

Review

Does being drunk or high cause HIV sexual risk behavior? A systematic review of drug administration studies[☆]

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ABSTRACT

HIV sexual risk behavior is broadly associated with substance use. Yet critical questions remain regarding the potential causal link between substance use (e.g., intoxication) and HIV sexual risk behavior. The present systematic review was designed to examine and synthesize the existing literature regarding the effects of substance administration on HIV sexual risk behavior. Randomized controlled experiments investigating substance administration and HIV sexual risk behavior (e.g., likelihood of condom use in a casual sex scenario) were included. Across five databases, 2750 titles/abstracts were examined and forty-three total peer reviewed published manuscripts qualified (few were multi-study manuscripts, and those details are outlined in the text). The majority of articles investigated the causal role of acute alcohol administration on HIV sexual risk behavior, although one article investigated the effects of acute THC administration, one the effects of acute cocaine administration, and two the effects of bupropion. The results of this review suggest a causal role in acute alcohol intoxication increasing HIV sexual risk decision-making. Although evidence is limited with other substances, cocaine administration also appears to increase sexual risk, while acute cannabis and bupropion maintenance may decrease sexual risk. In the case of alcohol intoxication, the pharmacological effects independently contribute to HIV sexual risk decision-making, and these effects are exacerbated by alcohol expectancies, increased arousal, and delay to condom availability. Comparisons across studies showed that cocaine led to greater self-reported sexual arousal than alcohol, potentially suggesting a different risk profile. HIV prevention measures should take these substance administration effects into account. Increasing the amount of freely and easily accessible condoms to the public may attenuate the influence of acute intoxication on HIV sexual risk decision-making.

1. Introduction

Alcohol and other drug use (hereafter referred to as “substance” use) has been identified as a significant risk factor in HIV transmission through mechanisms such as sexual risk behavior (e.g., unprotected sex, multiple partners) and needle sharing (Centers for Disease Control and Prevention [CDC], 2015a, 2016a; Scott-Sheldon et al., 2016). Sexual risk behavior is widespread among drug users, including alcohol users (Kalichman et al., 2007; Meade et al., 2014; Molitor et al., 1998); injection drug use, however, is relatively rare within many drug-using populations (e.g., roughly 10% for cocaine users, Chaisson et al., 1989; Hudgins et al., 1995; Morissette et al., 2007; 2.5% for prescription opioid users, Meade et al., 2014), and nearly non-existent in alcohol using populations (Mahdi and McBride, 1999). Unprotected sex

perpetually accounts for the largest proportion of new HIV infections globally (70–80%; CDC, 2011). Among people living with HIV, substance use is prevalent (22–40% alcohol; 6–29% other substances) and is a significant predictor of unprotected, risky sex (Scott-Sheldon et al., 2016; Beckett et al., 2003). Taken together, these data suggest that risky sexual behavior, as opposed to injection drug use, is the most prominent HIV transmission mechanism – and substance use plays a role in driving risky sexual decision-making associated with HIV transmission.

Various methods have been used to examine relations between risky sex and substance use (Halpern-Felsher et al., 1996) including global correlational studies (i.e., lifetime associations between substance users and HIV incidence and sexual risk behavior, e.g., Staton et al., 1999), and situational covariation studies (e.g., substance use and HIV sexual

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risk behavior within the past 30 days; e.g., Biglan et al., 1990). Global correlational and situational covariation studies have extensively demonstrated broad associations between amphetamine, methamphetamine, cocaine, alcohol or opioid use and increased HIV incidence and sexual risk behaviors (Buchacz et al., 2005; Molitor et al., 1998; Booth et al., 1993; Booth et al., 2000; Friedman et al., 2017; McCoy et al., 2004; Shuper et al., 2009, 2010; Halpern-Felsher et al., 1996; Scott-Sheldon et al., 2016; for reviews see e.g., Lan et al., 2016; Li et al., 2010; Heath et al., 2012; Kalichman et al., 2007). In addition to correlational studies, event-level methods (e.g., ecological momentary assessments, Wray et al., 2015; diary methods; Bailey et al., 2008) have also been used. Event-level analyses incorporate naturalistic data collection to enable participant recording of substance use and HIV sexual risk behavior within a defined temporal window (e.g., responses to random prompts to record recent substance use and HIV sexual risk behavior via a study cellular phone). A causal link between acute substance use and HIV sexual risk behavior, however, cannot be inferred from correlational or event-level methodologies.

