-based or delivered via an electronic device) and designed for administration outside of a controlled setting (although not always tested remotely). This strategy identified 29 new studies that utilized an RCT design and tested an electronic intervention for alcohol use within a sample of college students, reporting effects on one or more behavioral alcohol outcomes. These 29 studies are summarized in the table. Nearly all interventions were designed for delivery via the Web on a computer; therefore, unless otherwise stated, the reader should assume this is the method of intervention delivery. Effects on nonbehavioral outcomes, effects on use or consequences related to other drugs, comprehensive information on moderators and mediators of treatment effect, and full discussion of individual study limitations were considered beyond the scope of this review. Readers are referred to the original articles for more detailed information about a given study.

Branded Programs That Include PFI-Style Information

AlcoholEdu for College

AlcoholEdu for College incorporates personalized feedback regarding normative misperceptions and alcohol consumption, supplemented by education and skills training. Three studies reviewed by Cronce and Larimer (2011) (i.e., Croom et al. 2009; Hustad et al. 2010; Lovecchio et al. 2010) evaluated various versions of AlcoholEdu for College. Two additional publications reported on the effects of the intervention on alcohol use and consequences from a single multicampus study (Paschall et al. 2011*a,b*). Studies generally show reduced alcohol consumption and/or consequences (Hustad et al. 2010; Lovecchio et al. 2010; Paschall et al. 2011*a,b*) or a protective effect against increased alcohol use relative to assessment only (Lovecchio et al. 2010), at least in the short term (approximately 1 month). The largest study to date (Paschall et al. 2011*a,b*) utilized an intent-to-treat, campus-wide implementation strategy and randomly assigned 30 campuses to either an intervention or control group. Treatment effects were observed in the fall semester (following implementation in summer and early fall) that were no longer evident by spring. Although stronger effects were found among campuses with higher rates of intervention participation, the lack of endurance of effects requires further research, perhaps using a longitudinal versus panel design. Studies are not universally positive, however. Croom and colleagues (2009) found that AlcoholEdu participants reported less participation in drinking games but no changes in consumption or consequences.

AlcoholEdu for Sanctions

Whereas AlcoholEdu for College is advertised as a population-level prevention program for use with freshmen or the entire student body, AlcoholEdu for Sanctions specifically targets students who have been mandated to receive an alcohol intervention following a campus alcohol policy violation. The overall content of the program is similar to the original but emphasizes the prevention of future consequences and policy violations. One study reviewed by Cronce and colleagues (2011) (Carey et al. 2011) compared

Table Summary of Methodologies and Outcomes for Previously Unreviewed Studies Included in the Current Review

Authors Year	Group Studied	Intervention Condition	Behavioral Alcohol Assessment/Outcome Measures	Follow-up Assessment	Conclusions/Results For Electronic Intervention Condition(s)
Alfonso et al. 2013	Undergraduate students who were mandated to an alcohol intervention for violating university alcohol policies ($N = 173$).	Brief Alcohol Screening and Intervention for College Students (BASICS) (individual in-person brief motivational intervention [BMI]); CHOICES (group in-person); e-CheckUpToGo (individual personalized feedback intervention [PFI]).	Alcohol Timeline Followback; BAC; Rutgers Alcohol Problem Index.	3 months	e-CheckUpToGo was associated with significant within-person reductions in alcohol-related harms, which were similar to those observed for the BASICS condition. No reductions were evident on indices of alcohol use for those receiving e-CheckUpToGo.
Bewick et al. 2010	University students (ages 18–67; 95 percent undergraduates) reporting consumption of alcohol at least once every 6 months ($N = 1,112$); 57 percent of the sample scored 8 or higher on the AUDIT.	Immediate (weeks 1 through 7) vs. delayed (weeks 8 through 15) access to the Unitcheck electronic intervention vs. assessment only control.	Retrospective weekly drinking diary, AUDIT.	4 follow-up assessments across the 24-week study	Significant reductions in drinks per drinking occasion were evident in the delayed intervention and assessment-only conditions, with no effect in the immediate intervention condition. Those assigned to either intervention condition that completed more than two of the five total assessments showed greater reductions in drinking than those in the control condition.
Bingham et al. 2010	Freshmen college students who were living in dormitory housing ($N = 1,137$); sample divided into non-, low-, and high-risk drinkers for analyses. High-risk defined as consumption of an average of more than 14 (male) or 7 (female) drinks per week or 5 (male) or 4 (female) drinks in a row at least 2 times during the past 3 months. Nondrinkers reported no alcohol consumption in the 6 months preceding baseline.	Four sessions of online *Michigan Prevention and Alcohol Safety for Students* (M-PASS) program vs. assessment-only control.	Daily drinking questionnaire, 28-day Timeline Followback (TLFB), Young Adult Alcohol Problems Screening Test (YAAPST).	Posttest at end of intervention (9 weeks)	Among those assigned to M-PASS relative to control: high-risk male drinkers reported fewer episodes of heavy drinking; high-risk female drinkers reported lower total drinks on TLFB; low-risk female drinkers report fewer drinks per drinking day.
Bingham et al. 2011	3-month followup of sample reported in Bingham et al. (2010).	See Bingham et al. (2010).	See Bingham et al. (2010)	3 months after intervention end	Among those assigned to M-PASS relative to control: male and female high-risk drinkers reported fewer episodes of heavy episodic consumption and high-risk female drinkers also reported fewer alcohol-related consequences. Further, M-PASS showed protective effect among nondrinking women in terms of total drinks consumed.
Bryant et al. 2013	Students enrolled in first-year psychology courses ($N = 191$).	E-mailed PFI vs. e-mailed educational information about the risks of alcohol consumption.	AUDIT, Daily Drinking Questionnaire, Rutgers Alcohol Problem Index.	6 weeks	Relative to alcohol education, e-mailed PFI was associated with fewer drinks per week and fewer days drunk in the past 30 days.

Table Summary of Methodologies and Outcomes for Previously Unreviewed Studies Included in the Current Review *(continued)*

Authors Year	Group Studied	Intervention Condition	Behavioral Alcohol Assessment/Outcome Measures	Follow-up Assessment	Conclusions/Results For Electronic Intervention Condition(s)
Carey et al. 2013	College students who were mandated to an alcohol intervention for first-time campus alcohol policy violations ($N = 288$).	BMI or Alcohol 101+ program: self-chosen ($N = 147$) vs. randomly assigned ($N = 141$).	Daily Drinking Questionnaire; AUDIT; Brief Young Adult Alcohol Consequences Questionnaire.	1 and 2 months	Reductions in alcohol use and consequences were evident among those receiving the BMI relative to Alcohol 101+ at the 2-month followup. The absolute efficacy of Alcohol 101+ cannot be determined due to the absence of an assessment control condition; however, those who were randomly assigned to Alcohol 101+ showed greater reductions in drinks per drinking day and drinks per week relative to those who chose Alcohol 101+.
Donovan et al. 2012	High-school seniors and their parents ($N = 279$ parent–teen pairs, of which $N = 150$ who reported drinking and were included in analyses regarding alcohol use).	MyStudentBody-Parent (MSB-P) online intervention vs. attention control (e-mailed alcohol education newsletters).	Single question assessing number of heavy-drinking episodes in the past 30 days using 5/4 gender-specific criteria within 2-hour time frame on a given occasion.	1 week postintervention, 3 and 6 months	No treatment effect on proportion of teens reporting episodes of heavy drinking.
Doumas et al. 2010	First-year NCAA Division 1 intercollegiate athletes ($N = 106$); sample divided into low- and high-risk drinkers for analyses. High-risk defined as reporting one or more occasions of heavy drinking in the past 3 months using the 5/4 gender-specific criteria.	e-CheckUpToGo vs. Web-based alcohol education program.	Daily Drinking Questionnaire.	3 months	Relative to control, high-risk drinkers in the e-CheckUpToGo condition significantly reduced their weekly drinking, peak drinking quantity and frequency of drinking to intoxication. There were no differences among low-risk drinkers.
Doumas et al. 2011*a*	Freshmen college students randomly assigned as intact orientation groups ($N = 82$); sample divided into low- and high-risk drinkers for analyses. High-risk defined as reporting one or more occasions of heavy drinking in the past 3 months using the 5/4 gender-specific criteria.	e-CheckUpToGo vs. assessment-only control.	Daily Drinking Questionnaire; Rutgers Alcohol Problem Index; individual items assessing peak alcohol consumption and frequency of drinking to intoxication.	3 months	Relative to control, high-risk drinkers in the e-CheckUpToGo condition significantly reduced their peak drinking quantity and frequency of drinking to intoxication. However, only seven participants were in the high-risk e-CheckUpToGo condition.
Doumas et al. 2011*b*	Students mandated to university counseling services for violating university alcohol policies ($N = 37$).	Online e-CheckUpToGo feedback only (PFI) vs. counselor-facilitated review of e-CheckUpToGo feedback (BMI).	Daily Drinking Questionnaire; Rutgers Alcohol Problem Index; individual items assessing peak alcohol consumption and frequency of drinking to intoxication.	30 days	Participants in both conditions showed significant within-person reductions in weekly and peak drinking quantity, frequency of drinking to intoxication, and alcohol-related consequences. No significant differences were found between the groups.

