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The Role of Alcohol-Related Behavioral Risk in the Design of HIV Prevention Interventions in the Era of Antiretrovirals: Alcohol Challenge Studies and Research Agenda

William H. George[1], **Jessica A. Blayney**[2], **Cynthia A. Stappenbeck**[3], **Kelly Cue Davis**[4]

[1]Department of Psychology, University of Washington, Box 351525, Seattle, WA 98195-1525, USA

[2]Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA, USA

[3]Department of Psychology, Center for Research on Interpersonal Violence, Georgia State University, Atlanta, GA, USA

[4]Edson College of Nursing and Health Innovation, Arizona State University, Phoenix, AZ, USA

Abstract

HIV/AIDS remains a significant health threat and alcohol is a robust contributing factor. After 25 years of alcohol challenge studies investigating alcohol-related behavioral risk (ARBR), much has been learned delineating how drinking influences sexual transmission. We examine this research and consider its relevance for interventions in the era of antiretrovirals. We consider prototypic alcohol challenge methods, illustrative findings, and prevention/intervention implications, noting three perspectives: (a) scale up/extend existing interventions, including identifying under-targeted risk groups and intersecting with PrEP/PEP interventions; (b) modify existing interventions by cultivating psychoeducational content related to alcohol expectancies, alcohol myopia, sexual arousal, risk perception, sexual abdication, and condom use resistance; and (c) innovate new interventions through Science of Behavior Change approaches and repurposing ARBR paradigms. Finally, we suggest research directions concluding that until HIV incidence diminishes significantly, psychosocial interventions addressing the nexus of alcohol use, sexual transmission, and adherence to biomedical protocols will be an important priority.

Keywords

Alcohol; HIV risk; Sexual risk; Alcohol challenge; Intervention implications

Psychosocial and biomedical interventions aimed at curtailing the HIV/AIDS epidemic have made considerable progress. Psychosocial interventions were initially the predominant mitigation strategy, seeking to reduce sexual transmission risk behavior, such as condom nonuse. These psychoeducational and behavioral risk reduction programs proliferated over

✉William H. George, bgeorge@uw.edu.

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decades and have shown demonstrable—albeit limited—success in increasing condom use [1, 2]. A biomedical intervention then emerged—antiretroviral therapy (ART). ARTs consist of a combination of antiretroviral (ARV) drugs that suppress an infected individual's viral load (i.e., the quantity of virus in a given volume of body fluid), thereby stopping disease progression and preventing HIV transmission to uninfected individuals. ARVs have also been developed for those who are uninfected. These medications, known as pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP), prevent transmission when taken before or after HIV exposure. Overall, gains in mitigating the epidemic are evident in reduced rates of new diagnoses, the number of people living with HIV (PLWH), and AIDS-related deaths. Despite this progress, worldwide in 2019 there were approximately 1.7 million new infections, 38 million PLWH, and 690,000 deaths [3]. Thus, HIV/AIDS remains a significant health threat worldwide and continues to exact an enormous economic burden.

Until a true HIV vaccine emerges, further mitigating the epidemic will depend on developments in a variety of evidence-based components. First, advancing basic research for a more complete understanding of the factors associated with transmission risk behaviors serves as the foundation. The capacity to prevent HIV risk behavior ultimately hinges on scientists' ability to understand what drives it and what retards it. Second, etiology is prelude to intervention—exploiting the knowledge gains and insights derived from the aforementioned research efforts is critical to design, modify, and innovate HIV interventions. Third, in what now amounts to a newly reconfigured intervention landscape constituting a nexus between psychosocial and biomedical strategies, the future research and intervention agendas must attend not only to elucidating and preventing sexual risk behaviors, but also identifying and preventing deficiencies in medication adherence.

Alcohol is one of the most robust factors associated with HIV risk behavior. Broadly, HIV-related sexual risk behaviors, such as casual partnering, partner concurrency, and condom nonuse, have been associated with a host of alcohol variables, including alcohol expectancies, typical drinking quantity, and drinking before sex. For the present purposes, alcohol-related behavioral risk (ARBR) refers primarily to the link between indicators of acute alcohol intoxication and the proximal likelihood of engaging in sexual behaviors vulnerable to HIV transmission. For example, showing that rising acute intoxication increases the likelihood of condom nonuse during vaginal or anal sex is a demonstration of ARBR. In the era of ARVs, another ARBR path of note is alcohol's impact on variables linked to the prevention or acquisition of HIV, but less proximally so, such as reduced PrEP/PEP adherence.

The goal of this paper is to examine the implications of ARBR studies and how they might inform future research on intervention design, modification, and innovation. Specific aims are to first describe alcohol challenge experiments as a method for examining ARBR. "Alcohol challenge" has traditionally referred to laboratory procedures that involve administering alcohol (orally or intravenously) under controlled conditions to research subjects (human or animal) and has gained increasing usage to refer to any alcohol administration research protocols. In alcohol challenge ARBR experiments, acute intoxication is manipulated using an experimental design and its effects are evaluated on sexual risk variables measured under controlled laboratory conditions. Second, we describe

illustrative ARBR empirical findings and theory support that have resulted from alcohol challenge experiments. Third, we discuss implications for how ARBR research could inform future intervention work, noting three perspectives: (a) scaling up or extending existing interventions, (b) modifying existing interventions, and (c) innovating new interventions. Finally, future research directions will be considered.

ARBR and Alcohol Challenge Experiments

ARBR evidence began emerging from surveys conducted early in the HIV/AIDS epidemic [4]. Nonexperimental studies proliferated rapidly [5] and were essential to establishing initial empirical evidence linking alcohol with sexual behaviors vulnerable to HIV transmission. Since then, ARBR has been the subject of considerable research using a variety of methodological approaches, including qualitative interviews, quantitative surveys, and experiments. Broadly speaking, this research has addressed three overarching questions on ARBR: (a) What aspects of a person's background and prevailing social circumstances determine that they wind up in a situation in which there exists an opportunity for ARBR? (b) What aspects determine that they will experience acute alcohol intoxication in said situation and how intoxicated they become? (c) Finally, once in the situation, how is it that acute alcohol intoxication causally contributes to ARBR?

Both nonexperimental and experimental studies have been conducted to address the latter question about causality. Relying on prospective survey methods, including event-level [6], daily diary [7], and ecological momentary assessments [8], investigators have shown that alcohol contributes causally to ARBR. Such findings provide external validity corroborating alcohol challenge studies, which—through rigorous experimental methods—have established the internal validity of alcohol's capacity to exert a causal impact on sexual risk behaviors [5, 9–12].

Thus, the previously open-to-debate assertion of alcohol's causal role in sexual risk behaviors now stands as "settled law" —no longer subject to reasonable dispute. This assertion is especially true when appraising the body of evidence from alcohol challenge experiments and when stated with the following precision: Acute intoxication exerts a causal impact on sexual risk intentions and behaviors; and this is an augmentation effect that increases with dosage. An outstanding question to be informed by the growing body of event-specific prospective survey work concerns identifying factors influencing whether the established alcohol-sexual risk behavior causal effect materializes in any particular real-world instance. However, the foundational work establishing causality emerged as a result of alcohol challenge experiments.