Critical questions remain regarding the potential causal mechanisms of substance use and HIV sexual risk behavior. For example, the influence of disinhibitory effects while intoxicated, increased sexual arousal while intoxicated, or expectancy effects of drugs or alcohol (Rhodes and Stimson, 1994) on HIV sexual risk decision-making have yet to be disentangled. These factors are difficult or impossible to address, manipulate, and control in naturalistic settings or with retrospective correlational analyses.

Experimental drug administration methods constitute a complement to the correlational and naturalistic methods described above, and allow causal examination of the effects of drug and alcohol intoxication on HIV sexual risk behaviors. Drug administration experiments investigate hypothetical HIV sexual risk decision-making processes while under the influence of controlled doses of alcohol or other substances using placebo controlled designs to address potential influential variables (e.g., expectancy effects, arousal). For example, one decision-making model involves audio-video interactive role-play (e.g., Maisto et al., 2002), in which the participant is shown a video and asked how he/she might respond to the sexual situation presented, such as whether to have protected or unprotected sex with the partner in the video. Another example of a decision-making model involves isolating the influence of delay to condom availability on the likelihood of unprotected sex within the Sexual Delay Discounting Task (SDDT; Johnson et al., 2017). For example, one may prefer to use a condom with a casual partner because it decreases the risk of HIV transmission. However, if a condom is not immediately available, the same person might prefer immediate unprotected sex over waiting to obtain a condom, because the discounted value of delayed sex with a condom is lower than the immediate value of unprotected sex (Johnson and Bruner, 2012; Johnson et al., 2015). If acute substance use does indeed play a causal role in HIV sexual risk decision-making processes, then this would directly inform the development of interventions that could prevent HIV transmission.

The focus of this review, therefore, was on experimental laboratory methods explicitly designed to understand the causal pharmacological influences on sexual risk decision-making processes. For this reason we focus on acute substance administration in the context of controlled laboratory settings. The aim of this systematic review is to collate and synthesize studies investigating whether substance use, with specific emphasis on acute drug effects, causally influences HIV sexual risk decision-making.

1.1. Defining substance use and sexual risk behavior

1.1.1. Substance use

For the purposes of this review, substance use is defined as the use of a psychoactive substance, regardless of whether that use is in the context of a substance use disorder.

1.1.2. Sexual HIV risk behavior

Sexual HIV risk behavior can be defined as any sexual behavior putting individuals at risk for acquiring or transmitting HIV including sex with or without a condom with multiple partners, sex with or without a condom with unknown partners, and unprotected vaginal, anal, or oral sex (CDC, 2015b, 2013). Although the risk of transmitting HIV via oral sex is low, this risk increases if cuts or sores are present in the mouth or vagina, or on the penis, or if this behavior is repeated many times (CDC, 2016b). As condom protected as opposed to unprotected sex is a highly effective means of preventing HIV transmission among sexually active individuals (CDC, 2013), we place particular emphasis on reviewing studies that report decision-making processes related to condom use or unprotected sex, or likelihood of condom use or unprotected sex.

2. Methods

2.1. General search strategy

For this literature review, we conducted both automated and manual searches. Systematic searches were conducted across five psychology, health and multidisciplinary electronic databases (PsycINFO, GoogleScholar, PubMed, WorldCat, Catalyst) during October 2016 through January 2017. The search was conducted in conjunction with the guidelines for systematic reviews outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Moher et al., 2009). The search was conducted using systematic search vocabulary as key words in the title and abstract across all databases. Search terms spanned specific topics and methods serving the objective of this review: (1) Substance use (e.g., alcohol, cocaine), (2) Acute administration of drug, and (3) HIV sexual risk behavior (e.g., unprotected sex), and decision-making. Systematic combinations of the following search terms were used:

- “substance use” “addiction” “drug use” “acute drug effects” “drug administration” “alcohol administration” “alcohol”
- “HIV risk behavior” “sexual risk behavior” “condom use” “unprotected sex”
- “decision-making” “sexual delay discounting”

The reference sections of relevant publications were also examined for potential inclusion in this review.