Table Summary of Methodologies and Outcomes for Previously Unreviewed Studies Included in the Current Review *(continued)*

Authors Year	Group Studied	Intervention Condition	Behavioral Alcohol Assessment/Outcome Measures	Follow-up Assessment	Conclusions/Results For Electronic Intervention Condition(s)
Doumas et al. 2011*c*	8-month followup of sample reported in Doumas et al. (2011*b*) ($N = 83$).	See Doumas et al. (2011*b*).	See Doumas et al. (2011*b*).	8 months	Relative to those in the e-CheckUp-ToGo PFI condition, participants in the BMI condition showed significant reductions in weekly drinking quantity and frequency of heavy episodic drinking. Participants in the PFI condition showed increases on these drinking indices.
Ekman et al. 2011	Sophomore students from a single Swedish university who consumed 180/120 (men/women) grams of alcohol or more per week in the past 3 months and/or consumed 60/48 (men/women) grams of alcohol or more on two or more occasions in the past month ($N = 158$).	Personalized normative feedback (PNF) with harm reduction tips compared with a minimal feedback control (comparing the student's drinking to national safe drinking guidelines).	Items assessing average weekly alcohol consumption, frequency of heavy episodic drinking and peak BAC; specific measures used were not indicated.	3 and 6 months	Significant within-person reductions in weekly consumption in the PNF group, and significant within-person reductions in number of heavy drinking episodes in both conditions at both followups. No significant between-group differences for alcohol-related outcomes at either time point.
Hagger et al. 2012	Undergraduate students from a single university in the United Kingdom ($N = 238$).	Web-based instructions: 2 (mental simulation of achieving goal of keeping drinking within safe limits vs. no mental simulation) × 2 (intention to implement reduction in drinking vs. no implementation intention) design.	Items assessing number of alcohol units consumed and number of episodes of heavy drinking in the past 4 weeks using criteria applicable in the United Kingdom; specific measures used were not indicated.	1 month	Receipt of the mental simulation instructions without the implementation intention instructions was associated with reductions in number of units consumed and heavy episodic drinking.
Hendershot et al. 2010	College students of northeast Asian descent ($N = 200$).	Web-based ALDH2 genotype-specific feedback (ALDH2*1/*1, ALDH2*1/*2, or ALDH2*2/*2) vs. attention control.	Daily Drinking Questionnaire.	30 days	Participants heterozygous for the ALDH 2*2 allele (i.e., ALDH2*1/*2) who received genetic-risk feedback personalized to their genotype showed reductions in quantity and frequency of drinking relative to control.
Hester et al. 2012	College students who reported one or more occasion of heavy episodic drinking in the past 2 weeks using the 5/4 gender-specific criteria with an associated blood alcohol content [BAC] of .08%. (Two trials: $N = 130$ and $N = 81$).	College Drinkers Check-up (CDCU). In experiment 1, CDCU vs. assessment-only control; in experiment 2: CDCU vs. a delayed-assessment control group.	AUDIT, Brief Drinker's Profile, 19 items from the CORE Institute's alcohol survey related to negative consequences.	Experiment 1: 1 and 12 months; Experiment 2: 1 month	Experiment 1: Adjusting for multiple comparisons, reductions in peak BAC on two heavier occasions in the past month were evident at 1-month followup among those assigned to CDCU, but the effect was absent at 12 months. Experiment 2: CDCU associated with significant reductions in drinks per week, typical peak BAC, and average number of drinks and BAC on two heavier occasions in the past month.

Table Summary of Methodologies and Outcomes for Previously Unreviewed Studies Included in the Current Review *(continued)*

Authors Year	Group Studied	Intervention Condition	Behavioral Alcohol Assessment/Outcome Measures	Follow-up Assessment	Conclusions/Results For Electronic Intervention Condition(s)
Kypri et al. 2008	Students at a New Zealand student health service scoring 8 or higher on the AUDIT (*N* = 429).	Single-dose PFI vs. two-dose PFI vs. education-only control.	AUDIT, additional items assessing frequency of drinking, typical quantity per occasion, total volume, frequency of heavy drinking episodes (120/80 g, men/women), consequences of heavy drinking; specific measures used were not indicated.	1, 6, and 12 months	Reductions in frequency of drinking, total consumption, and academic consequences at 6 months in both PFI conditions relative to control. Additional reductions in frequency of drinking, typical quantity, and frequency of heavy episodic consumption at 6 months in the multidose PFI condition. Reductions in total consumption and academic problems were still evident at 12 months in the single dose PFI condition. Reductions in academic problems were also still evident at 12 months in the multidose condition, and effects on nonacademic consequences emerged. Reductions in AUDIT scores (alcohol problems) were evident in both PFI groups at 12 months.
Kypri et al. 2009	Undergraduates at a single Australian university who scored 8 or higher on the AUDIT and who exceeded Australian gender-specific standards for one or more episodes of heavy episodic drinking in the past 4 weeks (*N* = 1,904 at 1-month followup; 1,578 at 6 months).	Two-dose PFI vs. assessment only control.	AUDIT, Alcohol Problems Scale (APS), Academic Role Expectation and Alcohol Scale (AREAS), additional items assessing frequency and quantity of drinking, and heavy-drinking episodes.	1 and 6 months	Relative to control, participants in the PFI condition reported significant reductions in frequency and quantity of drinking (drinks per occasion and total consumption) at 1-month followup; effects on frequency of drinking and total consumption were maintained at 6 months.
Kypri et al. 2014	Non-Maori students at seven New Zealand universities who scored 4 or higher on the AUDIT-C (*N* = 2,850).	PFI including screening for, and feedback regarding, alcohol dependence vs. assessment only.	AUDIT-C, AREAS, additional items assessing alcohol use; for intervention participants only: AUDIT, Leeds Dependence Questionnaire.	5 months	PFI with dependence screening and feedback resulted in fewer drinks per drinking occasion at followup; however, analyses accounting for attrition call this finding into question. No effects evident on five other indices of alcohol use.
LaBrie et al. 2013	Heavy-drinking Caucasian and Asian undergraduates at two West Coast universities (*N* = 1,663).	Web-based PFI vs. eight Web-based PNF conditions differing on level of specificity of student-normative referent groups: typical same-campus student or a same-campus student at one (either gender, race, or Greek affiliation), or a combination of two, or all three levels of specificity vs. non-alcohol normative feedback control.	Daily Drinking Questionnaire, Quantity/Frequency Index, Rutgers Alcohol Problem Index.	1, 3, 6, and 12 months	Both the PFI and PNF groups reported significant reductions in indices of alcohol use relative to control, with participation in any PNF group also associated with significant reductions in alcohol-related negative consequences. PFI and PNF were no different than one another across alcohol use and consequence outcomes. Comparison among PNF conditions supports the use of the "typical student" normative referent.

Table Summary of Methodologies and Outcomes for Previously Unreviewed Studies Included in the Current Review *(continued)*

