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Meta-Analysis of Alcohol and Serodiscordant Condomless Sex Among People Living with HIV

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Abstract

While observational studies have found that alcohol consumption is associated with serodiscordant condomless sex among people living with HIV (PLHIV), no meta-analysis has yet examined this trend. We conducted a meta-analysis to synthesize empirical evidence on the association between alcohol and condomless sex with partners at risk of HIV acquisition. To meet inclusion criteria, studies: (1) specifically targeted PLHIV or provided stratified data for HIV-infected participants; (2) provided a quantitative measure of alcohol use; (3) provided a quantitative measure of condomless sex with serodiscordant partners; and (4) reported the results of statistical tests examining the relationship between alcohol use and serodiscordant condomless sex. Using random-effects models, weighted effect sizes were calculated. Three separate analyses were conducted to examine serodiscordant condomless sex in association with any alcohol consumption, binge/problematic drinking, and alcohol in a sexual context. A total of 36 independent effect sizes from 27 studies (including 25,065 HIV-infected participants) were pooled in the meta-analysis. Any alcohol consumption, binge/problematic drinking, and alcohol use in a sexual context were each associated with condomless sex with serodiscordant partners [OR 1.64 (95% CI 1.46–1.85); OR 1.65 (95% CI 1.14–2.39); OR 2.88 (95% CI 2.01–4.12), respectively]. Meta-analytic findings demonstrate a consistent positive relationship between alcohol use and serodiscordant condomless sex among PLHIV. Future public health programming for HIV-infected individuals needs to address the role of alcohol consumption in sexual risk-taking behavior.

Keywords

Condomless sex; Alcohol; HIV; Meta-analysis

Introduction

Nearly 37 million people are living with HIV globally with more than 2 million new infections occurring annually (UNAIDS, 2016). While recent biomedical advances in

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therapeutic options such as antiretroviral therapy “treatment as prevention” (Cohen et al., 2011) and preexposure prophylaxis (Baeten et al., 2012; Grant et al., 2010) have expanded the scope of HIV prevention strategies, condom use maintains a key behavioral role in the prevention of HIV transmission. Although being diagnosed with HIV has been associated with a significant reduction in sexual risk behavior (Fox et al., 2009; Gorbach et al., 2011; Steward et al., 2009), condomless sex is not limited to partners who are also HIV positive (Dia et al., 2010; Venkatesh et al., 2012) as a sizable minority of people living with HIV (PLHIV) continue to engage in sex without using condoms with partners at risk of acquiring the virus (Blair et al., 2014; Eaton & Kalichman, 2009; Heijman et al., 2012). For example, a meta-analysis found that the prevalence of unprotected anal intercourse with serodiscordant partners (those who were negative or of unknown serostatus) was 26% (Crepaz et al., 2009). More recent studies have found between one-quarter and one-half of HIV-positive gay, bisexual, and other men who have sex with men (MSM) report serodiscordant condomless sex (Pantalone, Tomassilli, Starks, Golub, & Parsons, 2015; Wilson et al., 2015). Importantly, while there are variations based on the HIV continuum of care, the majority of incident HIV cases in the U.S. are attributable to people diagnosed with HIV rather than those infected but undiagnosed (Skarbinski et al., 2015). Importantly, studies have consistently demonstrated that serodiscordant condomless sex remains a crucial risk factor for HIV transmission given the fact that many HIV-positive individuals do not achieve viral suppression (Levy et al., 2017; Rosenberg, Millett, Sullivan, Del Rio, & Curran, 2014; Van Den Boom et al., 2013). Consequently, behavioral interventions that reduce possible transmission risk behaviors are necessary to decrease HIV incidence.

From a public health standpoint, the identification of key risk factors for HIV acquisition and transmission is the cornerstone of prevention efforts. Given the well-established intersection of alcohol and HIV, the two are often considered twin epidemics as unhealthy alcohol use is a risk factor not only for HIV seroconversion (Vosburgh, Mansergh, Sullivan, & Purcell, 2012) but also for disease progression (Chander, Lau, & Moore, 2006). Furthermore, while reported past-month alcohol use is comparable between PLHIV and the general population (50.7 versus 52.7%, respectively) (Blair et al., 2014; Center for Behavioral Health Statistics and Quality, 2015), 30–60% of PLHIV have alcohol use disorders compared to only 6.4% in the general population (National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health, 2008; Center for Behavioral Health Statistics and Quality, 2015). Importantly, alcohol use is also directly linked with an increased risk of HIV acquisition (Baliunas, Rehm, Irving, & Shuper, 2010).

Previous research suggests that risky sexual behavior is more likely to occur in the presence of alcohol consumption (Hess et al., 2015; Kahler et al., 2015a; Sales, Brown, Vissman, & DiClemente, 2012; Seth, Wingood, DiClemente, & Robinson, 2011). Specifically among HIV-infected study populations, approximately one in four individuals reports consuming alcohol before or during sex (Blair et al., 2014) with additional evidence supporting a link between alcohol use and condomless sex (Gerbi, Habtemariam, Tameru, Nganwa, & Robnett, 2011; Hasse et al., 2010). Importantly, previous systematic reviews and meta-analytic studies with HIV-positive individuals have generally focused on the overall alcohol–sex relationship without particular attention to transmission risk potential. One review found a significant positive relationship between alcohol consumption and condomless sex

(Shuper, Joharchi, Irving, & Rehm, 2009). Another review similarly demonstrated a positive association between alcohol use and condomless sex reviewing only five studies published between 2012 and 2013 (Scott-Sheldon et al., 2013). Neither of these reviews, however, examined the effects of alcohol on high-risk sexual behavior explicitly with partners capable of acquiring HIV (i.e., partners who were HIV negative or of unknown serostatus). Despite their novel contributions to understanding the role of alcohol and general condomless sex among PLHIV, these studies were limited in the extent to which the serostatus of the partner was correlated with risky sex. Consequently, the nature of the linkage between alcohol consumption and condomless sex with HIV-negative or unknown serostatus partners (i.e., serodiscordant) is less clear. Previous studies have demonstrated that binge drinking (Hess et al., 2015) and alcohol use in the context of sex (Perry, Taylor, Elsesser, Safren, & O’Cleirigh, 2016) among MSM are correlated with serodiscordant condomless anal intercourse. Since condomless sex with a serodiscordant partner is considered to carry the greatest chance of HIV transmission risk (Doyle et al., 2014), we chose to investigate sexual behavior with serodiscordant partners to gain a better understanding of the role of alcohol and this particular type of sexual behavior.