Alcohol Challenge Experiments: Goals, Advantages, History, and Prototypic Methods

It is important to first delineate the goals of alcohol challenge experiments and provide an illustration of the methods before considering the findings and how they might inform intervention work. A goal of any controlled experiment is to evaluate the validity of a causal hypothesis. In addition to the obvious need to control extraneous influences that might contaminate the findings (e.g., pre-drink food consumption), the *sine qua non* of an alcohol challenge experiment is the random assignment of research participants to alcohol

versus control conditions (i.e., who is administered alcoholic beverages versus non-alcoholic beverages). As a consequence, any differences between the two groups on sexual risk variables measured under laboratory conditions can only be caused by alcohol and all other rival explanations ruled out. A distinct advantage of experimental methods for researching alcohol is that its constituent features can be disaggregated and evaluated as separate, yet interrelated alcohol variables, including the amount consumed, the expectancy set as to whether the consumed beverages contain alcohol or not, the breath alcohol concentration (BrAC) level achieved, subjective intoxication, speed of consumption, and the BrAC limb (i.e., whether BrAC is ascending or descending). These alcohol variables can be validated unequivocally. Another advantage is that alcohol challenge experiments permit a definitive determination of the causal ordering of events. Specifying that the drinking precedes sexual risk behavior is significant because it controls for the reverse-causation possibility. For example, in the real world, a person may decide to pursue an opportunity for risky sexual behavior and proceed to drink alcohol in anticipation, creating the artifactual impression that alcohol played a causal role. Finally, because experiments allow simultaneous consideration of distal and proximal determinants, they foster theory refinement and advancement based on identification, isolation, and evaluation of mediating and moderating mechanisms. Given these important advantages, alcohol challenge experiments have provided the best source of evidence for evaluating causal factors in ARBR.

Despite these advantages, alcohol challenge experiments have faced a seemingly insurmountable limitation—sexual behavior cannot be investigated directly. Indeed, most human subject research ethics regulations would prohibit direct observation and measurement of any naturalistic post-drinking sexual behavior. Further, the alternative method of sole reliance on participants' self-reports can be justifiably deemed suspect, owing to a variety of reporting biases and motives. For example, someone may exaggerate drinking to deflect responsibility for regretted sex. However, despite genuine constraints in measuring sexual behavior directly, researchers have succeeded in developing and establishing an array of laboratory methods for measuring constituent elements of ARBR, such as genital sexual arousal [13, 14], subjective sexual arousal [15], casual sex likelihood [16], condom use intentions [17, 18], condom negotiation skills [19, 20], condom use resistance [21], condom decision abdication [22], anticipated partner reactions to condom requests [23], and perceived risks of sex with a new partner [24].

Alcohol challenge experiments on ARBR began appearing in 1996—ten years after the Stall et al. [4] ARBR study [5]. An initial wave of ARBR experiments provided clear evidence of causal linkages between acute alcohol intoxication and sexual risk behavior. Impressively, this support emerged from five independent research teams [24–28]. Replication across different teams and protocols strengthened confidence in this linkage. This evidence also provided varying support for both prominent explanatory models of alcohol's effects: alcohol expectancy theory and alcohol myopia theory.

However, a limitation of this initial wave of alcohol challenge experiments was that protocols largely emphasized corollary factors constituting "cold state" variables (e.g., attitudes, knowledge) and simulations (e.g., non-eroticized third-person analogues) of sexual risk behaviors. Real-world sexual encounters occur in the "heat-of-the-moment." In fact,

apart from alcohol, high sexual arousal drives riskier sexual behavior than low arousal [29, 30] and insufficient incorporation of “hot state” variables (e.g., positive affect, sexual arousal) and simulations (e.g., eroticized second-person analogues) inherently limits face validity. Furthermore, research on cold-to-hot empathy gaps suggests that responding in real-life heat-of-the-moment encounters is more accurately predicted when participants are assessed in “hot state” rather than “cold state” protocols.

In first-wave ARBR experiments, representation of “hot states” known to impact real-world sexual risk behaviors was decidedly limited. As a result, a subsequent wave of alcohol challenge experiments ushered in a shift to emphasize “hot state” variables and simulations [31–34]. These second-wave ARBR experiments incorporated heat-of-the-moment paradigms in which participants projected themselves into a highly eroticized story depicting a credible sexual encounter. An overarching aim of these studies was to provide a comprehensive account of the states, motivations, perceptions, and processes that immediately precede and ultimately result in sexual risk taking.

Prototypic Methods in Heat of the Moment Protocols for Assessing ARBR

We and our colleagues have published more than two dozen reports utilizing heat-of-the-moment paradigms to evaluate a variety of dispositional and situational factors affecting ARBR. Our prototypic methods and procedures include the following components. (a) Participants of drinking age (21–30 years old) are recruited, screened for inclusion criteria (e.g., sexually active, but not in an exclusive relationship) and exclusion criteria (e.g., problem drinking), and scheduled for an individual laboratory session for which they are instructed to follow pre-experimental restrictions (e.g., zero BrAC level upon arrival, no food consumption in the prior four hours). (b) Upon arrival to the lab, and after informed consent, participants complete a questionnaire battery assessing a host of demographic, dispositional, and behavioral constructs as well as baseline affective and sexual arousal assessments. (c) Each participant is randomly assigned to either an alcohol condition with a specified target dosage (e.g., placebo, 0.04, 0.08, 0.10) or a control no-alcohol condition. The amount of alcoholic beverage (e.g., 80 proof, 100 proof, 190 proof) and mixer (e.g., juice or soda) administered is determined ideographically based on body weight and gender. To create a heavy episodic consumption experience, drinks are poured equally into three glasses and participants are instructed to consume each glass in three or four minutes. The amount of time allotted for alcohol absorption is also determined ideographically [35]. Therefore, participants in an alcohol condition are assessed for BrAC level every four minutes until they reach a predetermined criterion sub-peak BrAC level on the ascending limb of the BrAC curve. To equilibrate the absorption period and procedures across conditions, each control participant is yoked to an alcohol participant. (d) After achieving criterion BrAC level, the participants are instructed to read and project themselves into a story written in the second-person describing a sexual encounter in which the protagonist (i.e., the participant) is on a date with an attractive new or casual partner. The story is extensively piloted and calibrated to evoke high levels of realism, emotional response, and sexual arousal. Depending on the particular experiment and hypotheses, additional independent variables can be manipulated prior to the start of the story (e.g., instructions to maximize or inhibit sexual arousal) and/or within the story narrative (e.g., positive versus

negative emotional context, partner pressure to forgo condom use, differing rationales for condom use). As the story progresses, it becomes increasingly eroticized and is paused periodically to assess a variety of dependent measures, such as sexual arousal, perception of partner's characteristics and responses, desire and intentions to engage in various sexual acts, intentions to use a condom, willingness to abdicate sexual and condom decision making to the partner, etc. (e) At the end of the story, participants complete a number of ratings assessing manipulation checks, their degree of engagement with the story, and story realism. (f) Finally, participants are debriefed about the nature of the research and, in the alcohol condition, directed to a detoxication phase and retained until their BrAC drops below 0.03% (in accordance with recommendations for ethical administration of alcohol to human subjects [36]).

Because sexual behavior cannot be observed ethically in real time, all assessments of sexual risk behaviors encompass inherent sacrifices in validity. For instance, while nonexperimental surveys enjoy strong external validity, event-specific queries about ARBR are by necessity retrospective and thus subject to a variety of reporting biases—a challenge to internal validity. In the above prototypic heat-of-the-moment paradigm, as in all laboratory sexual risk behavior assessments, validity concerns arise. Two internal validity questions (Are participants truly intoxicated? Are participants sexually aroused?) get demonstrably affirmed. Breathalyzer assessments ascertain intoxication; and physiological and subjective indices attest to arousal [32]. Another internal validity question (Do participants effectively project themselves into the heat-of-the-moment paradigm?) is affirmed by post-experimental queries. In numerous studies using projection protocols, the evidence is highly robust based on ratings of relevance, realism, and ease of projection into the scenario. Clearly, with respect to internal validity, the acute "hot states" of import—intoxication and sexual arousal—are activated and exert proximal effects on ARBR measures. Regarding external validity or correspondence between projection protocols and real-world behavior, we found that participants' reports of their past and projected future condom use were significantly correlated with their likelihood of sexual risk behaviors [37, 38]. Finally, the truism that laboratory behavior has low external validity has been largely vanquished empirically. This has been best exemplified by an extensive analysis of effects sizes from over 38 laboratory versus field study pairs across a wide range of behaviors [39]. Overall, there is substantial conceptual and empirical support for the validity of experimental assessments of ARBR.