2.2. Inclusion criteria

For studies to qualify for inclusion, the published manuscripts were required to: 1) include a study abstract, 2) be published in English, 3) be a primary peer reviewed article, 4) present data on acute substance administration, 5) report data involving HIV sexual risk behavior while under the influence of substance in a controlled laboratory setting, 6) present data on decision-making processes related to condom use (e.g., likelihood of condom use, attitudes towards condom use, sexual abstinence, or similar metrics). To conduct the most inclusive literature review possible under the aforementioned criteria, no restrictions were placed on the type of substance administered within the experiment, the age of use, or the country or population of the study.

The first author reviewed the titles and abstracts of studies to determine initial relevance. In some cases the title and abstract did not provide sufficient information to determine relevance, and in these cases the first author reviewed and compared the study content to the inclusion criteria. To ensure accurate representation of the originally presented forms of drug use and HIV sexual risk behavior – original terms and concepts that were employed by the authors within the primary studies remain intact in this review (Heerde and Hemphill, 2016).

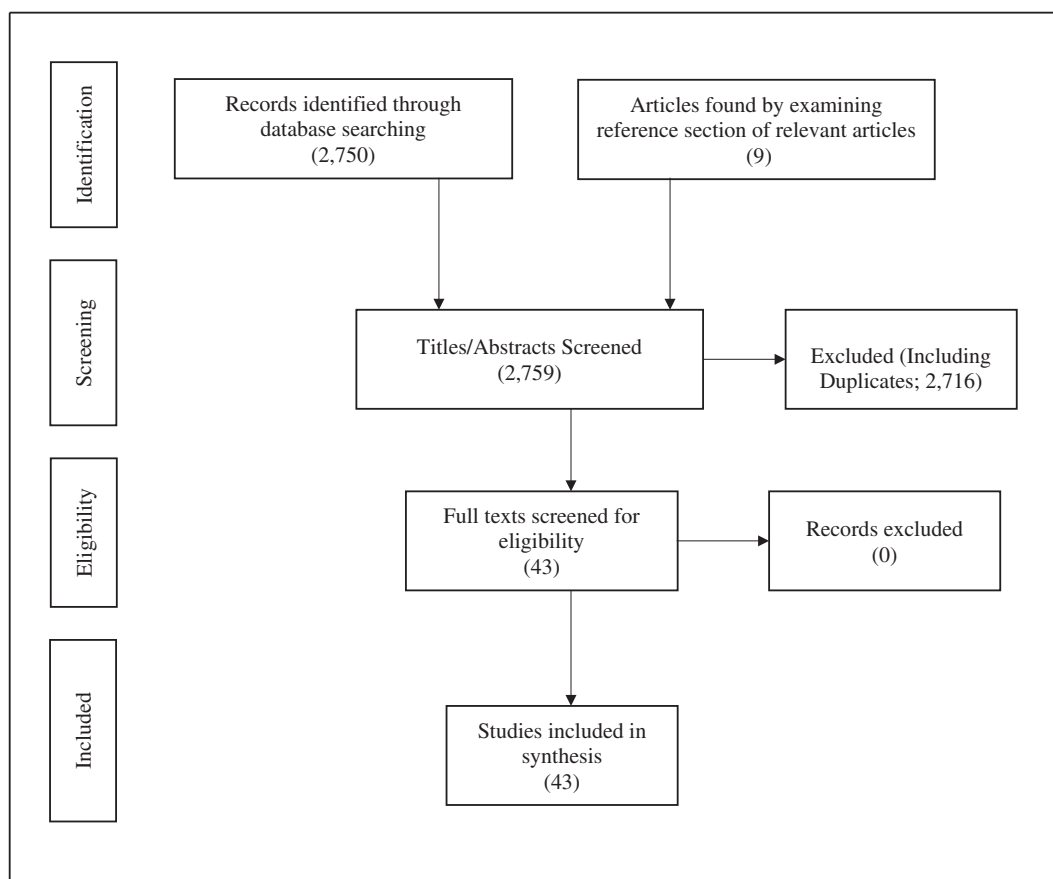


Fig. 1. Schematic diagram of Preferred Reporting Items for Systematic Reviews and Meta-Analyses of published studies qualifying for this review and synthesis.

3. Results

3.1. Summary of overall results

The initial search yielded 2750 manuscripts (see Fig. 1). Forty-three published manuscripts met all of the inclusion criteria and were therefore included for synthesis in this review. Thirty-nine studies focused on acute effects of alcohol intoxication on causal determinants of HIV sexual risk decision-making. These studies investigated acute effects of alcohol in samples that ranged from social or moderate drinkers (e.g., Davis, 2010; Jacques-Tiura et al., 2015) to heavy or heavy episodic-drinkers (e.g., Gilmore et al., 2013; Maisto et al., 2012), and across various populations at risk for HIV contraction including men who have sex with men (MSM one study; Maisto et al., 2012), heterosexual women (seventeen; or majority in sample were heterosexual e.g., Zawacki, 2011), heterosexual men (ten; e.g., Maisto et al., 2004b), or heterosexual men and women (eleven; or majority of participants in sample were heterosexual; e.g., Johnson et al., 2016). The remaining studies focused on acute effects of cocaine administration among male and female cocaine users (Johnson et al., 2017, specific