An incident HIV case originates from another individual who is infected with the virus. Consequently, condomless sex among PLHIV has direct relevance to the persistence of the epidemic (Shuper, Joharchi, & Rehm, 2016). Condomless sex is clearly associated with the probability of transmission to HIV-negative partners, and successful safer sex negotiation and decision making may be compromised in the context of alcohol use. For HIV-positive individuals, the potential consequences of condomless sex are uniquely different from HIV-uninfected individuals; consequently, the behaviors associated with sexual risk behavior may vary as well. In addition, there are persuasive reasons why the associations between alcohol use and sexual risk behavior in HIV-undiagnosed populations may not be generalizable for HIV-diagnosed individuals. For example, for some PLHIV, the stress of transmission risk potential may serve as motivation to use condoms consistently even in the presence of alcohol consumption (Kalichman, Weinhardt, DiFonzo, Austin, & Luke, 2002).

While previous research has demonstrated that alcohol consumption is associated with condomless sex, not all PLHIV who drink engage in condomless sex and, furthermore, not all drinking experiences in a sexual context coincide with condomless sex. Pinpointing potential moderators of this association, such as demographic characteristics of study samples or study features, may support greater understanding of the variation in the literature. First, sexual risk group is one potential moderator where the association between alcohol consumption and serodiscordant condomless sex may be stronger for certain subgroups of PLHIV. Previous studies among PLHIV have found alcohol use to be higher among MSM relative to heterosexual men (Golin et al., 2009), while in other studies, no differences in alcohol consumption were found between sexual risk groups (Julio et al., 2015). Furthermore, some studies have found lower rates of serodiscordant condomless sex among heterosexual women relative to MSM and heterosexual men (Blair et al., 2014; Golin et al., 2009; Przybyla et al., 2014; Venkatesh et al., 2012). Second, the relationship between alcohol consumption and sexual risk behavior may vary by country as the social and cultural norms regarding alcohol use and sexual behavior may differ (World Health Organization, 2014). While studies in the developed world have found variations in sexual risk behaviors

by partner serostatus (Mizuno et al., 2010; O'Dell, Rosser, Miner, & Jacoby, 2008), this pattern may not be observed in other countries (Venkatesh et al., 2012). Third, recruitment setting warrants consideration as a potential moderator. Clinic-based samples may be different from those recruited in community settings regarding their level of engagement in HIV care as well as the social desirability biases inherent in the reporting of both substance use and risky sexual activity. For example, PLHIV who have been diagnosed but are not engaged in medical care have higher HIV transmission rates relative to PLHIV who are retained in care and virally suppressed (5.3 transmissions/100 person-years versus 0.4 transmissions/100 person-years, respectively), a finding which suggests that engagement in clinical care is associated with a reduction in risk behavior (Skarbinski et al., 2015).

The aim of this paper was twofold: (1) to meta-analyze the contribution of alcohol on serodiscordant condomless sex among PLHIV and (2) to test relevant moderators hypothesized to account for heterogeneity among studies. In line with current literature on condomless sex, we expected larger effect sizes among MSM samples and community-based recruitment samples. Due to limited research regarding between-nation differences, no *a priori* hypotheses were made regarding the country in which the study was conducted. Given alcohol's role as a prominent risk factor for engaging in condomless sex, understanding the overall strength and consistency of this relationship using meta-analytic techniques may offer meaningful information to aid in future prevention and intervention strategies.

Method

Search Strategy for Identification of Studies

With the assistance of a health sciences librarian, we conducted a systematic search of four comprehensive online databases (PubMed, EMBASE, PsycINFO, and CINAHL) using PRISMA guidelines (Moher, Liberati, Tetzlaff, Altman, & PRISMA Group, 2009). We identified articles published in English through September 2014. Search terms and syntax, including combinations of free text and medical subject heading terms, were modified according to each database using a Boolean search strategy (see "Appendix" for search terms).

A total of 11,155 publications were identified and entered into a reference management software program (EndNote X7 for Windows). We also manually reviewed reference lists of previously published systematic reviews and meta-analyses for potentially relevant studies not identified in the initial search (4 were identified in this manner). The combined searches were filtered for duplicate records (4658 identified and removed) resulting in a unique set of 6497 abstracts for screening. Articles were evaluated carefully to ensure that the same data that may have been published in multiple articles would be included only once. In the instances of more than one report of the same data, we opted to include the article with the earliest published date. All database searches were conducted on September 30, 2014.