Authors Year	Group Studied	Intervention Condition	Behavioral Alcohol Assessment/Outcome Measures	Follow-up Assessment	Conclusions/Results For Electronic Intervention Condition(s)
Lee et al. 2014	Students intending to go on a spring break (SB) trip with friends as well as to engage in heavy episodic drinking (using the 5/4 gender-specific criteria) on at least 1 day of SB ($N = 783$; $N = 507$ who actually went on a SB trip).	Standard BASICS vs. SB-focused BASICS vs. SB-focused BASICS with a friend vs. SB-focused PFI vs. SB-focused PFI with a friend vs. attention control.	Modified Daily Drinking Questionnaire to assess SB drinking intentions (baseline) and actual consumption (followup), 12 items modified from the Young Adult Alcohol Problems Screening Test and the Young Adult Alcohol Consequences Questionnaire to measure anticipated (baseline) and actual (followup) alcohol-related consequences.	1 week after SB	Neither of the PFI conditions (with or without a friend) resulted in reductions in alcohol use or consequences. Only in-person SB-focused BASICS without a friend reduced drinking versus attention control.
Lewis et al. 2014	College students who reported being sexually active within the past year, typically with a member of the opposite sex, and who also reported at least one occasion of heavy episodic drinking in the past month using the 5/4 gender-specific criteria ($N = 480$).	Alcohol-only PNF (PNF-A), alcohol-related risky sexual behavior (RSB) only PNF (PNF-RSB), combined alcohol and alcohol-related RSB PNF (PNF-C), or assessment-only control.	Daily Drinking Questionnaire, Quantity/Frequency Index, Brief Young Adult Alcohol Consequences Questionnaire, additional individual items assessing risky sexual behavior and normative perceptions of sexual behavior adapted from prior work by the first author.	3 and 6 months	Compared with control, PNF-C and PNF-A were associated with reductions in drinking quantity and frequency at 3 months with most effects maintained at 6 months. PNF-C and PNF-RSB were effective in reducing frequency of drinking prior to sex at 3- but not 6-month followup. None of the interventions reduced alcohol-related negative consequences.
Martens et al. 2010	Intercollegiate college athletes ($N = 263$) from three colleges in the Northwest, Midwest, and Northeast.	PFI targeted to college athletes vs. standard PFI targeted to college students in general vs. alcohol education control.	Daily Drinking Questionnaire, Brief Young Adult Alcohol Consequences Questionnaire.	1 and 6 months	Those receiving the targeted PFI who were currently in their athletic season ($N = 57$) or who were heavier drinkers at followup ($N = 61$) reported fewer drinks per week and lower peak BAC, respectively, at 1 month. At 6 months, the effect of the targeted PFI on peak BAC was evident across all participants in that condition, and the standard PFI also showed reductions in peak BAC among heavier drinkers $N = 57$).
Mason et al. 2014	Undergraduates enrolled in psychology courses at a single Southeastern university who scored 8 or higher on the AUDIT ($N = 18$).	Automated personalized text messaging (four to six messages for 4 days that required a brief response) vs. assessment-only control.	AUDIT, additional items assessing quantity and frequency of alcohol use; specific measures used not specified.	1 month	No effects on alcohol use or problems.
Moreira et al. 2012	Freshmen and sophomore college students from 22 universities in the United Kingdom ($N = 876$ at 6 months, 1,050 at 12 months).	E-mailed PNF vs. repeated assessment-only control vs. posttest-only (at 12-month followup) control.	AUDIT, individual items developed by the authors assessing alcohol quantity, frequency and alcohol-related consequences.	6 and 12 months	Compared with repeated-assessment-only control, participants in the PNF group reported less weekly drinking at 6 months (looking at the full sample and a high-risk subsample), but this effect was absent at 12 months. No other effects of the intervention on alcohol use or consequences were evident.

Table Summary of Methodologies and Outcomes for Previously Unreviewed Studies Included in the Current Review *(continued)*

Authors Year	Group Studied	Intervention Condition	Behavioral Alcohol Assessment/Outcome Measures	Follow-up Assessment	Conclusions/Results For Electronic Intervention Condition(s)
Murphy et al. 2010, study 2	College students reporting at least one occasion of heavy episodic drinking in the past month using the 5/4 gender-specific criteria ($N = 118$).	BASICS vs. e-CheckUpToGo vs. assessment only.	Daily Drinking Questionnaire, individual item assessing number of heavy drinking episodes in the past month.	1 month	Participants assigned to e-CheckUpToGo showed within-person reductions in weekly drinking quantity ($d = 0.42$) and frequency of heavy episodic drinking ($d = 0.39$). The e-CheckUpToGo condition was not significantly different than BASICS in terms of reductions in heavy episodic drinking; however, it was also no different than assessment only on this variable or weekly drinking.
Neighbors et al. 2010	Freshmen reporting at least one occasion of heavy episodic drinking in the past month using the 5/4 gender-specific criteria ($N = 818$).	One- vs. four-dose gender-specific PNF vs. one- vs. four-dose gender-neutral PNF vs. attention control.	Daily Drinking Questionnaire, Alcohol Consumption Index, Rutgers Alcohol Problem Index.	6, 12, 18, and 24 months	Biannually administered gender-specific PNF was associated with decreased weekly drinking for men and women, and with fewer-alcohol related consequences for women only. No effects were evident for either of the single-dose PNF conditions or the biannual (four-dose) gender-neutral PNF.
Neighbors et al. 2012	Students intending to engage in heavy episodic drinking (using the 5/4 gender-specific criteria) on their 21st birthday ($N = 599$).	Standard BASICS vs. 21st birthday–focused BASICS vs. 21st birthday–focused BASICS with friend vs. 21st birthday–focused PFI vs. 21st birthday–focused PFI with friend vs. an attention control.	Modified Daily Drinking Questionnaire to measure 21st birthday drinking intentions (baseline) and actual consumption (followup), modified Young Adult Alcohol Problems Screening Test to measure anticipated (baseline) and actual (followup) alcohol-related consequences.	1 week after 21st birthday	21st birthday–focused PFI (without friend) was associated with lower BACs on participants' 21st birthday compared with control, similar to standard BASICS, but had no effect on total consumption or consequences. 21st birthday–focused PFI with friend reduced alcohol-related consequences relative to control, similar to all three BASICS conditions but did not reduce consumption or BAC.
Palfai et al. 2011	Introductory psychology students reporting two or more occasions of heavy episodic drinking in the past month using the 5/4 gender-specific criteria or who had an AUDIT score of 8 or higher ($N = 119$).	PFI vs. attention control.	Daily Drinking Questionnaire, Young Adult Alcohol Problems Screening Test.	1 month	Those with high (vs. low) levels of alcohol-related consequences at baseline who were assigned to the PFI showed significantly greater reductions in weekly drinking quantity and number of heavy-drinking episodes relative to control participants.
Paschall et al. 2011*a*	Multicampus study ($N = 30$ campuses, 5,074 college freshmen).	AlcoholEdu for College vs. control.	Individual items assessing past-30-day alcohol use, average number of drinks per occasion, and heavy episodic consumption.	N/A (fall and spring assessments were cross-sectional, not longitudinal)	Relative to control campuses, students at colleges assigned to AlcoholEdu for College reported reductions in past 30-day alcohol use and frequency of heavy episodic consumption in the fall; however, these effects were absent at the subsequent spring assessment.

Table Summary of Methodologies and Outcomes for Previously Unreviewed Studies Included in the Current Review *(continued)*

Authors Year	Group Studied	Intervention Condition	Behavioral Alcohol Assessment/Outcome Measures	Follow-up Assessment	Conclusions/Results For Electronic Intervention Condition(s)
Paschall et al. 2011*b*	Additional findings from Paschall et al. (2011*a*).	See Paschall et al. (2011*a*).	Rutgers Alcohol Problem Index.	See Paschall et al. (2011*a*)	Relative to control campuses, students at colleges assigned to AlcoholEdu for College reported reductions in alcohol consequences in the fall; however, these effects were absent at the subsequent spring assessment.
Patrick et al. 2014	Undergraduates (ages 18–21) who planned to go on a SB trip with their friends ($N = 263$).	Combined SB alcohol use and SB alcohol-related RSB PNF vs. assessment-only control.	Individual items assessing anticipated and actual alcohol use, sexual behavior, and associated consequences.	1 week after SB	No significant differences between PNF and control on alcohol use, risky sexual behavior or related consequences.
Schuckit et al. 2012	Freshmen who have never met criteria for DSM–IV alcohol or drug dependence, who reported any drinking in the past 6 months and who reported a low or high subjective level of response (LR) to alcohol ($N = 64$).	Prevention videos tailored to a low LR to alcohol vs. non-tailored prevention videos.	Individual items assessing alcohol use and associated consequences (drawn from the Rutgers Alcohol Problem Index).	Immediate posttest and 4 weeks following end of the intervention	Although all participants showed significant decreases in typical and peak drinks per occasion, participants with a low LR who were assigned to the tailored group showed greater reductions than those assigned to the nontailored group. Additionally, in terms of typical drinks per occasion, those with high LR assigned to the nontailored group showed greater reductions than those in the tailored group.

AlcoholEdu for Sanctions with a waitlist control group and at the 1-month followup found reductions in alcohol use, relative to the control group, for men only. Within-person reductions in alcohol use were reported in women in the intervention group, but no differences were found between women in the intervention and control groups. Likewise, within-person reductions in alcohol consequences were evident for men and women, but these reductions did not differ relative to the control group. No additional studies were identified, indicating a need for more research to establish efficacy.

Check Your Drinking (CYD)

All iterations of CYD have included a brief online assessment followed by presentation of personalized feedback. Two studies reviewed by Cronce and Larimer (2011) (Doumas and Haustveit 2008; Doumas et al. 2009) evaluated the efficacy of the original beta version of CYD, showing reductions in both alcohol consumption among mandated students and high-risk-drinking intercollegiate athletes at the 1- and 3-month followup, respectively. Although the original beta version still is available, the program now is in its third iteration (version 3.0). Whereas studies have been conducted in the general adult population, to date, CYD 3.0 does not seem to have been specifically evaluated among college students. Therefore, research is needed to establish the efficacy of the most current iteration in college populations.