Findings from ARBR Alcohol Challenge Studies

Findings from alcohol challenge experiments conducted to date highlight several points. First, —and this is important given the current zeitgeist of justifiable concern about replicability of psychological experiments—there is independent replication using a variety of protocols showing clear evidence of causal influences. Second, despite the pragmatic and ethical constraints on analogizing ARBR in the lab, investigators have succeeded in developing and implementing credible protocols. Third, these researchers have identified in-the-moment processes that immediately precede sexual risk behaviors and have demonstrated the theoretical importance of these constructs. Fourth, simultaneous consideration of distal and proximal determinants has advanced identification, isolation, and evaluation of mediating and moderating mechanisms. Several variables may function as

co-factors in ARBR situations. For instance, sexual sensation seeking [20], effortful control [7], alcohol expectancies [40], relationship factors [41, 42], and sexual victimization history [34] have been associated with ARBR in alcohol challenge experiments.

Furthermore, findings almost uniformly support the utility of alcohol myopia theory (AMT; [43] as the best framework to understand intoxicated sexual risk taking. This support is illustrated in experiments showing the following findings. (a) Alcohol effects increase with dosage [32], which would not be predicted from an alcohol expectancy framework. (b) Alcohol affects risk indirectly via relevant subjective states, including (i) positive mood [17, 44], (ii) sexual desire [17] and sexual arousal [32, 45–48], (iii) perceived intoxication [45], (iv) perceived sexual potential [49, 50], (v) implicit approach bias toward erotic stimuli [51], (vi) anticipated partner response to condom request [22, 23], and (vii) emotional numbing and refusal self-efficacy [52]. (c) Alcohol focuses the individual cognitively to impelling cues in the situation [49] and a weighted composite of impelling/inhibiting cognitions mediates alcohol's effects [15, 31]. In sum, the available science warrants the conclusion that alcohol can and does increase the likelihood of sexual risk taking through attuning intoxicated participants to internal states congruent with sexual gratification. Alcohol's capacity to focus the drinker myopically on impelling cues—despite extant risks in a sexual encounter—fosters sexual risk behaviors.

ARBR Prevention Implications: Three Perspectives

Three perspectives emerge in contemplating translational insights from alcohol challenge experiments. The landscape of existing HIV interventions is extensive, replete with a wide range of programs targeting a wide range of specialized populations. Therefore, an obvious starting point is to articulate how ARBR findings might be used to scale up or extend existing interventions that are already available. Second, rather than simply scaling up and extending, an alternative perspective is to explore how existing interventions could be modified to incorporate lessons gleaned from alcohol challenge experiments. Finally, a more adventure-some perspective is to consider how these lessons could be used as the basis for innovating new interventions.

Scale Up and Extend Existing Interventions

As noted, psychosocial interventions have been shown to be effective in reducing HIV risk-related behaviors. For example, in the United States, the CDC's Risk Reduction Chapter of its Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention lists 59 evidence-based interventions [53]. The majority of these programs are tailored for particular groups known to be at elevated risk for HIV, based on factors such as age, gender identity, sexual identity, race/ethnicity, serodiscordant coupling, incarceration history, risk patterns (sex work, injection drug use), STI status, or intersectionality of these factors. Summarizing across these programs, most consist of psychoeducation and cognitive-behavioral content delivered in individual, group, or video format across one or multiple sessions and target issues such as basic sex education, condom use and negotiation, HIV/STI testing, safer sex self-efficacy, social support, and partnering patterns (e.g., reducing partner concurrency). Other countries as well as multinational organizations similarly provide

guidance on evidence-based psychosocial prevention programs. However, targeting alcohol use and heat-of-the-moment factors is uncommon in most interventions. By demonstrating that alcohol has a causal effect, a clear implication of alcohol challenge experiments is that sexual risk behavior can be reduced indirectly by reducing alcohol consumption [54] and there has been documented success in this regard [55]. Some interventions have combined and/or integrated sexual behavior content with alcohol content and shown risk reduction [56].

Apart from the straightforward implication of scaling up and extending existing risk reduction interventions by better targeting alcohol use, it is important to consider the nexus of psychosocial and biomedical strategies. Thus, an emergent but critical point necessarily subsumed within our aim of identifying implications of alcohol challenge findings is this question: What implications might these findings have for the intersection of existing interventions and PrEP/PEP?

PrEP/PEP and Existing Interventions

With the expansion of biomedical approaches to include targeting of uninfected individuals, the idea of extending and scaling up interventions now necessitates consideration of the intersection between PrEP/PEP and existing psychosocial interventions. The advent of PrEP/PEP is still sufficiently recent that ideas for addressing this intersection in the context of ARBR are by necessity embryonic, but center on identifying psychosocial barriers to PrEP/PEP effectiveness and integrating with existing interventions targeting PrEP/PEP.

Psychosocial Barriers to PrEP/PEP Effectiveness

For HIV negative individuals, PrEP and PEP are two biomedical approaches found to be effective at preventing HIV infection. PrEP is an FDA-approved daily medication (i.e., Truvada™, Descovy™) that reduces HIV risk by over 90% and is recommended for use in conjunction with safer sex practices (e.g., consistent condom use, regular STI/HIV testing) [57]. PrEP is indicated for high-risk sexually active individuals exhibiting one or more of the following characteristics: inconsistent condom use, recent STI diagnosis, involvement with an HIV positive sexual partner, or having used multiple courses of PEP [58]. It is also indicated for injection drug users, but with slightly less efficacy (reduces HIV risk by 74%; [58]). Despite PrEP's potential in curtailing new HIV infections, uptake in the real-world has been slow, likely due in part to a number of individual and structural barriers (e.g., *individual level*: low PrEP awareness, low HIV risk perception, stigma, mistrust of the medical system; *structural level*: PrEP accessibility, medical provider PrEP knowledge and willingness to prescribe, insurance coverage) [59–63]. Among those who do initiate PrEP, medication non-adherence is a major concern as this reduces the level of medication in the blood needed to fight infection if exposed. Barriers to adherence in PrEP trials have included heavy drinking, forgetting, stress, side effects, changes in routine, and missed medical appointments [64–67].

Unlike PrEP, which is used daily to prevent risk of future infection, PEP is an emergency intervention taken after suspected exposure to HIV. PEP works by reducing the possibility of seroconversion post-exposure [57]. To be effective, it must be started within 72 h and taken

1–2 times daily for a total of 28 days [68]. PEP is indicated for individuals who are HIV negative, but who may have been exposed to HIV during sex, drug use, sexual victimization, or as part of their occupation (e.g., first responders, healthcare workers; [68]). For those who have used multiple courses of PEP—especially in the context of consensual sex or drug use—efforts to shift these individuals to PrEP is of high priority. However, similar to PrEP, adherence to PEP tends to be poor [69, 70].