Data Extraction, Content Coding, and Reliability

One author first screened titles and abstracts to remove clearly ineligible studies. Two reviewers completed the data abstraction independently. Using a standardized data

abstraction form, key study descriptive characteristics were extracted (e.g., authors, year of publication, sample size specifically for the alcohol–sex analysis, country where study was conducted, gender, and age). Second, alcohol measurement characteristics were coded including behavioral recall time period (e.g., 3 months) and a description of the measure. Specifically, we coded studies for variables that assessed any alcohol consumption, an indication of problematic or binge drinking, and an indication that alcohol was consumed prior to and/or during sexual activity (Shuper et al., 2009). Third, characteristics of sexual behavior with serodiscordant partners were extracted including behavioral recall time period. We defined serodiscordant condomless sex as any anal or vaginal intercourse with partners of HIV negative or unknown HIV serostatus when a condom was not used. Finally, studies were coded based on the alcohol–condomless sex association. We coded each effect size based on the type of drinking category measured in relation to sexual transmission risk behavior. Specifically, three effect sizes were categorized as assessing: (1) any alcohol consumption (yes/no), (2) binge/problematic drinking, and (3) alcohol consumption prior to/at the time of sex. We categorized binge/problematic drinking as a dichotomous measure that either (a) met established criteria indicative of hazardous or harmful alcohol use based on screening (e.g., AUDIT score greater than 7) or (b) met or exceeded the gender-specific threshold for number of drinks on a single drinking occasion (NIAAA, 2005). We calculated measures of association when they were not explicitly reported, but sufficient information was available for calculation (e.g., contingency tables). The majority of studies provided unadjusted odds ratios or contingency tables.

Intercoder agreement was assessed with an initial set of five studies coded independently by two authors (SP and GK). Once coding definitions were clear enough to produce consistent data across the two raters, the remaining studies were coded. Cohen's Kappa (κ) and the intraclass correlation coefficient (ICC) were used for categorical and continuous variables, respectively, to assess interrater reliability. For categorical variables, interrater agreement ranged from 87.5 to 100%; κ ranged from 0.82 to 1.0 with an average of 0.98 across all categories. Intercoder reliability based on the ICC was high for sample size (ICC = .96) and age (ICC = .99), respectively. Disagreement between reviewers was resolved by discussion and consensus.

Effect sizes were calculated with ORs as the majority of studies compared groups with a dichotomous outcome variable. Because unadjusted odds ratios were available for more than 90% of the studies, the research team's emphasis was positioned on unadjusted odds ratios (ORs). For those studies that reported means and standard deviations for continuous outcome variables ($k = 1$), we requested and obtained unadjusted ORs from the first author. For those studies that presented only multivariate data, we contacted authors to request unadjusted ORs since multivariate models differed across studies (two of the three contacted authors provided the requested additional information). In addition, when information was not sufficient to calculate effect sizes, we contacted corresponding authors in writing before we excluded those studies. Six were contacted, and five responded with the requested data. There were two instances in which corresponding authors were contacted without response yet sufficient data were available in a previously published meta-analysis and the necessary data were extracted for our analyses.

Data Analytic Plan

All analyses were conducted using Stata 14.0 using the metan, metareg, and heterogi commands (Sterne, Newton, & Cox, 2009). For 12 studies, we extracted the original data (the number of participants with and without alcohol use and the number reporting serodiscordant sex in the absence of condoms). For the remainder of the studies that did not report these numbers, we extracted the crude ORs and the 95% confidence intervals (CIs). The Stata software program has the capacity to combine both types of data to calculate pooled ORs and 95% CIs. Odds ratios were transformed into natural logarithm ORs for data analysis. Individual effect sizes were weighted by the inverse variance of each study. We used random-effects meta-analytic procedures for our analyses (Lipsey & Wilson, 2001) because it allows for study estimates to vary by setting, while fixed effects models assume that variation is due solely to chance (Riley, Higgins, & Deeks, 2011). Three separate analyses were conducted to examine serodiscordant condomless sex in association with: (1) any alcohol consumption, (2) binge/problematic drinking, and (3) alcohol consumption in a sexual context.

The Cochrane Q test and I^2 index and its corresponding 95% confidence intervals (CIs) were used to assess the presence and magnitude of heterogeneity among the calculated effect sizes (Higgins, Thompson, Deeks, & Altman, 2003). The Begg's test and Egger's test were used to measure the potential presence of publication bias (Begg & Mazumdar, 1994; Egger, Davey Smith, Schneider, & Minder, 1997). We also examined three a priori study and sample characteristics as moderators of the alcohol-serodiscordant condomless sex relationship that might account for any observed heterogeneity across studies. We used meta-regression for continuous moderators and an analog to the analysis of variance for categorical moderators. We followed Cochrane guidelines which recommend a minimum of 10 studies for each moderator (Higgins & Green, 2006). The following study-level characteristics were coded: (a) sexual risk group composition (men who have sex with men versus other); (b) country (U.S. versus other); and (c) study sample recruitment setting (clinic based versus community based). Effect sizes and their 95% CIs were calculated for these hypothesized moderators, which were subsequently compared using the Q_B statistic.

Results

Study Selection Criteria

Abstracts were independently reviewed by two authors to determine whether studies met the following eligibility criteria for inclusion in the meta-analysis: (1) specifically targeted PLHIV or provided stratified data for HIV-infected participants, (2) provided a quantitative measure of alcohol use (not in combination with other drugs), (3) provided a quantitative measure of condomless sexual activity with HIV-negative or unknown serostatus partners, and (4) reported the results of statistical tests that examined the relationship between alcohol use and serodiscordant condomless sex or provided sufficient descriptive data to calculate an effect size for the association of interest. Dissertations (indexed in PsycINFO) and published conference abstracts (indexed in EMBASE) were screened, but none met eligibility criteria. Combining the manual search results with the electronic database search results identified 222 articles that were retained for full text review. Ultimately, 195 studies were excluded

resulting in 27 studies that satisfied the eligibility criteria for the meta-analysis. Figure 1 summarizes the process for identifying, screening, and selecting articles included in the meta-analysis.

Descriptive Characteristics of Included Studies

The final sample of 27 studies included 25,065 participants (range 109–7309; mean = 895) dating between 2001 and 2014. Most studies (21) were conducted in the U.S., while 6 were conducted outside the U.S. (2 in France, 1 in South Africa, 1 in Switzerland, 1 in Thailand, and 1 in Togo). Ten articles included only MSM, 2 included a combination of heterosexual men and women, and 1 included only heterosexual women. Table 1 provides descriptive information for each included study, including sample characteristics and effect sizes.