College Drinker's Check-up (CDCU)

CDCU is a Web-based adaptation for college students of the well-established in-person intervention known as the Drinker's Check-up, originally developed for heavy-drinking adults. Like its predecessor, the CDCU begins with a screening instrument and incorporates decisional balance exercises (i.e., assessing and considering pros and cons of drinking) along with personalized feedback. A single two-trial study (Hester et al. 2012) has evaluated CDCU. In the first trial, reductions in peak blood alcohol concentration (BAC) were significant (correcting for multiple comparisons) at 1 month compared with repeated assessment but were absent at 12 months. The second trial, comparing CDCU to postassessment only (versus repeated assessment) found robust reductions across peak and typical drinking outcomes from baseline to 1 month. Although preliminary evidence suggests that this program may be efficacious, limited evidence, in addition to the sole finding of reduced peak BAC compared with repeated assessment, points to the need for further evaluation before the program should be widely adopted.

e-CheckUpToGo

E-CheckUpToGo, called e-CHUG in earlier versions, incorporates assessment, personalized feedback targeting normative misperceptions and other alcohol behaviors, education, and skills training. Three of the four previously reviewed studies on this approach demonstrated at least short-term positive effects on alcohol use (Doumas and Andersen 2009; Hustad et al. 2010; Walters et al. 2007) and alcohol-related consequences (Doumas and Andersen 2009). Five new studies have been published since the 2011 review by Cronce and Larimer, three of which show reductions in various indices of alcohol use (Doumas et al. 2010, 2011*a*) and/or consequences (Alfonso et al. 2013) relative to control subjects across follow-up periods ranging from 1 to 6 months. One study (Murphy et al. 2010) demonstrated no between-group differences at 1 month compared with assessment only, although the study did show within-group differences for e-CheckUpToGo. Another study showed successes compared with an in-person BMI at 1 month that were no longer present at the 8-month followup, with increased drinking evident in the e-CheckUpToGo group (Doumas et al. 2011*b*,*c*). Absence of an assessment-only control in this study leaves overall efficacy unclear. Although e-CheckUpToGo has been tested across an array of high-risk populations (e.g., mandated students, athletes, and freshmen), research on any one college population is relatively limited and would benefit from replication, especially given variation in specific effects on alcohol outcomes across studies.

MyStudentBody (MSB) and MyStudentBody-Parent (MSB-P)

MSB includes general education and skills training, along with assessment and personalized feedback discussing alcohol behavior, beliefs, and risks. One previously reviewed study (Chiauzzi et al. 2005) evaluated MSB among binge-drinking college students. Participants randomly assigned to MSB showed reductions in peak drinks per drinking day and composite drinking index scores at 1 month but were no different than an alcohol education control group at 3 months. Female, but not male, MSB participants showed reduced consumption on special occasions and fewer alcohol-related negative consequences relative to control subjects at followup. Additional research is needed to evaluate efficacy.

More recently, Donovan and colleagues (2012) examined MSB-P, a modification of MSB delivered to parents (only) that encourages parent–teen communications about alcohol. Parent–teen dyads were randomly assigned to either MSB-P or an attention control (i.e., receipt of an equal amount of material that is not expected to produce change, in this case, an alcohol education e-mail newsletter). Parents received the intervention 4 weeks prior to the start of their child's freshman year of college. Assessments through 6 months postintervention found no impact on students' binge drinking, which was the single alcohol use outcome variable.

Unitcheck

Unitcheck provides personalized feedback on alcohol consumption as well as related education and advice. One previously reviewed study (Bewick et al. 2008) demonstrated that drinks per drinking occasion were reduced at 12 weeks postintervention compared with assessment only. Subsequently, Bewick and colleagues (2010) randomly assigned students reporting alcohol use in the past 6 months to immediate access to the intervention (weeks 1 to 7), delayed access (weeks 8 to 15), or assessment only. Results were mixed. Reductions in drinks per drinking occasion occurred for the delayed and assessment-only conditions but not in the immediate condition. Across conditions, participants who completed a minimum of two of five assessments reduced drinking with additional reduction for those assigned to the intervention arms. This study demonstrated that repeated assessment alone may be effective at reducing alcohol consumption, and this may be enhanced by participation in an intervention such as Unitcheck. As with many programs, more research is needed.

Unbranded PFI-style and Personalized Normative Feedback (PNF) Programs

A number of studies have examined the effects of unbranded PFIs and/or single-component PNF interventions, the features of which differ, and any one version may only be represented by a single study. Two previously reviewed studies evaluated unbranded electronic PFIs with generally positive findings. Compared with a control group, Kypri and colleagues (2004) showed reduction of alcohol use and consequences, and, comparing a minimal versus enhanced version of PFI, Saitz and colleagues (2007) found within-person reductions in alcohol use and problem severity among women and in problem severity, but not consumption, among men across active interventions. Evaluating a brief computer-based PNF, Neighbors and colleagues (2004) found reductions in drinking persisting up to 6 months.

Twelve subsequent studies have tested other unbranded PFIs or PNFs. Similar to Saitz and colleagues (2007), Kypri and colleagues (2008) compared two versions of a PFI (a single vs. multiple dose) but also included an education-only control condition. Students scoring 8 or more on a 10-question screening instrument (i.e., Alcohol Use Disorders Identification Test [AUDIT]) were recruited from primary care. Relative to a control group, a single dose of a PFI resulted in lower frequency of drinking at 6-month followup, lower total consumption and academic consequences at both 6- and 12-month followup and reduced alcohol problems at 12 months. The multidose condition resulted in decreased typical quantity and frequency of drinking, lower total consumption, and reduced frequency of heavy episodic drinking at the 6-month followup; reduced academic consequences at both the 6- and 12-month followup, and

reduced non-academic consequences and alcohol problems at the 12-month followup.

Kypri and colleagues (2009) compared a two-dose PFI to assessment-only among Australian college students who scored 8 or more on the AUDIT and engaged in at least one occasion of heavy episodic consumption over the previous 4 weeks. Participants received assessment and feedback at baseline and again 1 month later, including additional feedback on alcohol use and consequences that occurred after the initial feedback. Of outcomes examined at 1-month followup, participants receiving the two-dose PFI reported a lower frequency of drinking, fewer drinks per occasion, and lower total consumption relative to those who received assessment only. Only the effects on frequency of drinking and total consumption were maintained at the 6-month followup. Negative-consequence variables did not differ at either time point. Overall differences in alcohol consumption differed by condition, with the intervention group consuming 17 percent less alcohol compared with an 11 percent reduction by the control condition. The authors indicated that this was primarily driven by reductions in frequency of drinking rather than amount consumed per episode.

Kypri and colleagues (2014) compared a PFI to assessment only among students scoring 4 or more on the AUDIT-C[2] at seven New Zealand universities. At the 5-month followup, those randomly assigned to PFI reported fewer drinks per typical drinking occasion; however, this effect was reduced to non-significance in sensitivity analyses designed to detect effects of differential attrition. No effects on the five other drinking-related outcomes assessed were evident.

Palfai and colleagues (2011) randomly assigned college students scoring 8 or more on the AUDIT to PFI versus attention control. At the 1-month followup, participants who received the PFI reported drinking fewer drinks per week overall. Subsequent analyses indicated that this effect was driven by those students who had reported a greater number of alcohol consequences at baseline, with no effect of the intervention among students with a lower number of baseline consequences. A similar effect was shown for heavy episodic consumption, with reductions in episode frequency evident among those with greater baseline consequences and not for those with fewer baseline consequences.

Martens and colleagues (2010) compared two forms of PFI—one targeted to college athletes and the other aimed at college students in general (generic)—against an alcohol education control group among varsity and club-sport athletes. At 6 months, those in the targeted PFI condition reported lower peak BAC compared with the control group and the generic PFI, with increases in peak BAC evident in these latter two groups. However, for heavy drinkers, reductions in peak BAC were evident for both PFI conditions compared with the control group. No effects were found for other alcohol-related indices.

Bryant and colleagues (2013) randomly assigned students to receive either a PFI or educational information on the risks of alcohol via e-mail. Followup at 6 weeks postintervention revealed that those who had received the PFI reported fewer drinks per week and fewer days drunk in the past 30 days compared with those who received education only. However, it must be noted that about 40 percent of students were lost to followup, and these individuals reported significantly higher values on all alcohol outcome measures at baseline.

LaBrie and colleagues (2013) compared a full PFI to eight versions of a PNF intervention (a component of the full PFI) that varied the specificity of the normative reference group and a generic non–alcohol-focused normative feedback control group in Caucasian and Asian students reporting one or more occasions of heavy episodic consumption in the past month. PFI participants reported lower peak drinking and fewer drinking days compared with control subjects, with no effects on alcohol consequences. Those receiving any PNF reported lower average total consumption, lower peak drinking, fewer drinking days, and fewer alcohol consequences compared with control subjects. Comparisons of PNF conditions indicated that use of the "typical student" reference group is most effective.