Interventions Targeting PrEP/PEP—A small, but growing number of psychosocial interventions have begun to target PrEP uptake and adherence. Less intervention work, however, has focused on PEP. To date, most research has focused on the feasibility and acceptability of PrEP programming in clinic settings with samples of men who have sex with men [71–73] or injection drug users [74, 75]. Interventions typically involve psychoeducation and problem solving, with an emphasis on providing accurate PrEP information (i.e., what it is, how it works, benefits and side effects), identifying barriers to PrEP initiation and/or adherence, and collaboratively problem-solving barriers. Less common is the inclusion of other sexual risk reduction strategies or discussion of alcohol and other drug use as contributing factors to PrEP non-adherence and/or sexual risk (for exceptions, see [72, 75]). These topics are particularly important given concerns for risk compensation (i.e., decreased condom use) as a result of PrEP initiation. Preliminary findings indicate that PrEP programming is both feasible and acceptable and some have shown improved rates of uptake and/or adherence. However, these studies are comprised of small samples, often lack control groups, or are pilot tests subsumed within larger medication trials. Further testing in the context of randomized controlled trials will reveal the true impact of these interventions as the PrEP literature continues to grow. If effective, these strategies could be easily translated to PEP interventions.

The lessons learned from ARBR can assist in scaling up and extending developing PrEP interventions. First, consistent with the CDC's agenda of high-impact prevention [76], increasing PrEP awareness among those at elevated HIV risk, including gay and bisexual men, other men who have sex with men, transgender women, injection drug users, and sex workers, must be expanded. Awareness campaigns are a key step to improving PrEP knowledge, reducing stigma, and increasing uptake. This information could also encourage frequent PEP users to shift to PrEP. However, to date, awareness efforts have largely focused on men who have sex with men [77]. Work within ARBR has identified other "hidden" populations at elevated HIV risk, such as women who drink heavily or women who have been sexually victimized [34], and who may exist within or outside of the CDC's high-impact prevention groups. Apart from medication trials, funding priorities have often left high-risk women out of PrEP programming [78], even though the majority of women's HIV infections are acquired from sex with men [79]. Greater inclusion of high-risk women into PrEP awareness campaigns could help reduce up to ¼ of new HIV infections if PrEP uptake were to increase in this group. Further, PrEP awareness efforts could have a particularly powerful effect in late adolescence and early young adulthood, when alcohol and sexual risk patterns begin to unfold. This, however, will require more creative outreach strategies to engage youth and young adults, such as social media campaigns, advertisements on streaming services, sexual health promotion at community events, targeting social and

community networks, and/or peer support models. As PrEP awareness campaigns are developed, researchers can draw on user centered design [80], an innovative approach from the technology sector, to incorporate high-risk groups into all stages of planning in order to ensure that awareness messaging is developmentally appropriate, understandable, and engaging. This is important because the decisions made early in prevention development (e.g., language used, message framing, delivery method) have the potential to greatly influence its impact—in this case—PrEP awareness and subsequent uptake.

As awareness increases so too will the need for interventions to support high-risk groups with PrEP uptake. Given that PrEP (and PEP) require a prescription, bundling interventions into health care services will be a critical step in this effort. The CDC has proposed a collaborative model to help coordinate PrEP care (i.e., screening, initiation, follow-up) between community-based organizations and medical clinics [81]. In this model, community organizations, such as health departments, LGBTQ centers, needle exchange, and sexual assault centers, can provide PrEP education and conduct initial screenings before referring high-risk individuals to clinics for initiation. This approach has the potential to capture hidden or hard-to-reach high-risk individuals who might not otherwise present to clinics for PrEP care [81], such as those identified as high risk within ARBR studies (e.g., women who drink heavily, women who have been sexually victimized). Early in the uptake process, community organization interventions could address initial barriers to uptake (i.e., information, access, cost and coverage) as well as support high-risk individuals with referral follow-through. In addition, community organization interventions could assist with ongoing PrEP (and PEP) support after initiation, such as medication adherence as well as alcohol and sexual risk reduction skills training. Collaborative models can be challenging to implement in the real-world, but represent an important untapped area for research and program development. To bypass these challenges, existing PrEP interventions have sought to embed themselves directly within medical clinics [71–75]. For these interventions, expanding clinic-based PrEP screening to include sexual victimization experiences (particularly in women), alcohol or other drug use, and history of PEP use could help identify hidden at-risk groups in need of PrEP. In addition to existing intervention components (i.e., psychoeducation, problem solving), alcohol and other drug use must be addressed, as substance use patterns can contribute to medication non-adherence [82], but also risky sexual partner selection, sexual abdication, and inconsistent condom use [22, 23]. Further, sexual risk reduction skills to reinforce condom use while on PrEP should be emphasized early and often. Similar programming can be incorporated for PEP. Given the time constraints faced in clinics, psychoeducation and skill building could be delivered by other staff (e.g., physician assistants, nurses, social workers), in skill building groups, or through technology.

As disparities in access to and use of technology continue to shrink, developing PrEP/PEP interventions can exploit key technology trends to improve uptake and adherence. Technology-based interventions (e.g., computer, phone, or text message delivered) have unique advantages relative to in-person administration, including reduced cost, ability to personalize content, privacy in accessing content, and improved reach and dissemination [83, 84]. For prevention interventions, technology can be used to promote PrEP information and awareness, especially in the context of risk behaviors, such as seeking out sexual

partners via hookup apps or websites. Further, technology-based interventions have been effective at increasing ART adherence for PLWH [85–87]. PrEP interventions delivered through technology are still in the early stages of testing, but suggest feasibility and acceptability with using text messages to provide daily medication reminders, supportive check-ins, and to a lesser degree, risk reduction messaging [75, 88]. These studies did not, however, examine how text messages influence behavior (i.e., adherence, condom use, alcohol or other drug use). Starting at PrEP/PEP initiation, behavioral adherence strategies, such as creating a dosing schedule, setting reminders, having physical cues for reminders, and planning ahead for routine changes, should be discussed and barriers problem solved. This should include problem solving around how alcohol use patterns can interfere with medication adherence. A personalized medication management plan could then be incorporated into app- or text-based reminders and sent daily to promote adherence and provide support. In addition, technology-based PrEP/PEP interventions can assist in teaching brief alcohol and sexual risk reduction strategies to reinforce consistent condom use in conjunction with medication. Sexual risk interventions are increasingly making their way online [83], but key to this delivery method is early participation from high-risk groups as part of intervention development. Without early involvement, we run the risk of creating interventions that aren't engaging and won't be used.

Modify Existing Interventions

Existing psychosocial interventions can be strengthened by incorporating modifications informed by alcohol challenge experiments. This overarching strategy involves identifying, cultivating, and integrating evidence-based content derived from prominent theoretical and empirical lines of work. Based on this work, modification emphases are indicated for alcohol expectancies, alcohol myopia, sexual arousal, risk perception, sexual abdication and partner risk, and condom use resistance. While alcohol challenge experiments addressing the era of ART have yet to emerge, the current findings have implications for interventions related to ARV/ART and will be explored.