Meta-Analysis of Alcohol and Serodiscordant Condomless Sex

Eighteen studies contributed independent effect sizes reflecting the association of any alcohol consumption and condomless sex with serodiscordant partners. Although individual study effect sizes ranged from 0.62 to 3.02, the overall effect size was 1.64 (95% CI 1.46–1.85) indicating that any alcohol consumption has a statistically significant positive association with condomless sex (see Fig. 2 for forest plot). There was homogeneity in effect sizes for any alcohol consumption [$Q(17) = 19.55$, $p = .30$; ($I^2 = 13.04\%$, 95% uncertainty interval 0.00–49.26)] indicating consistency across studies. Both the Begg's and Egger's tests suggest a low probability of publication bias ($p = .79$ and $p = .56$, respectively).

Ten studies examined binge/problematic drinking and serodiscordant condomless sex. Of these, six found statistically significant positive associations while one found a statistically significant negative association. While individual study effect sizes ranged from 0.72 to 5.54, the overall effect size was 1.65 (95% CI 1.14–2.39) indicating that binge or problematic drinkers were 65% more likely to report condomless sex (see Fig. 3 for forest plot). There was significant heterogeneity among effect sizes for binge/problematic drinking ($Q(9) = 62.66$, $p < .001$; $I^2 = 85.64\%$, 95% uncertainty interval 75.41–91.61). Tests for publication bias ($p = .53$ and $p = .31$ for Begg's and Egger's tests, respectively), were not significant.

Eight studies examined alcohol consumption in the context of sexual activity and condomless sex. Of these, seven found a statistically significant association, whereas one found no significant association (see Fig. 4 for forest plot). The point estimate for the combined studies was 2.88 (95% CI 2.01–4.12), which indicates that those PLHIV who reported alcohol use before or during sex were nearly three times as likely to be classified as engaging in serodiscordant condomless sex compared to those who did not. Significant heterogeneity was detected among effect sizes for alcohol use in sexual contexts ($Q(7) = 28.24$, $p < .001$; $I^2 = 75.21\%$, 95% uncertainty interval 50.12–87.68). The p values of the Begg and Egger tests were $p = .32$ and $p = .05$, respectively, which suggests possible publication bias, indicating that small studies may not be adequately included in the analysis.

Moderators of Alcohol Use and Serodiscordant Condomless Sex

Led by our findings of heterogeneity in the relationship between binge/problematic drinking and serodiscordant condomless sex, we examined the effect of potential moderating variables at the study level (see Table 2). Analyses revealed that sexual risk group ($Q_B[8] = 47.13, p < .001$), study location ($Q_B[8] = 52.65, p < .001$), and recruitment setting ($Q_B[8] = 61.85, p < .01$) significantly moderated the effects of binge/problematic drinking on serodiscordant condomless sex. Specifically, effect sizes were significantly greater in samples with only MSM (compared to only heterosexual samples), studies conducted outside the U.S. (versus in the U.S.) and studies with community-based recruitment settings (versus clinic recruitment sites). As only 8 studies contributed effect sizes for the relationship between alcohol use in a sexual context and serodiscordant condomless sex, meta-regression was not conducted since the minimum threshold of 10 studies was not achieved (Higgins & Green, 2006).

Discussion

The role of alcohol has received attention as one of the critical factors that may be associated with serodiscordant condomless sex which increases the risk of HIV transmission. This study provides the first meta-analytic evaluation of the association between alcohol use and risky sexual behavior among PLHIV with partners at risk of HIV infection. Pooling data from more than 25,000 HIV-infected individuals, results demonstrated that those who reported any alcohol use were significantly more likely to report condomless sex with a serodiscordant partner compared to those who did not. A positive association was also found for binge/problematic drinking and alcohol consumption in a sexual context. While alcohol use posed its greatest risk within a sexual context, this finding should be interpreted with caution given the low number of studies for this particular analysis. Overall, this meta-analysis demonstrates that alcohol is associated with serodiscordant condomless sex among HIV-infected adults. Our findings are consistent with earlier reviews among PLHIV that have examined condomless sex more broadly (Scott-Sheldon et al., 2013; Shuper et al., 2009). The relative magnitudes of calculate effect sizes are generally consistent with that found by Shuper et al. (2009) though our results had wider confidence intervals for two of the three analyses. Importantly, our results build upon these prior findings by explicitly focusing on sexual transmission risk potential since the analyses focused on condomless sex with partners at risk of acquiring HIV. Importantly, the statistically significant association was evident across different risk groups, using different timeframes for assessing condom use, and within study samples in multiple countries, all of which provide solid evidence for the robustness of this effect.

The nature of the relationship between alcohol consumption and sexual risk-taking behaviors among PLHIV is complex. Arguably, the association of most interest is the most direct one (alcohol use in the context of sexual encounter and the likelihood of condomless sex with a partner at potential risk of HIV acquisition). Being under the influence of alcohol may lower one's inhibitions and affect sexual decision making. Several mechanisms may be involved in this association. First, the tendency of alcohol to focus an individual's attention to immediate rather than distal events (i.e., alcohol myopia) may lead PLHIV to engage in

serodiscordant condomless sex when drinking while discounting HIV transmission risk potential (Steele & Josephs, 1990). Alcohol's constraint on a person's cognitive capacity contributes to a focus on salient cues such as sexual arousal and a shift away from distant cues such as HIV transmission risk in the absence of condoms. Unlike HIV-uninfected individuals, PLHIV often are challenged to find and maintain a balance between pleasure and risk reduction strategies (Kelly, Lohan, Alderdice, & Spence, 2011). Importantly, the use of behavioral strategies (e.g., condom use) varies according to the serostatus of the sexual partner (Mitchell, 2013) and alcohol consumption may interfere with condom decision-making processes, disrupting the risk management calculation of HIV transmission potential. Since alcohol consumption also increases an individual's willingness to take risks, PLHIV may be less cognizant of or concerned about the potential consequences of their sexual risk behavior. This may include not only risk of HIV transmission to an HIV-uninfected partner but also opens the possibility of sexually transmitted infection (STI) acquisition for the HIV-infected individual (Cook & Clark, 2005).