Lewis and colleagues (2014) expanded targets of PNF to include alcohol-related risky sexual behaviors (RSB) in addition to alcohol-related behaviors. Students were stratified by gender and level of drinking and randomly assigned to an alcohol-only PNF, an alcohol-related RSB-only PNF, a combined alcohol and alcohol-related RSB PNF, or assessment only. The alcohol-only and the alcohol-related RSB-only PNFs each reduced their target behaviors and the combined intervention reduced both sets of outcomes relative to control subjects. None of the interventions reduced alcohol-related consequences. Results indicate that combining related treatment targets may be an effective strategy.

Ekman and colleagues (2011) compared a minimal feedback intervention, in which participants' own drinking was compared with safe-drinking guidelines, to PNF with harm reduction advice among students at a Swedish university. Retention rates at the 3- and 6-month followup were quite low (between 24 percent and 38 percent), and although some significant within-person reductions in alcohol use and risk were evident, given the small sample size, it was not surprising that no significant between-groups effects emerged.

Moreira and colleagues (2012) evaluated PNF against assessment-only and delayed (posttest–only) assessment in a sample of students drawn from multiple universities in the United Kingdom. Although retention was poor (50 percent) at the 6-month followup, a significant decrease in weekly drinking was evident in the PNF group compared with control subjects. However, this effect was absent at the 12-month followup, and no effects were observed on any of the other alcohol outcome measures.

Neighbors and colleagues (2010) tested gender-specific versus non–gender-specific PNF as a single- versus four-dose (biannual) intervention against an attention control group among heavy-drinking freshmen. At 6 months, those

[2] The AUDIT-C is a three-item alcohol screening test that is scored on a scale from 0 to 12.

in the four-dose, gender-specific PNF condition reported lower weekly drinking compared with the control group. Women, but not men, who received the four-dose, gender-specific PNF decreased their alcohol problems compared with control subjects. No differences were found on any outcome between the control group and the gender-specific single-dose PNF or non–gender-specific PNF groups.

Finally, Mason and colleagues (2014) randomly assigned students with hazardous drinking to either an assessment-only control condition or a very brief (four to six texts over 4 consecutive days) automated text intervention including personalized information on drinking frequency, social norms, social risk, and protective behavioral "boosts," if requested. The amount of personalized information contained in the intervention is most consistent with a PNF versus a PFI; however, the inclusion of skills training and the MI framework used for the texts go beyond a standard PNF. This was a small-scale proof-of-concept investigation to determine feasibility. Although there were no significant group differences on behavioral alcohol outcomes, this was not surprising given the very small sample size. The results did show changes in potential mediators of intervention efficacy (i.e., readiness to change), suggesting further research may be warranted.

Event-Specific Prevention (ESP)

Electronic interventions targeting general alcohol misuse have been adapted to proactively address alcohol use and consequences for specific events associated with extreme alcohol consumption (i.e., 21st birthdays, spring break [SB]). In an ESP study reviewed by Cronce and Larimer (2011), Neighbors and colleagues (2009) randomly assigned participants to receive an electronic card 2 days before their 21st birthday that contained a hyperlink to personalized feedback about their drinking intentions and anticipated BAC for their 21st birthday, associated normative information, education on BAC effects, and suggestions for protective behavioral strategies. The intervention (which is most consistent with PNF) reduced reported BAC levels on the day of participants' 21st birthdays compared with an assessment-only control condition. This effect was pronounced for those with baseline intentions to reach higher BACs.

Three subsequent ESP studies were identified. In the first, Neighbors and colleagues (2012) tested a 21st birthday–specific in-person BASICS, a Web-based 21st birthday PFI, a general in-person BASICS condition, and attention control. Two additional conditions tested augmented versions of the 21st birthday–specific interventions by incorporating a friend of the participant who was supplied with alcohol education and harm reduction tips for their friend's birthday celebration. Students with reported intention to "binge drink" on their upcoming 21st birthday were randomly assigned to one of the six conditions. Results were mixed. None of the interventions reduced the number of drinks consumed compared with the control group. The 21st birthday PFI without the friend component, but not with, resulted in lower BACs compared with control subjects, as did the general in-person BASICS. Unlike the 21st birthday PFI without the friend component, the 21st birthday PFI with the friend component reduced consequences relative to the control group, as did all three in-person conditions.

With a similar design to Neighbors and colleagues (2012), Lee and colleagues (2014) conducted a large RCT examining five different intervention conditions against an attention control with the goal of reducing drinking and negative drinking consequences over SB. Two of five interventions included a PFI that was designed specifically to address SB drinking; one with a friend component, one without. Neither SB-PFI, with or without a friend, nor the original in-person BASICS, was shown to be effective in reducing SB drinking. Only the in-person SB-BASICS intervention without a friend reduced drinking compared with control subjects. Of note, the same intervention with the friend component was not effective.

Lastly, Patrick and colleagues (2014) applied a PFI modified to address both alcohol-related behavior and alcohol-related RSB, similar to Lewis and colleagues (2014), as an ESP to target SB alcohol use. Students between the ages of 18 and 21 who planned to go on SB trips with friends were randomly assigned to PFI or assessment only. Although normative perceptions were reduced, there were no main effects on any of the primary alcohol-related behavioral outcomes.

Other Programs with Minimal Personalization

In addition to unbranded PFIs, other interventions have taken advantage of technology-based delivery methods that include some personalization but which cannot be considered a full PFI or PNF intervention. For example, Cronce and Larimer (2011) reviewed a study by Weitzel and colleagues (2007) that compared 2 weeks of repeated (daily) assessment on a handheld (HH) computer plus tailored feedback on avoiding alcohol consequences, based on baseline levels of reported self-efficacy and drinking outcome expectancies, to repeated assessment alone. Those who received the tailored feedback messages reported fewer drinks per drinking day on the HH device during the daily assessment period. However, no group differences in drinking outcomes were evident on the retrospective assessment for the same period completed at the 2-week followup.

Hendershot and colleagues (2010) tested an intervention that targeted the $ALDH_2$ genotype, found almost exclusively in individuals of northeast Asian descent, which can convey a protective effect against alcohol misuse. Students of 100 percent Chinese, Korean, or Japanese heritage underwent genotyping and were randomly assigned to personalized genetic feedback that included their $ALDH_2$ test results and information specific to their genotype ($ALDH_2$ 1/1, $ALDH_2$ 1/2, $ALDH_2$ 2/2), or attention-control feedback that provided normative information about nonalcohol behaviors. At the 1-month followup, only the group with one of two affected alleles ($ALDH_2$ 1/2) demonstrated a

reduction in alcohol-related measures (i.e., peak quantity, typical weekend quantity, drinking frequency). However, this is an encouraging result as this genotype is most at risk for alcohol-related cancers.

Schuckit and colleagues (2012) examined a prevention paradigm based on another genetically linked trait, subjective levels of response (LR) to alcohol (high vs. low). Freshman were randomly assigned to either (1) a low LR–based prevention group (LRB group), which watched four 45-minute Internet-based videos that included, in addition to prevention messages, information on how low LR to alcohol may promote heavy drinking; or (2) a non-LRB comparison group, which saw the same prevention messages without the LR framework. Self-reported usual and maximum drinks per drinking occasion decreased significantly for all participants regardless of LR status or condition. Low-LR students showed the greatest decreases in the LRB condition and high-LR students showed greater decreases in the non-LRB condition, demonstrating support for tailoring prevention messages to specific predisposing factors such as LR. Because the study design did not include an assessment-only control group, general efficacy information is unknown.

Hagger and colleagues (2012) randomly assigned students from the United Kingdom to one of four instruction conditions delivered using Web and e-mail: implementation intention only (setting specific intentions to reduce alcohol intake), mental simulation only (visualizing achieving goals), a combination of the two, and an assessment-only control. Only the students in the mental simulation–only condition reduced alcohol consumption and heavy episodic drinking occasions over the subsequent month compared with the control group. Students with the highest baseline use, however, had a greater reduction in alcohol consumption in the combined condition than any of the other conditions.

Alcohol 101+

Alcohol 101+, a Web-based modification of the earlier CD-ROM–based Alcohol 101 program, provides alcohol education and skills training using a "virtual campus," modeling potential drinking situations and discussing possible consequences and alternatives, with personalized BAC calculations provided. Three studies were identified, two of which (Carey et al. 2009, 2013) included Alcohol 101+ as a control condition, limiting the ability to evaluate efficacy. The third (Carey et al. 2011), previously reviewed by Cronce and Larimer (2011), compared Alcohol 101+ with a waitlist control group and found reductions in alcohol use for male mandated students compared with wait-listed students at 1 month. However, only within-person reductions (no between-groups effects) were found for female mandated students. In terms of alcohol consequences, women assigned to Alcohol 101+ actually fared worse compared with waitlist students, and there were no intervention effects for men at 1 month.