sexual orientation not required), THC administration among male and female regular cannabis users (one; Metrik et al., 2012, specific sexual orientation not required/specified), and bupirone maintenance or acute bupirone administration among male and female cocaine users (e.g., Bolin et al., 2016; Strickland et al., 2017; specific orientation not required). The majority of the studies were conducted in the U.S., and several were conducted in Canada (see Table 1).

3.2. Summary of administration methods and HIV sexual risk decision-making outcomes

Methods used to examine the influence of acute substance intoxication on HIV sexual risk decision-making processes varied widely. These methods included double blind placebo-controlled designs (e.g., Abbey et al., 2006), as well as unblinded designs (e.g., Davis et al., 2007). In all cases, active substance or placebo was administered either across subjects (thirty-seven) or within subjects across multiple sessions (six). All studies involved substance administration followed by HIV sexual risk decision-making questions, often in the context of hypothetical sexual scenarios. One study arranged a social interaction with a confederate following beverage consumption, and hypothetical risky sexual decision-making questions related to the confederate (Zawacki, 2011). We outline the first reviewed experiment in greater detail to provide context of the overall experimental model.

A wide variety of methods were also used to quantify HIV sexual risk decision-making including reported likelihood of condom use, various other assessments of unprotected sex intentions, attitudes towards condoms, and reported sexual abdications (allowing a partner to decide what to do; e.g., whether to use a condom or not). In some studies condom use likelihood was reported (e.g., Bolin et al., 2016; Johnson et al., 2017). Other studies combined risky sexual decision-making metrics such as condom use likelihood questions, unprotected sex intentions, or attitudes towards condom use (e.g., Maisto et al., 2004a, b). Still other studies used and reported general risk behaviors (including non-sexual risk taking) and participant answers to these questions were combined and reported as a conglomerate risk-taking scale. For example, the Cognitive Appraisal of Risky Events (CARE or the CARE Revised; Metrik et al., 2012) questionnaire measures substance use, aggression, sex without protection, and perceived risks and

Table 1
Basic characteristics of qualifying studies including author, year of publication, sample size and study location, number of substance conditions, dose, resulting BAC where appropriate and within or between subject design.