Alcohol consumption may be an indicator of particular risky personality traits which may help explain the alcohol–condomless sex connection among PLHIV with serodiscordant partners. In fact, evidence from a systematic review suggests sexual compulsivity and sensation seeking may be indirectly associated with motivations and ability to use condoms through their links to substance use (Shuper, Joharchi, & Rehm, 2014). The role of sexual compulsivity in the relationship between substance use and serodiscordant condomless sex has been suggested in cross-sectional studies (Woolf-King et al., 2013) but warrants further attention via prospective studies. Another possible interpretation for our meta-analytic findings may be alcohol's association with greater intentions to engage in condomless sex (Scott-Sheldon et al., 2016). There exists the potential for both intentional condomless sex and unintentional condomless sex as a consequence of the disinhibiting effects of alcohol (Kahler et al., 2015b). While some HIV-infected individuals may engage in unintentional sexual risk behavior (i.e., serodiscordant sex in the absence of condoms) stemming from alcohol use, others may have conscious motives to use alcohol as a catalyst for condomless sexual activity (Kahler et al., 2015a). Finally, the potential causal linkage between alcohol and HIV transmission risk behavior may also be influenced by the contributory biological effects of alcohol on the immune system (O'Leary & Hatzenbuehler, 2009; Shuper et al., 2010). PLHIV who consume alcohol are more likely to have increased viral loads and more rapid disease progression which can increase the likelihood of viral transmission to an uninfected partner (Azar, Springer, Meyer, & Altice, 2010; Bagby et al., 2015; Chander et al., 2006).

We found evidence of moderation in the association between binge/problematic drinking and serodiscordant condomless sex. First, the relationship was stronger for samples with exclusively MSM relative to heterosexual samples. This finding is consistent with previous research (Bruce, Kahana, Harper, & Fernández, 2013; Julio et al., 2015) on excessive alcohol consumption and risky sex among HIV-positive MSM relative to men who have sex with women and offers support for the notion that MSM may use the disinhibiting effects of alcohol as a cognitive escape from the ceaseless attentiveness to engage in condom-protected sex (McKirnan, Vanable, & Ostrow, 2001). Second, studies conducted outside the U.S. had larger effect sizes than those conducted in the U.S. It is important to note that this variable

was dichotomized; consequently, additional research is warranted to better understand differences across various nations that were collapsed in comparison to the U.S. Third, study recruitment setting moderated the link between binge/problematic drinking and serodiscordant condomless sex which lends support to the idea that engagement in clinical care among PLHIV is associated with a reduction in sexual risk behavior (Skarbinski et al., 2015).

What is less clear, and perhaps more complex, is the relationship between alcohol use more generally and condomless sex with partners at risk of HIV acquisition. Future studies may consider additional moderators of the alcohol–sexual transmission risk association that were not assessed in the current meta-analysis. First, undetectable viral load has been associated with increased sexual risk behavior including serodiscordant condomless sex (Bruce et al., 2013; Prestage et al., 2009; Van Den Boom et al., 2013). Correspondingly, because of the availability of antiretroviral therapy, HIV-negative people may perceive a lower threat of HIV acquisition contributing to serodiscordant condomless sex (Bajunirwe, Bangsberg, & Sethi, 2013). The impact of high adherence to antiretroviral therapy or an undetectable viral load on the relationship between alcohol use and sexual behavior with serodiscordant partners, however, has not been extensively investigated. Second, while HIV-infected adults with high condom intentions (Widman, Golin, & Noar, 2013) and more positive attitudes toward condoms (Widman, Golin, Grodensky, & Suchindran, 2013) are less likely to engage in serodiscordant condomless sex, the role of any alcohol consumption in this observed association is largely unexplored. Third, partnership characteristics (e.g., primary/main, casual or anonymous partners) may also play a role in the odds of condomless intercourse with serodiscordant partners in the presence of alcohol. Studies with primarily or exclusively HIV-negative samples have consistently demonstrated that drinking alcohol is linked with not only condomless sex (Fisher, Cook, & Kapiga, 2010; Hess et al., 2015; Kutner, Nelson, Simoni, Saucedo, & Wiebe, 2017; Wen, Balluz, & Town, 2012) but also sex with new or casual partners (Parks, Hsieh, Collins, & Levonyan-Radloff, 2011). A cross-sectional U.S.-based study of MSM found that both alcohol use during sex and sex with non-main partners were associated with higher odds of serodiscordant anal or vaginal intercourse (Tieu et al., 2014). However, a longitudinal study of HIV serodiscordant couples in Southern Africa found that alcohol use was associated with condomless sex with main partners (Joseph Davey et al., 2017). The relevance of relationship characteristics to alcohol use and high-risk sexual behavior among HIV-infected populations is in need of future investigation. Relatedly, the use of preexposure prophylaxis (PrEP) by the partner not known to be infected with HIV may play a pivotal role in transmission risk likelihood. Behavioral studies are still in their infancy to determine the role of PrEP use among serodiscordant partners and its impact on the relationship between alcohol use and condomless sex. With notable exceptions (see Kahler et al., 2015b; Maisto et al., 2010), few studies to date have assessed sexual motives for drinking among PLHIV. While studies of HIV-uninfected populations have demonstrated that positive expectancies about alcohol's effect on sexual behavior can influence sexual attitudes as well as intentions (Maisto, Carey, Carey, Gordon, & Schum, 2004; Maisto, Palfai, Vanable, Heath, & Woolf-King, 2012), the extension of this line of research among HIV-positive populations is warranted, particularly for those with serodiscordant partners. Finally, the role of serosorting, or choosing sexual partners of the

same HIV status, is a behavioral approach to reduce risk of HIV transmission. Studies on serosorting strategies have demonstrated that while many individuals adapt their sexual risk behaviors after an HIV diagnosis, this behavior change is not absolute (Gorbach et al., 2011; Khosropour et al., 2016). Alcohol consumption may play a role in serosorting behaviors. For example, among HIV-infected MSM with the intention to serosort, those who frequently used alcohol were more likely to report potentially serodiscordant condomless sex acts compared to non-drinkers (Chen, Vallabhaneni, Raymond, & McFarland, 2012).