Michigan Prevention and Alcohol Safety for Students (M-PASS)

M-PASS comprises 4 10- to 15-minute online MI sessions delivered over 9 weeks. Sessions were tailored based on the participants' general drinking profiles, readiness to change and self-efficacy, and included some personalized information (i.e., drinking norms based on participant's demographics). One study has evaluated the efficacy of the M-PASS program, with findings from posttest (Bingham et al. 2010) and 3-month followup (Bingham et al. 2011) published separately. Treatment effects, relative to the control group, varied somewhat by gender, with lower binge drinking frequency among high-risk drinking men, fewer total drinks consumed over the past 28 days among high-risk drinking women, and fewer drinks per drinking day among low-risk drinking women at posttest. At 3 months, male high-risk participants in M-PASS continued to show lower frequency of heavy episodic consumption compared with control subjects; however, the effect would not have been significant if a correction for multiple comparisons was applied. Treatment effects for women differed at the 3-month followup relative to posttest, with lower frequency of heavy episodic consumption and fewer alcohol related consequences among high-risk women relative to control subjects. The availability of a single study and the variability of findings over time indicate that additional research is needed before strong conclusions regarding efficacy can be drawn.

Discussion

College student alcohol use remains a critical issue. Fortunately, there have been successful advances in prevention strategies targeting individuals to reduce the harms associated with college student drinking. It is important to stress that no one program or approach is sufficient to prevent or reduce high-risk drinking, and an overall strategic plan should incorporate multiple approaches targeting every level of intervention (i.e., universal, selective, and indicated). Whereas the amount and quality of research on any one program varies, the extant evidence suggests that electronic interventions may be one piece of an effective overall strategic plan.

Although the general PFI approach (grouping together commercially branded and unbranded programs) and PNF approach seem to be efficacious on the whole, data are insufficient to make general recommendations regarding the best program for adoption. Moreover, overall conclusions regarding the efficacy of electronic interventions globally, and any one program, must be tempered by the limitations of the individual studies (e.g., small sample sizes, poor retention) as well as the challenges and limitations imposed by rapidly changing technology (e.g., devices and Web browsers are not universal, requiring unique adaptations of interventions; innovations make hardware outdated within 1 year) and specifics of the campus environment and resources (e.g., availability of programming staff to monitor

compliance; ability to impose contingencies on students who do not complete the intervention, such as holding grades or preventing registration). Certainly, additional research is needed, and efforts to replicate existing findings are indicated. Of note, many of the programs reviewed have been subject to modifications over time, resulting in multiple iterations or versions. Colleges wishing to implement one of these programs should conduct due diligence before adoption to understand which variant they are considering and to determine the empirical support for that specific version, as efficacy research on one version may not apply to others. For commercially available programs, colleges can, and should, request articles supporting efficacy for the current version that would be adopted on their campus to evaluate the potential benefit of implementation.

In addition to program choice, campuses may wish to consider for whom such approaches should be made available (e.g., first-year students, athletes, Greek members, mandated students, etc., which can be informed by research efforts to determine for whom these approaches are most helpful) and must also critically consider potential limitations of electronic interventions. For example, research has shown that without incentives or penalties for noncompliance, students are unlikely to complete interventions of their own volition (see Paschall et al. 2011*a*,*b*). Likewise, without face-to-face interaction with a person who can assess and confirm the degree to which a student is paying attention (as would be the case in an intervention like BASICS), a potential limitation includes the degree to which students are engaged in, connected to, and even multi-tasking during the intervention. Additionally, given the high variability in length and content across different electronic interventions, the appropriate intervention "dose" given to any individual student to decrease his or her alcohol use (and the consequences he or she has experienced) needs to be more firmly established (as does the need for any "booster" sessions beyond the initial intervention to potentiate and/or sustain effects). Although the effect of electronic interventions on alcohol-related negative consequences does not seem to be as robust as in-person BMIs (as they are only evident in a minority of the studies detailed here), followup generally has been shorter in studies of PFIs and PNF interventions relative to BMIs and it may be that longer followups are needed to demonstrate an effect on consequences. Other factors also may be at work, such as differences across studies in assessment tools used to measure consequences. Thus, more research is needed to specifically address under what conditions electronic interventions produce reductions in negative consequences.

In terms of future research, there are several interesting and important questions that need to be addressed in order to maximize the potential of electronic interventions. Briefly, these include the study of:

- *Additional interventions.* Other available programs would benefit from more thorough empirical validation, such as Alcohol-Wise, an educational program that contains e-CheckUpToGo, or MyPlaybook, a program targeted toward athletes. Although preliminary findings have been presented at informal academic venues, no peer-reviewed published RCTs were identified for these programs.

- *Timing of the intervention.* Many campuses require first-year students to complete an alcohol intervention prior to matriculation. Although this may convey the seriousness with which a campus takes alcohol prevention and serve to get students on the "same page" regarding alcohol information, students may not yet have a sense of general college norms, what goes on at their school, or what pressure to drink is like. Research could explore what, if any, boosters might be needed once students arrive on campus and if there is an optimal time for intervention delivery.

- *Opportunities for reaching more advanced students.* Given the emphasis on entering/first-year students, how might electronic interventions systematically be offered to students in later years of study? For example, research by Neighbors and colleagues (2009, 2012) suggests that students turning 21 could be invited to participate in an ESP. However, when not required (as with entering students), how might we attract students to participate in such interventions?

- *Electronic PFIs as a referral option.* Alcohol screening in campus health and counseling centers helps identify students struggling with substance use and reduce the likelihood of students "slipping through the cracks." Hingson (2010) suggested that if schools implement such screenings, there would be an impact at the campus level through referral to empirically supported interventions. As primary care–based BMIs typically are in person, determining what circumstances and for whom referral to an electronic PFI (adjunct or standalone) would be effective should be examined.

- *Keeping abstainers in mind.* Studies have shown a protective effect of personalized feedback for those who do not drink. For example, in a mailed feedback intervention, Larimer and colleagues (2007) demonstrated that abstainers who received the feedback were twice as likely to be abstaining 1 year later compared with control participants. With increased risk for addiction associated with earlier onset of use, delaying the initiation of use can be of great public health importance. The role of electronic interventions in achieving this goal should be explored and abstainers considered as schools develop a strategic plan.

- *Duration/length and formatting of interventions.* How brief can a brief intervention be and still be effective? Without a facilitator present, how much information is necessary to have an impact? In addition, as more online information is viewed on smaller tablets and phones, the

ability to impact change in a time- and space-efficient way will increase in importance.

Conclusion

As reviewed here, the existing evidence gives us reason to be excited about the potential of electronic feedback interventions in reducing high-risk drinking and related harm among college students. That said, the field is still young and research must be done to establish the parameters of successful intervention, as well as the reliability, relative efficacy, and longevity of effects related to specific electronic programs. PFI-style programs have the most research support to date, but the increasing variety of style and content of PFIs, including among electronic programs with different iterations, makes it harder to group these programs together when discussing efficacy but also points to the potential for campuses to develop their own PFI based on features of programs with promising outcomes. Whereas this review summarizes the existing base of information on electronic alcohol feedback interventions, research is always advancing. Campuses wishing to adopt a given program are again advised to "do their homework" to ensure their expenditure of resources and dedication to one specific program is based on the most up-to-date and accurate information.

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Gaps in Clinical Prevention and Treatment for Alcohol Use Disorders

Costs, Consequences, and Strategies

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Heavy drinking causes significant morbidity, premature mortality, and other social and economic burdens on society, prompting numerous prevention and treatment efforts to avoid or ameliorate the prevalence of heavy drinking and its consequences. However, the impact on public health of current selective (i.e., clinical) prevention and treatment strategies is unclear. Screening and brief counseling for at-risk drinkers in ambulatory primary care has the strongest evidence for efficacy, and some evidence indicates this approach is cost-effective and reduces excess morbidity and dysfunction. Widespread implementation of screening and brief counseling of nondependent heavy drinkers outside of the medical context has the potential to have a large public health impact. For people with functional dependence, no appropriate treatment and prevention approaches currently exist, although such strategies might be able to prevent or reduce the morbidity and other harmful consequences associated with the condition before its eventual natural resolution. For people with alcohol use disorders, particularly severe and recurrent dependence, treatment studies have shown improvement in the short term. However, there is no compelling evidence that treatment of alcohol use disorders has resulted in reductions in overall disease burden. More research is needed on ways to address functional alcohol dependence as well as severe and recurrent alcohol dependence. **KEY WORDS: Alcohol use, abuse, and dependence; heavy drinking; alcohol use disorders (AUDs); alcohol-related problems; alcohol burden; burden of disease; morbidity; mortality; prevention; treatment; prevention strategy; treatment strategy; screening and brief intervention; primary care; cost-effectiveness of AOD health services**

Heavy drinking takes a high toll on society. Other articles in this issue summarize the disease burden and economic cost to society attributable to alcohol use, which provide a powerful incentive to develop and implement ways to reduce them. The focus of this article is on the role of selective (i.e., clinical) prevention and treatment approaches for heavy drinkers and people with alcohol use disorders (AUDs) in reducing the burden associated with excessive alcohol use. As used here, selective, or clinical, prevention refers to strategies targeted at individuals at higher risk of experiencing adverse alcohol effects, such as screening and brief counseling of heavy drinkers in health care settings or internet-based screening and advice provided to college students. The term "treatment" refers to services for alcohol dependence provided by a professional, such as a counselor, social worker, nurse, psychologist, or physician. Community peer-led support groups such as Alcoholics Anonymous are considered to be distinct from professional treatment services, much like a diabetes support group would be distinguished from endocrinology services. The article focuses on the following three questions: (1) Can selective prevention and treatment reduce the disease burden attributable to heavy drinking? (2) Are some treatment approaches more cost-effective than others? (3) Do gaps exist in the current continuum of care? After addressing these issues, the review suggests research priorities to help close existing gaps and reduce the burden of disease.