| Author | Year | n; population, study site | Number of substance conditions | Dose if reported (and resulting BAC for alcohol studies) | Within/ between subject |
|----------------------|-------|---|--|--|-------------------------|
| Abbey et al. | 2009 | n = 72 male; ≥ 1 drink in the past 30 days, and ≥ 4 on one occasion in past 12 months; U.S. | 3: alcohol, placebo, control | 2.00 g/kg body weight ratio (resulting BAC 0.08%) | Between-subject |
| Abbey et al. | 2005 | n = 180 (90 female, 90 male); ≥ 1 drink in the past 30 days, and ≥ 4 on one occasion in past 12 months; U.S. | 3: alcohol, placebo, control | 2.00 g/kg body weight ratio male; 1.85 g/kg female (resulting BAC 0.08%) | Between-subject |
| Abbey et al. | 2006 | n = 120 (60 female, 60 male); ≥ 1 drink in the past 30 days, and ≥ 4 on one occasion in past 12 months; U.S. | 3: alcohol, placebo, control | 2.00 g/kg body weight ratio male; 1.85 g/kg for female (resulting BAC 0.08%) | Between-subject |
| Bolin et al. | 2016 | n = 9 male and female; recent cocaine use, and positive benzoyllecgonine urine screen; U.S. | 2: buspirone, placebo | 30 mg/day, 0 mg (placebo) | Within-subject |
| Cho and Span | 2010 | n = 200 male and female; ≥ 5 drinks on one occasion in past 12 months; U.S. | 3: alcohol, placebo, control | 2.30 ml/kg body weight for male; 2.09 ml/kg body weight for female (resulting BAC 0.08%) | Between-subject |
| Davis et al. | 2009 | n = 150 male and female; moderate social drinkers (not explicitly defined); U.S. | 2: alcohol, control (yoked) | 0.82 g/kg body weight for male; 0.68 kg/g for female (target BAC 0.08%) | Between-subject |
| Davis et al. | 2007 | n = 61 male and female; ≥ 5 drinks/week, and ≥ 5 on one occasion in past 6 months; U.S. | 2: alcohol, control, (yoked) | 0.988 g/kg for male, 0.790 g/kg for female (resulting BAC 0.10%) | Between-subject |
| Davis | 2010 | n = 124 male; ≥ 5 drinks on one occasion in past 6 months; U.S. | 2: alcohol, control (yoked) | 0.82 g/kg body weight (resulting BAC 0.08%) | Between-subject |
| Davis et al. | 2014 | n = 436 female; ≥ 4 drinks in 2 h in past 12 months; U.S. | 2: alcohol, control (yoked) | 1.0 ml/kg body weight (resulting BAC 0.10%) | Between-subject |
| Ebel-Lam et al. | 2009 | n = 79 male; ≥ 1 drink per month, but less than one drink per day; Canada | 3: alcohol, placebo, control | 2.22 ml/kg body weight (resulting BAC 0.08%) | Between-subject |
| Fromme et al. | 1999 | Study 1: n = 161; Study 2: n = 135 male and female; ≥ 6 drinks/week, and ≥ 3 drinks on one day, and ≤ 5 drinks on 5 days during the past week; U.S. | 3: alcohol, placebo, control | Study 1 & 2: 2.39 ml/kg body weight (resulting BAC 0.08%) | Between-subject |
| Fromme et al. | 1997 | Study 1: n = 107; average of 18 drinks/week; Study 2: average of 12 drinks/week; n = 88; male and female; U.S. | 2: alcohol, control | 2.55 ml/kg body weight (resulting BAC 0.08%) | Within-subject |