Although the meta-analytic findings presented are an important first step in understanding the strength of the relationship between alcohol consumption and serodiscordant condomless sex, future research should move away from examining global associations as cross-sectional study designs are likely to have little impact on the broadening of knowledge in this area. This methodological limitation has challenged our ability to establish a clear causal link between alcohol consumption and sexual transmission risk behaviors among PLHIV and suggests the need for future experimental methods to be considered, such as laboratory experiments that involve the manipulation of alcohol consumption and its impact on condomless sex intentions (Rehm, Probst, Shield, & Shuper, 2017; Scott-Sheldon et al., 2016) or studies that involve the use of ecological momentary assessment to assess the co-occurrence of these behaviors in real time.

Limitations

Our meta-analytic findings should be interpreted in the context of a few key limitations. First, as is the case in any meta-analysis, we were limited by the statistical information provided in published reports and the responses from authors to obtain additional data when requested. Second, alcohol and sexual behaviors were determined based on retrospective self-report in most included studies which may be affected by recall and/or social desirability biases. This limitation restricts our ability to infer causal effects. Third, although most of the studies included in the meta-analysis considered some confounding variables in evaluating the relationship between alcohol and condomless sexual activity, adjustment was typically limited to sociodemographic variables (e.g., age, sex). Additional variables may confound the examined relationship. For example, the role of partner alcohol use, particularly before or during sex, was not assessed in our analysis as it was not reported in any included study. While previous research has suggested that partner type is an important moderator of the relationship between overall substance use and condomless sex among PLHIV (Starks, Millar, & Parsons, 2015), most studies that met inclusion criteria failed to provide information on the partnership characteristics. Some ($n = 3$) focused exclusively on primary/regular partners, while one focused exclusively on casual partners. The remaining studies combined all partnership types preventing our research team from examining partnership type as a moderator. Fourth, most studies (77.8%) were based in the U.S. and had samples that were primarily (22.2%) or exclusively (37%) comprised of MSM, thus limiting the generalizability to other subgroups of PLHIV. Finally, there was wide variation in the operationalization of both alcohol use and condomless sex in the studies included in the meta-analysis. While some studies included in the meta-analysis used AUDIT scores, others used much broader definitions of alcohol use using varied timeframes which may have likely contributed to the significant heterogeneity across studies. The combination of

binge drinking with indicators of probably alcohol use disorder may have contributed to the heterogeneous findings given that binge drinking is a widely varying marker of heavy and problematic use. In addition, the definitions of the outcome of interest varied considerably with respect to both the type of sexual risk behavior (e.g., condom use either at any sexual encounter or a specific type including vaginal versus anal sex, insertive versus receptive sex) and the time period. Importantly, the risk of HIV transmission through condomless sex differs substantially for different sexual behaviors (Baggaley, White, & Boily, 2010; Jin et al., 2010). For example, per-contact risk of transmission ranges from 4 per 10,000 exposures for insertive penile–vaginal sex to 138 per 10,000 for receptive anal sex (Patel et al., 2014). While some included studies in the meta-analysis separated unprotected vaginal sex from unprotected anal sex, others combined these behaviors. In addition, unprotected insertive anal sex was often merged with unprotected receptive anal sex in many studies, particularly those that included only MSM. An understanding and consideration of the mechanism by which these varying risk behaviors influence decision making around condom use by PLHIV and their sexual partners are needed.

Conclusion

Our meta-analytic findings are an essential initial step in understanding the magnitude of the relationship between alcohol use and serodiscordant condomless sex among PLHIV as a means to reduce the sexual transmission of the disease. Future prospective studies that evaluate potential moderators to better understand circumstances in which alcohol use is likely to influence condomless intercourse with serodiscordant partners are warranted. For example, identifying mechanisms such as clinical factors (e.g., viral load detectability), intrapersonal influences (e.g., sexual motives for drinking), and interpersonal elements (e.g., partner characteristics) that elucidate the link between alcohol and condomless sex will improve future risk reduction interventions. The accumulated evidence suggests that we should focus prevention efforts on alcohol and its role in sexual transmission risk behavior among HIV-infected individuals. Effectively addressing alcohol consumption among people living with HIV and its potential impact on condomless sex with serodiscordant partners may be an opportunity to impact HIV incidence.

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Appendix: Search Terms

For PubMed, search terms were: (“alcohol drinking”[mh] OR liquor OR alcohol[tiab] OR “substance use”[tiab] OR binge[tiab] OR drink*[tiab]) AND AIDS[sb] AND (sex[tiab] OR condom* [tiab] OR “unprotected sex”[tiab] OR “unsafe sex”[tiab] OR “risky sex”[tiab] OR sexual partner*[tiab] OR sexual behavior[tiab] OR “condomless sex”[tiab] OR “serodiscordant”[tiab] OR discordant[tiab] OR intercourse[tiab]).

For EMBASE, search terms were: (“alcohol drinking” OR liquor OR alcohol OR “substance use” OR binge OR drink*) AND (AIDS OR HIV OR “acquired immune deficiency syndrome” OR “Human immunodeficiency virus”) AND (sex OR condom* OR “unprotected sex” OR “unsafe sex” OR “risky sex” OR sexual partner* OR sexual behavior OR “condomless sex” OR “serodiscordant” OR discordant).