Alcohol Expectancies

ARBR findings point to the importance of alcohol expectancies, defined as the expected effects of drinking alcohol. Investigators have primarily operationalized alcohol expectancies either by contrasting placebo drink conditions (expect-alcoholic-drinks/receive-nonalcoholic-drinks vs. expect-nonalcoholic-drinks/receive-nonalcoholic-drinks) [28], by administering questionnaires assessing the expected effects/consequences of drinking [89], or by using both operationalizations within the same study [19, 20, 24–26]. Generally, with few exceptions, placebo-only studies have demonstrated little support for the importance of expectancies for sexual risk. However, studies using both operationalizations or questionnaire-only operationalizations have generally provided robust support for the importance of alcohol expectancies as moderating or mediating factors [9], suggesting that one approach for modifying existing interventions is to develop content devoted to expectancies. Alcohol Expectancy Theory and corroborating empirical evidence indicate that (a) alcohol's sexual effects are not strictly a result of pharmacology—expectancies matter; (b) alcohol expectancies shape decisions to drink and how much one drinks;

(c) self-fulfilling prophecies about what is expected sexually from drinking alcohol and deviance disavowal expectancies about alcohol as an excuse for disinhibited sexual behavior both shape how one behaves after drinking begins; and (d) alcohol expectancies are malleable and can be targeted through cognitive restructuring. A clear implication is to develop psychoeducation that can be modularized and grafted onto existing intervention programs. For instance, one emphasis in such content could focus explicitly on challenging the conventional wisdom that alcohol's effects are determined by solely pharmacological processes rather than psychological processes. This emphasis aims to demonstrate that post-drinking sexual risk-taking is largely a product of modifiable cognitions and choices rather than strictly biological determinism. This line of messaging directly contradicts the conventional wisdom and instead advances the counternarrative that sexual risk mitigating cognitions and choices can be adopted and implemented before, during, and after consuming alcohol.

Another important implication of this line of ARBR work is simply that alcohol expectancies are measurable. Numerous questionnaires have been developed and validated to measure expectancies [90–93], including sex-related alcohol expectancies [94–96]. Such measures can gauge pre-to-post-treatment changes in alcohol expectancies, thereby evaluating the mechanism driven impact of psychoeducation and cognitive restructuring. Relatedly, such measures can be useful in risk reduction interventions by enabling clinicians and researchers to identify individuals at particularly high risk for pre-sex drinking and/or post-drinking sexual risk taking, thereby evaluating an idiographic influence that could moderate intervention impact.

Yet another implication involves the "Expectancy Challenge" intervention [97]. This intervention has been shown to be effective at reducing endorsement of alcohol expectancies as well as alcohol consumption [98, 99]. The challenge is "designed to illustrate the effects of alcohol-related expectancies through experiential learning in a group setting" [99, p. 394]. In the original procedure for this intervention, participants were randomly assigned to consume alcoholic or placebo drinks and engage with co-participants in a group activity involving playing games and evaluating the sexual attractiveness of women in photos. Afterwards, participants judged who had consumed alcohol or placebo. The resulting high error rates proved to be a powerful demonstration of the potent influence of alcohol expectancies, providing mutative insight into psychologically driven "alcohol" effects. Several adaptations of this intervention have been implemented in a number of clinical trials [99]. The Expectancy Challenge could readily be adapted as a module for existing HIV interventions as an experiential springboard to expectancy modification.

Alcohol Myopia

Experimental studies have found strong support for the AMT, and the Inhibition Conflict Model of AMT [43, 100], in explaining ARBR. The unstipulated version of AMT posits that a pharmacologically driven reduction in cognitive capacity narrows a drinker's attention toward salient—often impelling—cues, and away from less salient—often inhibiting—cues. When applied to sexual decision making, AMT would suggest that in a typical sexual situation, a drinker may focus on the salient cue of sexual arousal, which would therefore

be the driver of ARBR, over less salient or distal cues that may otherwise inhibit risk taking behavior when sober, such as the partner's potential sexual risk. The Inhibition Conflict Model of AMT further stipulates that alcohol facilitates disinhibitory behavior only under conditions of high conflict—when impelling and inhibiting cues are both strong—as opposed to conditions when either impelling or inhibiting cues are strong and the other is weak or when both are weak. Hence, alcohol would have its strongest effects in situations in which there are strong instigatory and strong inhibitory cues. When impelling cues dominate, the behavior is likely to happen regardless of whether the individual is intoxicated or not.

A recent meta-analysis of alcohol challenge experiments evaluating alcohol effects on sexual decision making concluded that, consistent with the AMT, individuals who consumed alcohol reported higher sexual arousal and were more likely to report sexual risk intentions compared to those who received placebo or no alcohol beverages [12]. In a series of studies, MacDonald et al. [101] concluded that sexual arousal is a strong internal impelling cue, even in sexual situations involving disease risk. Further, when intoxicated, men's ability to consider inhibiting risk cues is impaired and they instead focus on salient arousal-related impelling cues, resulting in an increased likelihood of ARBR. Indeed, intoxicated men and women report greater attention to impelling cues and thus greater sexual risk intentions than their sober counterparts, and it was the attention to cues that explained the association between intoxication and risk intentions [31], particularly when the impelling cue was subjective—rather than physiological (e.g., sexual arousal; 32). Additionally, in an experiment that manipulated sexual arousal and alcohol conditions, Simons et al. [51] found that men who were aroused or intoxicated exhibited a bias toward approaching (versus avoiding) sexual stimuli and a bias toward sexual stimuli relative to condoms as assessed by a reaction time task. These results further support the AMT and highlight the importance of acute intoxication relative to alcohol expectancies in the process of attending to cues consistent with impellance (sexual stimuli) versus inhibition (condoms).

Importantly for ARBR interventions, alcohol intoxication has been found to reduce sexual risk taking in some individuals [102]. Although this may initially seem contrary to AMT, in fact it further supports AMT and its potential for modifying existing interventions. Indeed, if inhibitory cues are more salient than impelling cues, alcohol intoxication results in reduced risk taking relative to sober conditions presumably by harnessing the drinker's reduced cognitive capacity and narrowing of attention to focus on inhibitory cues as a way to facilitate less risky behavior [101, 103]. Although more research is needed to evaluate the impact of enhancing the salience of inhibitory cues to reduce ARBR, this provides a promising empirically supported approach for future interventions to incorporate.

Sexual Arousal

Alcohol challenge studies substantiated empirically what was understood intuitively—sexual arousal is a potent motivational state and plays an influential role in ARBR. The nature of the influence varies based on gender, the arousal dimension, and alcohol dosage or limb. Generally, for both men and women, the subjective dimension of arousal exerts a causal impact on sexual risk behavior and mediates alcohol's impact. That is, alcohol increases

self-reported arousal, which in turn increases sexual risk taking. Ironically, the genital dimension of arousal—when assessed physiologically—has little impact [32]. For men at low to moderately high dosages (BrAC ≤ 0.10), genital arousal is largely unaffected by alcohol; and, although it correlates with subjective arousal, genital arousal has no direct effect on sexual risk taking. For women at equivalent dosages, alcohol actually decreases genital arousal, which in turn has no relation to either subjective arousal or sexual risk taking. For both men and women, these alcohol-arousal-risk relationships are specific to the ascending limb of the BrAC curve, and are not evident on the descending limb [45]. These findings and others have notable implications for cultivating intervention content.

Now that there exists a robust empirical basis—which was not previously well established—for the alcohol-arousal-risk link, prevention interventions can and should include psychoeducation directly addressing this nexus. Key psychoeducational messaging is that alcohol enhances sexual risk taking through heightened subjective sexual arousal—regardless of whether this is understood via alcohol expectancies, alcohol myopia, or a combination thereof. By simply identifying and acknowledging this evidence base, intervention programming can legitimize targeting self-regulation of intoxicated sexual arousal as an explicit risk management objective. Further, the current evidence base specifies several other important points: (a) Alcohol's impact enhancing arousal is not reliant on genital physiology; the prepotent impact is on one's subjective self-perception of being highly sexually aroused. (b) Sexual arousal, subjective and genital, is subject to volitional control; and, this holds true even during states of low to moderately high levels of intoxication [13, 32]. (c) The alcohol-arousal-risk nexus is not a singular moment; instead, alcohol-involved sexual risk encounters are progressive sequences with generically discernable and describable phases (e.g., early- versus late-sequence arousal). The importance of the latter point lies in the possibility that risk reduction tactics and strategies could be construed as phase dependent [46]. For instance, through the use of heat-of-the-moment paradigms, we have identified early sequence arousal phases (i.e., before heavy petting and disrobing) that may be construed as prompting a "safety check" necessitating inquiries about condom availability and emphasizing arousal regulatory tactics and skills (for self and partner). This can be distinguished from late sequence arousal phases, which can be instead construed as prompting emphasis on condom request assertiveness, condom self-efficacy, sex refusal assertiveness, and safe extraction/escape strategies.