| George et al. | 2009 | Study 1: n = 115, Study 2: n = 165, Study 3: n = 173 male and female; average of 6 drinks/week; U.S. | Study 1: 3: alcohol low dose, alcohol high dose, control; Study 2: 4: alcohol low, alcohol moderate dose, alcohol high dose, control, Study 3: 4: alcohol low, alcohol moderate, alcohol high dose, control (yoked) | Dose not reported: Study 1: low dose (resulting BAC 0.04%); high dose (resulting BAC 0.08%); Study 2 & 3: low dose (resulting BAC 0.06%); moderate dose (resulting BAC 0.08%); high dose (resulting BAC 0.10%) | Between-subject |
| George et al. | 2016 | n = 408 female; ≥ 4 drinks in 2 h once in past 12 months; U.S. | 2: alcohol, control (yoked) | 1.0 ml/kg body weight (resulting BAC 0.07%) | Between-subject |
| George et al. | 2014 | n = 436 female; ≥ 4 drinks in 2 h once in past 12 months; U.S. | 2: alcohol, control (yoked) | 1.0 ml/kg body weight (resulting BAC 0.10%) | Between-subject |
| Gilmore et al. | 2013 | n = 144 female; consumed between 1 and 40 drinks/week, and ≥ 4 drinks on one occasion in past 6 months; U.S. | 2: alcohol, control (yoked) | 0.68 g/kg body weight (resulting BAC 0.08%) | Between-subject |
| Gordon et al. | 1997 | n = 60 male; mostly heavy drinkers, 3–4 drinking episodes per week; US | 3: alcohol, placebo, control | Dose not reported (resulting BAC 0.065%) | Between-subject |
| Jacques-Tiura et al. | 2015 | n = 162 female; self-defined social drinkers; U.S. | 3: alcohol low dose, alcohol high dose, control (yoked) | Low dose: 0.0325 g/kg body weight (resulting BAC 0.04%); high dose: 0.682 g/kg body weight (resulting BAC 0.08%) | Between-subject |
| Johnson et al. | 2017 | n = 12 male and female; used cocaine for at least 1 year, and in the past month; U.S. | 3: cocaine low dose, cocaine high dose, placebo | Low dose: 125 mg/70 kg of cocaine HCl; high dose: 250 mg/70 kg of cocaine HCl | Within-subject |
| Johnson et al. | 2016 | n = 23 male and female; 4–5 drinks per episode occasionally; U.S. | 2: alcohol, placebo | 1 g/kg alcohol dose (resulting BAC 0.093%) | Within-subject |
| Kruse et al. | 2005 | Study 1: n = 80, Study 2: n = 60, male; ≥ 5 drinks on one day of the week during previous 3 months; U.S. | 2: alcohol, placebo | 2.082 ml/kg body weight (resulting BAC 0.06%) | Between-subject |
| MacDonald et al. | 2000a | Study 1: n = 65, Study 4: n = 44, male; ≥ 1 drink per month; Canada | 3: alcohol, placebo, control | Dose not reported (resulting BAC 0.08%) | Between-subject |
| MacDonald et al. | 2000b | n = 358 male; drinking levels not specified; Canada | Study 2 & 4: 3: alcohol, placebo, control | Dose not reported (resulting BAC 0.08%) | Between-subject |
| MacDonald et al. | 1996 | Study 1: n = 54; Study 2: n = 55, male; consumed alcohol when in social situations; Canada | Study1: alcohol, control; Study 2: alcohol, placebo, control | Dose not reported (resulting BAC 0.084%) | Between-subject |
| Maisto et al. | 2004a | n = 60 female; moderate or heavy drinkers, 3–4 drinks ≤ (moderate) or ≥ (heavy) half of drinking episodes; | 4: alcohol high dose, alcohol low dose, placebo, control | Low dose: 0.35 g alcohol/kg body weight (resulting BAC 0.031); high dose: 0.70 g alcohol/kg body weight (resulting BAC 0.031) | Between-subject |