For PsycINFO, search terms were: AB (hiv OR AIDS OR human immunodeficiency virus OR acquired immune deficiency syndrome) AND AB (alcohol OR drink* OR binge OR substance use) AND (sex OR unprotected OR unsafe OR risk* OR “sexual partner*” OR “condomless sex” OR intercourse OR condom* OR serodiscordant OR discordant).

For CINAHL, search terms were: S1: AB hiv OR AB aids OR AB human immunodeficiency virus OR AB acquired immune deficiency syndrome; S2: AB alcohol OR AB binge OR AB drink* OR AB substance use; S3: (S1 AND S2); S4: (S3) AND AB sex OR AB unprotected OR AB unsafe OR AB risk* OR AB sexual partner* OR AB “condomless sex” OR AB condom* OR AB serodiscordant OR AB discordant OR intercourse; S5: (S3 AND S4).

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Fig. 1.
Study search and selection

Fig. 2.

Forest plot of any alcohol consumption and serodiscordant condomless sex

Fig. 3.
Forest plot of binge/problematic drinking and serodiscordant condomless sex

Fig. 4.
Forest plot of alcohol in sexual context and serodiscordant condomless sex

Table 1

Summary of data for included studies

First author, publication year	Study design and location	Sample size for alcohol–condomless sex association and associated characteristics	Age	Alcohol definition and timeframe	Condomless sex definition and timeframe	Alcohol–condomless sex association OR (95% CI)
Aidala, 2006	Prospective cohort, USA	N = 744 (186 MSM, 246 MSW, and 315 women)	M = 39.2	PD: positive score on the CAGE measure or usual drinking pattern of 5 + drinks at least weekly	Any experience of sex without a condom with partners who was not HIV positive or was of unknown serostatus, 6 months	PD: 1.72 (1.32–2.36)
Beckett, 2003	Cross-sectional, USA	N = 1278	Not reported	AAU: any alcohol consumption, 1 month SC: alcohol use before or during sex, 6 months	Any incident of unprotected anal or vaginal sex with an HIV-negative or unknown serostatus partner, 6 months	AAU: 1.67 (1.19–2.34) SC: 2.47 (1.77–3.44)
Benotsch, 2001	Cross-sectional, USA	N = 294 (198 MSM, 44 MSW, 44 women)	M = 40.5	AAU: any alcohol use, 3 months	Unprotected insertive and receptive anal or vaginal intercourse with non-HIV-positive partners, 3 months	AAU: 0.99 (0.50–2.01)
Bouhnik, 2007	Cross-sectional, France	N = 285 MSM with non-concordant partners	M = 42.6	PD: 6+ drinks on a single occasion, 12 months	Inconsistent condom use with a serodiscordant regular partner, 12 months	PD: 2.94 (1.94–4.46)
Bouhnik, 2007	Cross-sectional, France	N = 663 (390 MSM and 273 women)	M = 42.0	PD: 6+ drinks on a single occasion, 12 months	Inconsistent condom use with a serodiscordant regular partner, 12 months	PD: 2.22 (1.31–3.74)
Brennan, 2010, USA	Cross-sectional, USA	N = 346 MSM	Mdn = 43	AAU: never drinking vs. moderate (<once a week) and regular drinking (>once a week), 3 months	Unprotected anal intercourse with a partner of serodiscordant or unknown HIV status, 3 months	AAU: 2.54 (1.54–4.20)
Bruce, 2013, USA	Cross-sectional, USA	N = 200 MSM	M = 21.2	SC: unprotected sex after drinking alcohol despite intention to use condom, 90 days	Unprotected insertive or receptive anal intercourse with HI-negative or unknown status partners, 90 days	SC: 12.48 (3.65, 42.67)
Chin-Hong, 2005	Cross-sectional, USA	N = 168 (133 MSM, 17 MSW, and 18 women)	Mdn = 45	AAU: any alcohol consumption, 4 months	Unprotected receptive or insertive anal or vaginal intercourse with HIV-uninfected or unknown serostatus partners	AAU: 2.85 (0.81–10.04)
Clarke, 2012	Cross-sectional, Thailand	N = 512 (286 Men and 226 women)	Mdn = 39	AAU: any alcohol intake, 30 days	Unprotected sex with partners of negative or unknown HIV status, 30 days	AAU: 1.10 (0.51–2.47)
Friedman, 2009	Cross-sectional, USA	N = 602 (250 MSM, 168 MSW, and 184 women)	M = 41.3	AAU: any alcohol consumption, 90 days PD: affirmative response on validated alcohol abuse screening instrument, 90 days	Non-condom use for insertive and receptive anal and vaginal sex with main and non-main partners of known negative and unknown HIV serostatus partners, 90 days	AAU: 1.96 (1.23–3.11) PD: 0.80 (0.48–1.36)
Golin, 2009	Cross-sectional, USA	N = 1050 (496 MSM, 227 MSW, and 327 women)	M = 40.9	PD: 5+ drinks per day, 3 months	Unprotected insertive and receptive anal or vaginal intercourse with HIV-negative or unknown serostatus partners, 3 months	PD: 0.72 (0.54, 0.97)
Hasse, 2010	Prospective cohort study, Switzerland	N = 7309 (1650 MSM, 2840 MSW, 1934 women, and 885 IDU)	M = 44.2	AAU: WHO definition of severe, moderate, light, and no alcohol use, 6 months	Unprotected sexual contacts with stable partners whose HIV status was negative or known, 6 months	AAU: 1.40 (1.08, 1.82)