Finally, the above evidence and suggestions collectively provide "added value" to psychoeducation aimed at debunking common myths and misconceptions about sexuality. For instance, one myth depicts male physiology as an uncontrollable and indisputable determinant of sexual outcomes. Another portrays risky outcomes as inevitable consequences of drinking. Yet another depicts a sexual "point of no return" at which diversions to safer or non-sexual outcomes are definitively unavailable. The available ARBR science from alcohol challenge experiments involving sexual arousal now provide substantial psychoeducational bases for refuting these and related myths and misconceptions about sexuality and alcohol.

Risk Perception

Alcohol reduces one's ability to perceive risk, including sexual risk [24, 26, 40], and alcohol expectancies about the disinhibiting effects of alcohol on sexual behavior are associated with greater perceived positive consequences of sexual risk taking and greater endorsement of sexual risk [24]. Norris et al. [104] articulated the Cognitive Mediation Model to explicate the process whereby women make sexual decisions. However, this model has broader utility —beyond women—for understanding alcohol's role in reduced risk perception. It posits that a series of primary and secondary appraisals of contextual and environmental factors influence an individual's decision about engaging in sexual behavior. Primary appraisals refer to cognitive evaluations of the situation regarding its congruence with one's goals and the likelihood of achieving one's goals. Secondary appraisals include cognitive evaluations of the harm or benefit that could result from the situation in relation to one's overall goals.

Evaluations of the processes outlined in the Cognitive Mediation Model revealed that alcohol (both the pharmacological and expectancy effects) exerted its direct influence on individuals' primary appraisals [49, 105], specifically increasing positive evaluation of the situation's sexual potential. Alcohol's amplification of the level of sexual potential early in a situation influenced the subsequent secondary appraisals via an increased focus on impelling cognitions and reduced focus on inhibiting cognitions [105]. This reduced focus on inhibiting cognitions, including the partner's potential disease risk, increases the likelihood of engaging in ARBR. Conversely, heightened perceptions of the partner's potential disease risk are associated with less likelihood of ARBR [23].

Stemming from these findings, sexual risk reduction programs should target perceptions (and potential misperceptions) of sexual risk and sexual benefits early in a social encounter in which sex, particularly unprotected sex, is possible, especially when the encounters include drinking. There are many possible approaches for such an intervention, including providing psychoeducation and correcting normative misconceptions about alcohol's role in sexual behavior. Borrowing from the AMT literature, cueing inhibiting factors earlier in the encounter when an initial appraisal of the situation's sexual potential is made could serve to tip the scale toward a primary appraisal regarding sexual safety and thus a less risky behavioral response. Additionally, expectancy challenge or decision matrix approaches could be applied in this context to influence beliefs about the consequences versus benefits of alcohol's disinhibitory effect on sexual behavior.

Sexual Abdication and Partner Risk

Sexual abdication refers to "the willingness to forsake decisional power in a sexual encounter by letting a partner decide what happens sexually" [22], p. S136) and has been operationalized generally (e.g., letting the partner "decide how far to go sexually") and specifically (e.g., letting the partner "decide whether or not to use a condom"). Findings from ARBR experiments indicate that relationship potential [41], ambivalence about having sex [106], perceived condom-related conflict (i.e., wanting to use a condom, but perceiving that the partner does not; [107]), and anticipated negative partner reactions to condom requests [22, 23] predict sexual abdication; and abdication is associated with a lower likelihood of condom use [23, 41, 107]. In alcohol-involved sexual encounters, acute

intoxication not only decreases the desire to use a condom, but also increases perceptions that a sexual partner will not either [107]. Further, when there is moderate to high pressure to forego condoms, intoxication can increase expectations of a negative partner reaction to a condom request and subsequent abdication [22, 23].

Though this work has focused primarily on women, findings could also translate to men's condom use decisions. Existing psychosocial interventions focus on promoting condom use through strategies such as sexual communication, sexual assertiveness, and condom negotiation [53]. Biomedical interventions, however, do not typically include content on safer sex behavior outside of medication adherence (for exceptions, see [72, 75]). In modifying existing interventions, it is important that prevention messaging be framed within positive sexuality, thereby increasing individual motivation and self-efficacy in sexual decision making. This is consistent with findings that eroticizing sexual prevention strategies improves sexual attitudes, communication, and condom use [108]. In addition, building in psychoeducation around how relationship potential as well as high pressure situations can influence sexual decision making will be important. This content should also include how alcohol intoxication (through multiple pathways) increases sexual abdication and decreases condom use. Training in behavioral skills will be critical, such as identifying motivational factors that influence decision making (e.g., wanting a relationship, reducing conflict), decisional balance exercises to enhance safer sex behaviors, and practicing how to respond to high pressure situations with sexual assertiveness and refusal skills. Skills training with this additional content in mind can help promote sexual empowerment and agency for those who might otherwise let their sexual partners make key decisions that can affect sexual health in the short- and long-term.

Addressing sexual abdication and condom use is important as ARBR survey studies indicate a link between involvement with riskier sexual partners and STI/HIV risk above and beyond sexual patterns [109]. Partner risk characteristics can vary, but higher risk histories tend to include previous incarceration, intravenous drug use, sex with men, sexual concurrency, and previous STI history [109, 110]. In many cases, individuals tend to underestimate their sexual partners' risk [111] or believe their relationships are monogamous when they are in fact not [112]. Sexual history is not always discussed with new or casual partners, and when it is, partners can leave out important information that might otherwise influence condom use decisions. Psychosocial interventions do not typically target sexual partner selection or risk characteristics, but instead focus on improving safer sex behaviors more generally. Modifications to existing interventions can build on ARBR findings by increasing psychoeducation content on sexual partner risk and how alcohol can influence risk perception, partner selection, and subsequent condom use. Further, discussion around engaging in less risky sexual behaviors and consideration of PrEP as an extra source of protection for those who engage with higher risk sexual partners or sexual partners of unknown HIV status would be critical additions.

Condom Use Resistance

While psychosocial interventions often focus their efforts on motivating individuals to engage in more effective condom negotiation and increase their condom use, recent research

demonstrates that intentional resistance of condom use is also a worthy intervention target. Condom use resistance refers to active, deliberate attempts to avoid using a condom with a partner who wants to use one [113]. Individuals report using a variety of condom use resistance tactics that range from non-coercive behaviors (e.g., telling a partner that you have been tested for STIs with negative results) to coercive behaviors (e.g., lying to a partner about not having an STI). While both women [114, 115] and men [113] report engaging in condom use resistance, alcohol's influence on this sexual risk behavior has primarily been studied in men. For example, Davis et al. [21] reported that acute intoxication increased men's positive attitudes and social norms about condom use resistance as well as their condom use resistance self-efficacy and intentions. Moreover, several studies have demonstrated that acute intoxication interacts with preexisting individual factors such as depressive symptomology [116], hostility towards women [117], childhood sexual abuse [118], and sexual aggression history [119] to predict condom use resistance intentions, suggesting potential high-risk groups that would merit increased intervention efforts. Finally, Davis and colleagues have reported in two separate alcohol administration studies [120, 121] that aggression-related alcohol expectancies play a crucial role in intoxicated men's condom use resistance intentions through their effects on proximal emotional states such as anger. Such findings indicate that future research should evaluate the effectiveness of interventions that (a) are aimed towards men with stronger alcohol-aggression expectancies and (b) incorporate content regarding emotional states proximal to sexual risk behaviors. In sum, although empirical evidence is needed regarding the influence of alcohol on women's condom use resistance, research findings to date clearly and consistently demonstrate that alcohol increases men's engagement in this risky sexual behavior and suggest potential paths forward for targeting and tailoring interventions to reduce men's alcohol-involved condom use resistance.