Selective Prevention and Treatment: Effectiveness, Cost-Effectiveness, and Disease Burden

Screening and brief advice for at-risk (i.e., nondependent) drinkers, commonly known as screening and brief intervention (SBI), is effective at reducing drinking for a year or more and in many studies also has been shown to reduce alcohol-related harms, such as motor-vehicle crashes and driving violations. Its efficacy is supported by numerous randomized controlled trials and multiple meta-analyses; as a result, the U.S. Prevention Task Force has listed it as a Type B recommendation for medical prevention services (Babor et al. 2007; Whitlock et al. 2004). The evidence is strongest for nondependent heavy drinkers who present for primary care services in ambulatory settings. Unfortunately, a recent meta-analysis of studies of SBI in primary care settings failed to show significant reductions in subsequent health care utilization (Bray et al. 2011). The efficacy of SBI in other settings, such as emergency departments (EDs) or hospitals, has not been established, although several randomized controlled trials have been conducted (Field et al. 2010). One explanation for the observed differences may be the patient populations analyzed. Thus, in most of the outpatient primary care studies, participants with alcohol dependence were excluded from the analysis, whereas that generally was not

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the case for studies conducted in EDs or hospital settings. Moreover, patients with alcohol dependence are much more commonly encountered in ED and hospital settings than in primary ambulatory care. In summary, at this time, SBI in primary care ambulatory settings for adults can be strongly recommended as highly efficacious, whereas SBI in EDs or hospitals cannot.

SBI also seems to be effective among select groups when delivered through internet-based or computerized applications. In particular, there is strong evidence that digital SBI can effectively reduce drinking and associated consequences among college students (Moreira et al. 2009). It is not clear whether or to what extent this finding might generalize to other population subgroups, but it is certainly plausible that it could, provided the target population has easy access to computers and is computer literate. The same holds true for other methods, such as telephone-based SBI or use of the relatively new publication and Web site called Rethinking Drinking, which is published by the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

Despite the evidence supporting its effectiveness, SBI is not yet being implemented widely (Hingson et al. 2012). Widespread dissemination of information about recommended drinking limits and easy access to screening and brief counseling has the potential to make a significant public health impact. Because at-risk drinkers are much more numerous than alcohol-dependent people, at-risk drinking contributes a much greater disease burden than alcohol dependence. Accordingly, widespread implementation of SBI has the potential to reduce a greater proportion of disease burden than even very effective treatment, a concept known as the prevention paradox (Rose 1981). Therefore, more research is needed to expand the implementation of SBI in the at-risk population and further increase its effectiveness.

Estimating the effectiveness and cost-effectiveness of treatment is more complex. Most reviews conclude that treatment is effective at reducing drinking and associated consequences. Multiple behavioral treatment approaches—such as cognitive– behavioral therapy, motivational enhancement therapy, 12-step facilitation, behavioral marital therapy, and community reinforcement—have similar and relatively high levels of short-term success in reducing drinking and associated consequences, at least when treatment is provided by the highly trained, motivated, and closely supervised clinicians participating in clinical efficacy trials (Project MATCH Research Group 1998). Why these technically diverse counseling techniques produce almost identical drinking outcomes is unclear. Three alternative explanations have been offered:

- The specific technique is less important than other, mostly unidentified, factors associated with psychotherapy.
- Each approach works via different mechanisms but produces similar results on average, much like different antidepressants acting through different mechanisms produce similar outcomes in the treatment of depression.
- Professional treatment only has a small effect in determining outcome compared with other, nontreatment factors, such as social control (e.g., driving-while-intoxicated laws, family pressure, or employer mandate), natural history of alcohol dependence, and the tendency to revert to usual levels of drinking following resolution of a crisis where drinking had peaked (i.e., regression to the mean).

This last explanation is supported by recent research demonstrating that changes in drinking habits begin weeks before treatment entry (Penberthy et al. 2007). Likewise, in another study of treatment of alcohol dependence that examined events leading to treatment seeking (Orford et al. 2006), the findings suggested that the change point occurred prior to treatment entry. Thus, it is unclear how much of the positive change can be attributed to the treatment processes themselves as opposed to other factors leading to and following treatment seeking.

What is clear, however, is that researchers and clinicians do not yet understand how or why some people change in response to treatment and others do not. To address this issue, NIAAA led the way at the National Institutes of Health (NIH) in shifting the focus of behavioral treatment research to identifying the mechanisms of behavior change rather than encouraging more comparisons of different psychotherapy approaches (Willenbring 2007). The NIH subsequently developed a major initiative on basic behavioral research (Li 2009). This research initiative provides an opportunity to investigate many obvious questions. For example, what are the social forces that either support or impede positive health behavior change? What determines their impact, in terms of the response of the individual? Why and how do people begin to change, and what determines the resilience of that change? What is the basic science underlying behavior change, at all levels from genetic and genomic to cellular, organic, individual, and social interactions? Research elucidating the basic science of behavior change is an exciting and promising area that has the potential to substantially change the types of interventions that are available, making them more powerful, available, and cost-effective.

The lack of clarity about what causes change in drinking behavior also results in uncertainty as to whether treatment of alcohol dependence reduces disease burden. The community prevalence of alcohol dependence, which is about 4 percent in any year, has not changed substantially in recent years (Substance Abuse and Mental Health Services Administration 2011). Earlier studies found a cost offset of treatment—that is, lower health care costs after treatment than before treatment (Holder 1998). More recent studies, however, have found that heavy drinkers who are not in crisis underutilize health care, at least in an employed population, suggesting that the observed cost reduction is more a reflection of the natural history of drinking behavior and of a regression to the mean (Finney 2008; Zarkin et al. 2004). In other words, people suffering from any disease tend to seek treatment when their condition is most severe. In the case of alcohol dependence, treatment seeking therefore would be preceded by an escala-

tion of drinking, complications, and utilization of medical services and, consequently, high costs before treatment entry. Because chronic conditions such as alcohol dependence wax and wane, most people will tend to improve after a period of greater severity, even without effective treatment, so that subsequent reduced costs may not necessarily be associated with treatment. Also, every patient's disease trajectory is different, so that when drinkers are assessed before and after treatment, some of them will be well at followup, whereas for others their condition will be more severe. The average severity, however, will be less following treatment, because for all patients studied, their disease severity at treatment entry will have been high. The most rigorous study of cost-effectiveness of alcoholism treatment, the COMBINE trial, found that treatment was cost-effective, especially pharmacotherapy with medical management (Zarkin et al. 2008, 2010). The interpretation of these findings is limited, however, by the study's highly rigorous trial design, intensive follow up, and exclusion criteria (Anton et al. 2006), and it is unknown to what extent these findings generalize to community treatment programs and participants.

Another limitation when estimating the effects of treatment on public health is that relatively few affected people seek treatment. For example, among people who develop alcohol dependence at some point in their lives only 12 percent seek treatment in a specialty treatment program (Hasin et al. 2007). Among people who have AUDs and who perceive a need for treatment, almost two-thirds (i.e., 65 percent) fail to obtain it because they are not ready to stop drinking or feel they can handle it on their own. Other common reasons for the failure to seek treatment include practical barriers, such as lack of health insurance, the cost of treatment, and lack of transportation or access to treatment, which are reported by 59 percent of respondents, and stigma, which is reported by 31 percent (Center for Behavioral Health Statistics and Quality 2012).[1] Thus, more people might seek treatment if it was less expensive, stigmatizing, and disruptive than most treatment approaches. Efforts to improve access, affordability, and attractiveness of treatment, especially for individuals with less severe AUDs should be encouraged.