First author, publication year	Study design and location	Sample size for alcohol–condomless sex association and associated characteristics	Age	Alcohol definition and timeframe	Condomless sex definition and timeframe	Alcohol–condomless sex association OR (95% CI)
Hatfield, 2009	Cross-sectional, USA	<i>N</i> = 675 MSM	<i>M</i> = 42.0	AAU: any alcohol consumption, 3 months PD: 12+ drinks per day, daily for 30 days	Serodiscordant unprotected anal intercourse, 3 months	AAU: 2.35 (1.65, 3.36) PD: 5.54 (2.98–10.29)
Kahler et al., 2015b	Retrospective cohort, USA	<i>N</i> = 109 MSM	<i>M</i> = 42.5	AAU: any current alcohol consumption (AUDIT) PD: 6+ drinks on a single occasion	Unprotected receptive or insertive anal intercourse with partners of negative or unknown HIV status, daily for 30 days	AAU: 1.34 (0.79–2.26) PD: 1.76 (1.010, 3.07)
Kalichman, 2011	Prospective cohort, USA	<i>N</i> = 256 (201 men and 55 women)	Not reported	AAU: any alcohol consumption, 1 month PD: AUDIT score 8 or higher SC: any alcohol use before sex, 1 month	Unprotected anal or vaginal intercourse with HIV-negative or unknown status partners, 4 months	AAU: 1.76 (0.83–3.71) PD: 1.13 (0.53–2.41) SC: 2.69 (1.21–6.00)
Long, 2009	Cross-sectional, USA	<i>N</i> = 91 women	<i>M</i> = 37.0	AAU: any alcohol consumption, 6 months	Sex with person who was HIV negative or of unknown serostatus without condom, 6 months	AAU: 0.62 (0.16–2.44)
Martin, 2013	Cross-sectional, USA	<i>N</i> = 303 (207 MSM, 47 MSW, 47 women, and 2 transgender)	<i>M</i> = 43.7	AAU: any alcohol consumption, 3 months	Unprotected vaginal or anal sex with an HIV-negative or known serostatus partner, 3 months	AAU: 2.02 (0.99–4.11)
Metsch, 2009	Cross-sectional, USA	<i>N</i> = 1038 (644 men and 394 women)	<i>M</i> = 44.0	PD: heavy alcohol use, 6 months	Unprotected sexual intercourse with HIV negative or unknown serostatus, 6 months	PD: 1.91 (1.27–2.89)
Morin, 2005	Cross-sectional, USA	<i>N</i> = 1910 (1870 MSM and 40 MSM/W)	Not reported	AAU: any alcohol use, 3 months	Any act of insertive or receptive anal or vaginal intercourse without condom with HIV-negative or unknown serostatus partner, 3 months	AAU: 1.81 (0.85–3.85)
Purcell, 2005	Cross-sectional, USA	<i>N</i> = 1168 MSM	Not reported	AAU: any alcohol use, 90 days SC: alcohol use before or during sex, 90 days	Any unprotected insertive or receptive anal sex with HIV-negative or unknown serostatus casual partner, 3 months	AAU: 1.47 (1.20, 1.80) SC: 1.82 (1.53–2.16)
Purcell, 2001	Cross-sectional, USA	<i>N</i> = 456 MSM	<i>M</i> = 37.0	AAU: any alcohol use, 3 months SC: alcohol use before or during sex, 3 months	Unprotected insertive or receptive anal intercourse with HIV-negative or unknown serostatus partners, 3 months	AAU: 1.76 (1.16, 2.68) SC: 2.98 (1.52–5.82)
Sikkema, 2009	Cross-sectional, USA	<i>N</i> = 122	<i>M</i> = 42.2	AAU: any alcohol use, 4 months	Unprotected anal or vaginal sexual behavior with HIV-negative or serostatus unknown partner, 4 months	AAU: 3.02 (1.38–6.62)
Skeer, 2012	Cross-sectional, USA	<i>N</i> = 503 MSM	<i>M</i> = 41.9	AAU: drinking at least once per week, 3 months PD: 5+ drinks in a single day, 3 months	Unprotected insertive or receptive anal intercourse with partners of HIV-negative or unknown status, 3 months	AAU: 1.47 (1.02–2.13) PD: 1.25 (0.80–1.97)
Tieu, 2014	Cross-sectional, USA	<i>N</i> = 1458 MSM	<i>Mdn</i> = 29	AAU: any alcohol use, 3 months SC: any alcohol use during sex, 3 months	Serodiscordant/serostatus unknown unprotected anal or vaginal intercourse, 3 months	AAU: 1.45 (0.77–2.70) SC: 5.84 (3.43–9.95)

First author, publication year	Study design and location	Sample size for alcohol–condomless sex association and associated characteristics	Age	Alcohol definition and timeframe	Condomless sex definition and timeframe	Alcohol–condomless sex association OR (95% CI)
Tieu, 2011	Cross-sectional, USA	<i>N</i> = 205 MSM	Not reported	SC: any alcohol use within 2 h before sex, not reported	Serodiscordant/serostatus unknown unprotected anal intercourse, last sex	SC: 1.62 (0.88–3.00)
Yaya, 2014	Cross-sectional, Togo	<i>N</i> = 217 (83 men and 134 women)	<i>M</i> = 37.3	SC: any alcohol use before sex, not reported	Unprotected sex with HIV-negative or unknown serostatus partner, 3 months	SC: 2.96 (1.38–6.37)

MSM men who have sex with men, *MSW* men who have sex with women, *AAU* any alcohol consumption, *PD* problematic drinking, *SC* sexual context, *M* mean, *Mdn* median

Table 2
Moderators of the association between binge/problematic drinking and condomless sex

Moderator	Category	k	<i>Q_B</i>	OR	95% CI
Sexual risk group	MSM only	3	47.13***	1.95	0.81–4.72
	Heterosexual only	7		0.51	0.21–1.24
Study location	USA	7	52.65***	0.75	0.27–2.05
	Outside USA	3		1.34	0.49–3.67
Recruitment setting	Clinic	8	61.85***	0.78	0.24–2.51
	Community	2		1.29	0.40–4.17

p < .001