(continued on next page)

Table 1 (continued)

| Author | Year | n; population, study site | Number of substance conditions | Dose if reported (and resulting BAC for alcohol studies) | Within/ between subject |
|-------------------|-------|--|--|--|-------------------------|
| Maisto et al. | 2004b | U.S. n = 48 male; moderate or heavy drinkers, 3–4 drinks ≤ (moderate) or ≥ (heavy) half of drinking episodes; U.S. | 3: alcohol, placebo, control (yoked) | BAC 0.067% 0.65 g/kg body weight (resulting BAC 0.059%) | Between-subject |
| Maisto et al. | 2012 | n = 117 male; moderate or heavy drinkers, ≤ 3–4 drinks (moderate) or ≥ 3–4 drinks (heavy) on half of drinking episodes; U.S. | 3: alcohol, placebo, control (yoked) | 0.70 g/kg body weight (resulting BAC 0.07%) | Between-subject |
| Maisto et al. | 2002 | n = 102 female; moderate or heavy drinkers, ≤ 3–4 drinks (moderate) or ≥ 3–4 drinks (heavy) on half of drinking episodes; U.S. | 3: alcohol, placebo, control (yoked) | 0.65 g/kg body weight (resulting BAC 0.06%) | Between-subject |
| Metrik et al. | 2012 | n = 136 male and female; cannabis use ≥ once per week in past month, and ≥ 10 uses in past 6 months; U.S. | 2: cannabis, placebo | 2.8% THC | Between-subject |
| Murphy et al. | 1998 | n = 82 female; social drinkers; U.S. | 2: alcohol, control | 0.6 g/kg body weight (resulting BAC 0.056) | Between-subject |
| Norris et al. | 2013 | n = 328 female; nonproblem drinkers; U.S. | 3: alcohol low dose, alcohol high dose, control | Low dose: 0.325 g/kg body weight (resulting BAC 0.04%); high dose: 0.682 g/kg body weight (resulting BAC 0.08%) | Between-subject |
| Norris et al. | 2009a | n = 173 female; consumed between 1 and 40 drinks/week; U.S. | 4: alcohol low dose, alcohol high dose, placebo, control (yoked) | Low dose: 0.325 g/kg body weight (resulting BAC 0.04%); high dose: 0.682 g/kg body weight (resulting BAC 0.08%) | Between-subject |
| Norris et al. | 2009b | n = 173 female; consumed between 1 and 40 drinks/week; U.S. | 4: alcohol low dose, alcohol high dose, placebo, control (yoked) | Low dose: 0.325 g/kg body weight (resulting BAC 0.04%); high dose: 0.682 g/kg body weight (resulting BAC 0.08%) | Between-subject |
| Prause et al. | 2011 | n = 44 male and female; non-dependent to dependent levels of drinking (< 10 on MAST); U.S. | 3: alcohol low dose, alcohol high dose, control | Dose not reported; low dose (resulting BAC 0.08%) | Within-subject |
| Purdie et al. | 2011 | n = 230 female; between 1 and 40 drinks/week; U.S. | 4: alcohol low dose, alcohol high dose, placebo, control | Dose not reported; low dose (resulting BAC 0.025%); high dose (resulting BAC 0.08%) | Between-subject |
| Schacht et al. | 2010 | n = 64 female; social drinkers; U.S. | 4: alcohol low dose, alcohol medium dose, alcohol high dose, placebo | Dose not reported; low dose (resulting BAC 0.06%); medium dose (resulting BAC 0.08%); high dose (resulting BAC 0.10%) | Between-subject |
| Staples et al. | 2015 | n = 131 female; ≥ 5 drinks/week, and at least 1 episode of ≥ 5 drinks on one occasion in past 6 months; U.S. | 2: alcohol, control | Dose not reported (resulting BAC 0.10%) | Between-subject |
| Stoner et al. | 2007 | n = 115, male and female; consumed an average of 3 drinks 1–2 days/week; U.S. | 4: alcohol low dose, alcohol high dose, control | Low dose: 0.35 g/kg for females, 0.41 g/kg for males (resulting BAC 0.04%) high dose: 0.69 g/kg for females; 0.82 g/kg for males (resulting BAC 0.08%) | Between-subject |
| Stoner et al. | 2008 | n = 161 female; average of 10 drinks/week; U.S. | 5: alcohol low dose, alcohol high dose, low dose control, high dose control, placebo, (yoked) | Low dose: 0.02 ml (resulting BAC 0.04%); high dose: 1.75 ml (resulting BAC 0.08%) | Between-subject |
| Strickland et al. | 2017 | n = 11 male and female; recent cocaine use, and positive benzoyllecgonine urine screen; U.S. | 4: buspirone low dose, buspirone high dose, triazolam (positive control), placebo (negative control) | 4: low dose: 10 mg buspirone; high dose: 30 mg; 0.375 mg triazolam | Within-subject |
| Wray et al. | 2015 | n = 113 male; drinking levels not specified; U.S. | 3: alcohol, placebo, control | Dose not reported (resulting BAC 0.08%) | Between-subject |
| Zawacki et al. | 2009 | n = 161 female; between 1 and 40 drinks/week; U.S. | 4: alcohol low dose, alcohol high dose, placebo, control (yoked) | Low dose: 0.325 g/kg body weight (resulting BAC 0.04%); high dose: 0.682 g/kg body weight (resulting BAC 0.08%) | Between-subject |
| Zawacki | 2011 | n = 132 female; ≥ 1 drink in past month, and ≥ 4 drinks on one occasion in past 12 months; U.S. | 3: alcohol, placebo, control | 0.45 ml/lb. (resulting BAC 0.08%) | Between-subject |