Exploring Psychoeducational Content about ARV

ARVs, whether taken to prevent or control HIV infection, are critical to the health of high-risk individuals. As discussed, central to biomedical interventions (i.e., PrEP, PEP, ART) is providing accurate medication information and counseling high-risk individuals to be adherent to their medication regiments. Important to uptake and adherence is ARV- and HIV-related stigma. Use of ARVs, especially to prevent HIV infection, is highly stigmatized. For HIV negative individuals, beliefs that PrEP users are promiscuous ("Truvada Whore") or HIV positive is widespread [122, 123]. These misconceptions are especially problematic given that medication stigma has been linked to less willingness to initiate PrEP [124], particularly among racial and ethnic groups at elevated HIV risk [125].

Minority stress models [126] posit that unique stress-ors associated with stigmatized identities can increase risk for substance misuse. In this light, individuals who are stigmatized as a result of ARV use, whether to prevent or control HIV infection, may have greater motivation to drink to cope with related distress, resulting in more problematic alcohol use patterns. Heavy drinking can influence medication adherence in a number of ways [82], including missed doses due to hangover, disrupted sleep, vomiting, or forgetting. Incorporation of harm reduction and other protective behavioral strategies to reduce alcohol use and consequences could be a critical addition to combined psychosocial and biomedical

interventions. This could include discussion of specific strategies to reduce problematic alcohol use, such as setting drink limits, alternating alcohol and non-alcoholic drinks, and planning to stop drinking at a predetermined time. In addition, drinking to cope may have a proximal impact on risk through acute intoxication and sexual risk taking. In conjunction with alcohol-related protective behavioral strategies, sex-related protective behavioral strategies can be incorporated, including taking your medication before going out, always carrying condoms with you, having a plan to discuss safe sex with your sexual partner, and bringing extra medication with you if you are planning not to go home. These strategies can be taught and reinforced throughout uptake and into the support stages.

Innovation of New Interventions

As delineated in previous sections, multiple promising interventions exist for the reduction of sexual risk behavior and improvement of medication adherence. However, many of these interventions require scaling up in order to add specific targeting of alcohol factors. In conjunction with adding alcohol-specific foci to existing approaches, the development of new and novel interventions is warranted. Such development can capitalize on recent scientific advances, including prioritization of the Science of Behavior Change (i.e., the experimental medicine approach), development of innovative methodological techniques, and focusing on novel risk groups that would benefit from targeted and tailored interventions.

Science of Behavior Change

Recognizing a gap between mechanism-focused basic science and outcome-focused clinical science, the National Institutes of Health have developed the Science of Behavior Change program with the intent of creating a unified, trans-disciplinary approach to investigating behavioral change by targeting mechanisms (e.g., neurological, affective, cognitive, interpersonal, behavioral) to improve clinical outcomes [127]. Rather than relying on interventions with multiple components that target numerous possible mechanisms and outcomes, the Science of Behavior Change program instead recommends taking an experimental medicine approach to behavior change. The tenets of this approach include the identification and measurement of specific malleable intervention targets and testing the role of these targets in creating behavior change across a variety of clinical outcomes through either experimental methods or the implementation of interventions designed to engage the stipulated targets. Thus, rather than focus on *whether* interventions work, this approach places emphasis on understanding *how* interventions work [127]. Because complex, multicomponent interventions are resource-intensive, an understanding of which specific intervention components work and through which specific mechanisms they create behavioral change can guide our efforts toward crafting the most parsimonious—yet effective and resource efficient—interventions. Unfortunately, most existing intervention research does not adequately assess mechanisms of behavior change. For example, a recent systematic review of National Institutes of Health funded medication adherence studies found only two that reported testing hypothesized mechanisms [128], leaving both researchers and interventionists in the dark about the reasons for intervention success or lack thereof. Overall, a greater focus on testing and explicating the mechanisms underlying

ARBR could not only improve the effectiveness of interventions, but also advance the field of intervention science more broadly.

Novel Methodological and Technological Approaches

Several methodological and technological innovations can facilitate a Science of Behavior Change approach to developing and testing interventions targeting ARBR. One particularly useful method is the proximal change experiment [129, 130]. Proximal change experiments test interventions that focus on "small, specific, measurable behavior changes," thereby providing preliminary evidence of an intervention's proximal effects and demonstrating that an intervention target is both malleable and a mechanism of behavior change [130, p. 165]; [131]. Such evidence of immediate effects can then serve as the empirical foundation for more resource-intensive, large-scale clinical trials focused on distal outcomes [130]. For example, interventions targeting the mechanisms underlying partner risk perception could be targeted and tested proximally, then scaled up if (a) the tested mechanism is indeed proximally improved by the intervention, and (b) the change in the mechanism results in proximal improvements in partner risk perception.

For interventions targeting ARBR, of critical concern is not only whether an intervention is effective after alcohol has been consumed, but also whether different mechanisms underlie sober versus intoxicated risk-taking behavior. The proximal change experiment is advantageous in this regard as it facilitates the use of an alcohol administration paradigm which can provide a rigorous evaluation of intervention efficacy and activated mechanisms during both sober and intoxicated states. Evidence obtained from such an approach can inform the development and adaptation of interventions that differentially and specifically focus on behavior change targets that may vary by states of intoxication and sobriety. For example, in one of the first examinations of state-specific intervention efficacy on sexual outcomes, Davis and colleagues [132] reported that alcohol intoxication dampened proximal intervention efficacy on hypothesized mechanisms underlying sexual aggression (e.g., emotion regulation, emotional states). This novel investigation not only provides evidence that proximal change experiments can be useful for examining the efficacy of interventions for sexual risk behavior that occurs in intoxicated states, but also highlights the role of proximal states, like emotions and arousal, in sexual decision making.

Although existing interventions sometimes acknowledge the role of proximal states and their influence on sexual decision-making (e.g., discussing emotional triggers that facilitate poor decision-making), these influences are discussed in a didactic rather than experiential way. As noted, heat-of-the-moment paradigms have been used in ARBR research to investigate the proximal factors underlying ARBR. However, their use could also be expanded to ARBR interventions [133]. For example, heat-of-the-moment paradigms could be utilized for pre- and post-intervention efficacy assessment. Additionally, such modules may serve as "reflective tools" for intervention participants, guiding them to consider their choices within different situations, contexts, and personal states. As such, heat-of-the-moment paradigms can provide opportunities for behavioral rehearsal during ARBR relevant states, such as intoxication and sexual arousal. While existing paradigms are typically in written format, technological advances may soon enable virtual reality heat-of-the-moment approaches to

be more feasible, potentially offering an even more immersive—and effective—intervention experience.