Despite these limitations, some tentative conclusions can be drawn as to which approaches to treating alcohol dependence are more cost effective. Studies found no significant difference in outcomes between residential and outpatient treatment and no clear relationship between intensity of treatment and outcome (Fink et al. 1985; Longabaugh et al. 1983; McCrady 1986). For example, medical management plus pharmacotherapy with naltrexone generated similar outcomes to more expensive counseling approaches, even when counseling was performed once weekly and on an outpatient basis (Anton et al. 2006; O'Malley et al. 2003). These studies suggest that a more individualized, outpatient, and medically based approach may provide a cost-effective alternative to approaches favoring intensive psycho-education, which often are provided in residential settings. Treatment provided in residential rather than outpatient settings may add considerable expense without a commensurate improvement in outcomes. In addition, confidential treatment by their usual primary care physician involving only routine clinic visits may attract more people, thus expanding access to effective treatments.

Gaps in the Continuum of Care

There are several gaps in the continuum of care that deserve attention, affecting drinkers across the spectrum of alcohol involvement. Recent epidemiological research has demonstrated that alcohol involvement varies along a continuum ranging from asymptomatic heavy drinking (i.e., at-risk drinking), through functional alcohol dependence, and to severe and recurrent alcohol dependence (Willenbring et al. 2009). The continuum of care ideally should correspond to this epidemiology but does not at this time. Most studies and treatment approaches have focused on the more severe end of the spectrum—that is, people with severe, recurrent dependence. However, the vast majority of heavy drinkers either does not have alcohol dependence or has a relatively milder, self-limiting form (Moss et al. 2007). This spectrum of severity is similar to that for other chronic diseases, such as asthma. Likewise, examining treatment seekers in the current system of care yields similar results to studying hospitalized asthmatics: thus, heavy drinkers in treatment exhibit more severe dependence, more comorbidity, less response to treatment, and a less supportive social network compared with people who do not seek intensive treatment (Bischof et al. 2003; Dawson et al. 2005; Sobell et al. 2000). In contrast, people with functional alcohol dependence[2] predominantly exhibit "internal" symptoms, such as impaired control; a persistent desire to cut down on their drinking but finding it hard to do; and alcohol use despite internal symptoms such as insomnia, nausea, or hangover. These individuals generally drink much less than more seriously affected people (Moss et al. 2007). Functional alcohol dependence typically resolves after a few years, mostly without requiring specialty treatment (Hasin et al. 2007). Large gaps in services exist for people at both ends of the spectrum of dependence severity—that is, both for people at the milder end of the spectrum (i.e., at-risk drinkers and people with functional alcohol dependence) and for those at the most severe end (i.e., with recurrent, treatment-refractory dependence).

There currently are few services for at-risk drinkers and people with functional alcohol dependence. In primary medical care, very few patients are screened and positive screening results addressed (McGlynn et al. 2003). Furthermore, functional alcohol dependence largely is ignored because although these individuals meet diagnostic criteria for dependence, they rarely seek treatment in the current system (Moss et al. 2007). These gaps are significant from a public health perspective because the prevalence of at-risk drinking

[1] The numbers add up to more than 100 percent because respondents could endorse multiple reasons.

[2] People with functional alcohol dependence are those who meet the criteria for a medical diagnosis of alcohol dependence but remain functional in society (i.e., in their jobs, families, and social lives).

and functional dependence is much higher than that of more severe disorders and these conditions therefore account for the majority of excess morbidity, mortality, and associated costs attributable to alcohol consumption (Centers for Disease Control and Prevention 2012). Whether wider implementation of SBI would result in a reduction in disease burden is not known at this time. However, enhancement of these approaches, especially among young people and community-dwelling heavy drinkers not seeking medical care, might reduce disease burden, although the two populations require somewhat distinct approaches. More studies of secondary prevention efforts outside of medical settings therefore are needed.

SBI in primary care settings to identify people with AUDs at the milder end of the severity spectrum is effective and may be cost-effective (Solberg et al. 2008), but many questions remain. For example, is it more cost-effective to target higher-risk groups (e.g., young people) for routine screening or is universal screening better overall? And when should screening occur (e.g., only during annual prevention visits or at every new patient visit) and how often should it be repeated? However, the biggest problem remains that effective selective prevention interventions such as SBI are not widely implemented. Although implementation has worked well in situations where additional grant funds were available, it still is unknown whether physicians will engage in this widely or how to best facilitate implementation. The Veterans Affairs health services system has been the most effective at implementing annual screening, but this system is unique in its structure and hierarchical nature. Implementation of such approaches in private health care organizations is much more complex and difficult. Therefore, more research is needed on low-cost ways to encourage wider adoption of SBI in primary care settings. Additional research should focus on SBI in other medical settings, especially mental health settings and medical specialties particularly affected by heavy drinking, such as gastroenterology (with patients with alcohol-related liver disease, gastritis, and pancreatitis) and otolaryngology (with patients with alcohol-related head and neck cancers).

Because so many hospitalized heavy drinkers have dependence, SBI is much less effective in this group (Saitz et al. 2007) and its effectiveness with patients in EDs or trauma centers also is unknown. Although some early studies showed positive results, subsequent research has yielded as many negative as positive findings (Field et al. 2010). Current efforts to implement SBI in these more acute-care settings therefore are premature, and more research is needed to determine if heavy drinkers encountered in such settings require more intensive services, linkage to ambulatory care services, or both.

People with functional alcohol dependence likely require more than brief counseling, but there is a major gap in research concerning optimal treatment strategies. Currently, few, if any, services are available for this group because they fall between at-risk drinkers and those with severe recurrent alcohol dependence (who are most likely to enter the current specialty treatment system). Pharmacotherapy (e.g., antirelapse medications) combined with medical management offers an attractive possible approach for this group, and evidence suggests that this combination yields comparable results to state-of-the-art counseling (Anton et al. 2006; O'Malley et al. 2003). Such an approach would allow most people with functional dependence to be treated in primary care and mental health care settings, similar to people with mild to moderate depression. More research, especially regarding effectiveness and implementation, is needed on this approach. Although most people with functional alcohol dependence eventually recover without any treatment (Hasin et al. 2007; Moss et al. 2007), their period of illness is associated with less severe but still significant dysfunction, such as absenteeism, attending work or school while sick (i.e., presenteeism), and reduced productivity. Early identification and treatment could reduce or hopefully eliminate these costs to the affected individuals and society.

Gaps in treatment also exist for people with severe recurrent alcohol dependence—the group that most people tend to think of when they think of "alcoholism." A recent exhaustive report examining the current treatment system concluded that "Most of those who are providing addiction treatment are not medical professionals and are not equipped with the knowledge, skills or credentials necessary to provide the full range of evidence-based services to address addiction effectively," (p. 3) and that "Addiction treatment facilities and programs are not adequately regulated or held accountable for providing treatment consistent with medical standards and proven treatment practices." (National Center on Addiction and Substance Abuse at Columbia University 2012, pp. 3–4). The current addiction treatment system first was conceptualized in the middle of the last century, as documented by White (2002), and has changed little since. No other chronic disease is treated with brief stints in a program with limited follow up care. Instead, for other chronic conditions patients are followed closely by physicians and other professionals over long periods of time, with the goal of minimizing symptoms and relapses, treating complications, and maximizing function. In these cases, care is provided indefinitely, often for life. Such a longitudinal-care approach also offers considerable promise in treating people with severe recurrent alcohol dependence. Several studies have found a highly significant positive effect for longitudinal care in people who have one or more medical complications of alcohol dependence (Kristenson et al. 1984; Lieber et al. 2003), including two studies that found significant reduction in 2-year mortality (Willenbring and Olsen 1999; Willenbring et al. 1995). Some findings also indicate that integrating treatment for substance use disorders into that for severe and persistent mental illness may be effective at reducing substance use, although no high-quality randomized controlled trials of this approach have been published (Drake et al. 2006). Pharmacotherapy for AUDs also may be effective in people with severe mental illnesses (Petrakis et al. 2004, 2005, 2006; Salloum et al. 2005). Finally, the ongoing need for recovery support and maintenance should be addressed.

Thus, more research is needed on the best long-term management strategies for recurrent alcohol dependence.

Conclusion

At this time no solid conclusions can be drawn as to whether current approaches to prevention of and treatment for AUDs reduce the disease burden attributable to heavy drinking, although these strategies have shown positive outcomes in the short term. SBI for at-risk drinkers in ambulatory primary care settings has the strongest evidence for efficacy, and some evidence supports its cost-effectiveness and associated reduction in excess morbidity and dysfunction. However, these benefits do not necessarily indicate that health care costs for these patients are reduced. Widespread implementation of SBI for nondependent heavy drinkers outside of the medical context has the potential to have a large public health impact. For heavy drinkers with more severe conditions (i.e., recurrent alcohol dependence), time-limited counseling may improve short-term recovery rates, but its long-term impact is less clear. Moreover, recent research findings have not been widely implemented. Scientifically based, medically anchored treatment approaches may provide a more attractive and cost-effective approach than the current intensive but time-limited treatment. More research is needed on ways to address functional alcohol dependence as well as severe and recurrent alcohol dependence. ■

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