Technological advances will likely further augment researchers' ability to integrate multi-method approaches to ARBR investigations. For example, continued advances and improvements in wearable alcohol biosensors can offer investigators a means of capturing real-time and real-world alcohol intake proximal to actual risky sexual behavior. Such data could be integrated with data from alcohol challenge studies on a within-person basis in order to triangulate in upon alcohol's role in sexual risk through both internally valid lab experiments and ecologically valid field studies. Similarly, improvements in continuous, congruous measures of alcohol consumption, when coupled with other similar measures potentially relevant to sexual risk behavior (e.g., anxiety and other emotional responses) also gathered through wearable biosensors, may yield greater understanding of how these processes unfold at micro-levels (over minutes), meso-levels (over a situation), and macro-levels (over weeks or months). As another example, given the ubiquitous availability of cell phones, just-in-time adaptive interventions can utilize text messages, application push notifications, and the like to deliver a tailored intervention for the right individual at the right time. In these and likely myriad other ways, continued technological progress may not only be useful in further refining our understanding of the etiology of ARBR, but may also enhance our delivery of interventions effective for reducing ARBR.

Novel Populations

While specific populations (e.g., gay, bisexual, and other men who have sex with men, injection drug users) are viewed as having elevated risk for HIV transmission and certainly merit targeted interventions, other populations also should be considered when designing interventions to target ARBR. That is, individuals with certain characteristics or histories may be at greater risk of engaging in ARBR, and tailored interventions may be required to target the specific mechanisms that drive sexual risk in these populations. Although there are likely many predictors of increased risk for ARBR, one consistent predictor is a history of sexual victimization as well as a history of sexual aggression perpetration. In the following, we describe how ARBR interventions could specifically target and tailor their efforts towards individuals with such histories.

Decades of research has substantiated that women who have experienced sexual victimization in childhood, adolescence, or adulthood report elevated sexual risk indices compared to women without such histories, including greater engagement in ARBR [17]. Although a thorough review of this literature is beyond the scope of this paper, we highlight some aspects of this work to illustrate the implications of developing innovative interventions for this population. First, the extant literature indicates that the mechanisms underlying ARBR differ for women with and without sexual victimization histories. For example, because women with victimization histories are more likely than those without to use alcohol and sex to cope with negative emotions [134], they may benefit from interventions with a greater focus on adaptive emotion regulation skills. Laboratory research has also demonstrated that during states of acute intoxication, women's victimization history severity is predictive of anticipating that their partner will respond negatively to a condom

use request, and that such anticipation predicts greater likelihood to abdicate the decision about using a condom to their partner [22]. Such findings demonstrate that women with victimization histories may have specific proximal concerns that affect their behavioral risk, and that these considerations may result in decisions not typically addressed in risk reduction interventions (i.e., condom-decision abdication). As noted in Andrasik et al. [133], heat-of-the-moment paradigms could be an especially important reflective tool for tailoring interventions to these victimization history-specific nuances, particularly when used in conjunction with a proximal change experiment that includes both sober and intoxicated decision-making tasks. Tailoring of intervention content in this way would require routine screening of victimization history in order to target such content effectively.

Research has also consistently demonstrated that men with a history of sexual aggression have elevated sexual risk indices, including having more sexual partners, inconsistent condom use, and condom use resistance [135]. Routine screenings of sexual aggression would enable interventionists to tailor content to meet the specific needs of these men. For example, because men with a perpetration history are more likely than other men to use coercive tactics such as deception and emotional manipulation to resist condom use, psychoeducation around issues of consent regarding sex generally, and condom use specifically, may be warranted for this population. For example, a recent alcohol administration proximal change experiment demonstrated that a brief, emotion regulation-focused cognitive restructuring intervention resulted in greater use of emotion regulation skills, relative to the control group, which then predicted decreased sexual coercion intentions [132]. This suggests that such approaches could be useful for identifying and targeting the mechanisms underlying alcohol-involved coercive condom use resistance.

Future ARBR Directions: Research Agendas

The body of work we have presented is rich with suggestions on future directions for applied research agendas. We outlined numerous ways ARBR findings can be leveraged to inform extending and scaling up existing psychosocial interventions. We focused on expanding extant applications to elevated risk groups that are currently under-targeted, such as heavy episodic drinkers, women with sexual victimization histories, and men who engage in condom use resistance. The body of research on existing psychosocial interventions targeting PrEP/PEP is still in its nascent stage and we outlined several possible future directions, which included expanding inclusion of “hidden” risk groups targeted for awareness campaigns, identifying and overcoming barriers to medication uptake and adherence, capitalizing on emergent technology such as user-centered design, integrating psychoeducational content about alcohol and other drug use, and networking with extant community resources and service providers. Modifying existing interventions in light of ARBR experiments constitutes another agenda for applied research. There is much to be accomplished in cultivating evidence-based psychoeducational and experiential content that is largely absent from existing interventions. We discussed modification ideas derivative of empirical and theoretical ARBR findings about alcohol expectancies, alcohol myopia, sexual arousal, risk perception, sexual abdication, and condom use resistance. These ideas can spawn a wide-ranging set of modularizable intervention components that can be evaluated separately and jointly in treatment efficacy and effectiveness trials. Finally, in contemplating

potential innovation for new interventions, we emphasized the utility of applied and basic research strategies that incorporate Science of Behavior Change approaches for identifying and evaluating specific mechanisms for proximal change impact. We also identified specific ARBR research procedures that lend themselves to intervention utilization, such as the heat-of-the-moment paradigm, which can be deployed both as an assessment tool and as an experiential skill building exercise.

Agendas for future basic research are also evident. Insistent questions first concern the transferability of risk reduction skills across sober and intoxicated states. Can risk reduction strategies and skills be acquired and/or implemented during states of acute alcohol intoxication? If risk reduction skills are learned and acquired while sober, can those skills be effectively utilized during alcohol-involved sexual encounters? Does the logic of state-dependent learning apply, suggesting value in teaching skills in varying states of intoxication? The same questions can be posed about high levels of emotional or sexual arousal. Second, given demonstrable emotional processes, more work is needed to determine how emotion regulation models pertain to ARBR. For example, do individual differences in emotion regulation tendencies or habits (e.g., drink-to-cope motives or sex-to-cope motives) play significant roles in ARBR? Do individual differences in emotion dysregulation (e.g., emotion nonacceptance or limited regulation strategies) influence ARBR? Further, in the era of ARV, additional research is needed to investigate the relationship between alcohol use and medication adherence. How does alcohol use interfere with adherence or adherence intentions? Is the interference a function of memory processes, motivational processes, or both? How can such interference be countered? Such questions lend themselves both to basic behavioral laboratory research designs and applied ecological mHealth technology protocols.

Conclusions

In the quarter century since alcohol challenge experiments began [27, 136], the data and theory harvest has been voluminous in delineating how drinking influences HIV/STI transmission. Many of the original questions that launched this body of work have been answered. Alcohol exerts a causal impact explainable via alcohol expectancies and/or alcohol myopia. Important mediating and moderating factors have been identified. While some basic research questions remain, our synopses presented here indicate that we now understand a great deal about ARBR. Therefore, future research necessarily pivots primarily toward capitalizing on the knowledge gains accrued and directing those gains in the service of intervention work. We have offered extensive suggestions in how those gains can best be exploited and leveraged for expanding and modifying existing psychosocial interventions and for innovating new ones. In the era of ARVs, it is worth noting that practically all biomedical interventions necessitate expertise about behavioral compliance. Thus, until incidence of new infections is significantly curtailed, psychosocial interventions addressing the nexus of alcohol use, sexual transmission risk, and adherence to biomedical protocols will be an important priority for the foreseeable future.

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