benefits of unprotected sex. We focus on direct measures of condom use likelihood (or attitudes towards condoms, or unprotected sex intentions etc.) and risky sexual decision-making (e.g., sex, either protected or unprotected with an unknown partner) to the extent possible based on variables reported in the studies reviewed.

Because several measurements are common throughout studies and also straightforward, we do not define each of these measurements for each study, but rather outline them briefly here. “Arousal” or “desire” refers to subjective sexual excitement and is often measured on a Likert-type scale (e.g., not at all aroused to extremely aroused). “Expectancy effects” refers to the beliefs about the effects of alcohol on behavior. Expectancy effects are often measured using a scale similar to that used Leigh (1990), with questions such as “I enjoy sex more when I drink”, and “I am less nervous about sex when I drink” with each question the participant rates “Does alcohol have this effect on you?” and “Is this the reason you drink?” rated on a 1 (not at all) to 4 (very much) scale. “Condom use negotiation skills” and “safer sex behavior skills” are similar measures typically assessed by evaluating statements made by the participant during interactive video role-play that express desire for condom use (e.g., “I would feel more comfortable having sex if we used a condom”). Similar concepts such as likelihood of condom use, unprotected sex intentions, or attitudes towards condoms are measured on a 0–100% scale or Likert-type scales examining one or more questions regarding unprotected sex (e.g., “how likely are you to engage in unprotected sex?”, “how likely are you to allow Nick to put his penis in your vagina without a condom on?”, “My having sexual intercourse in this situation is”: irresponsible – not irresponsible [1–9 scale]).

3.3. Organization of remaining review results

The vast majority of experiments examined alcohol as a potential causal factor driving HIV sexual risk decision-making. For this reason, we first synthesize studies by alcohol and gender, and then by remaining substances examined (i.e., cocaine, THC, buspirone). Potential differences in HIV sexual risk behavior between females and males – and resulting best practices regarding sexual education that is tailored to the sexes – remains an active area of inquiry. For this reason, we first outline studies that included both women and men in the sample (regardless of if explicit comparisons between female and male participants were made) to compare potential differences or similarities in the effects of alcohol on female and male HIV sexual risk decision-making. Next, we outline studies that only included women, followed by those that only included men. Among each of these subsections, the studies are organized by primary themes and measures investigated (e.g., expectancy effects). Further, the main findings of each study are reported in the text, and doses as reported by the authors, dosing conditions, as well as populations under study (e.g., sample size, location) are reported in Table 1.

3.4. Alcohol administration studies examining HIV sexual risk decision-making

3.4.1. Alcohol administration studies among heterosexual women and men

Eleven studies examined the causal effects of alcohol versus placebo among heterosexual women and men. Acute alcohol intoxication tended to directly or indirectly increase risky sexual decision-making, particularly in the form of unprotected sex. As expected, these studies reported complex interactions between alcohol and multiple variables including levels of arousal, sexual risk cues, expectancy effects, and partner type in driving HIV sexual risk decision-making. In particular, the pharmacological effects of alcohol combined with expectancy effects lead to significantly riskier sexual-decision making. The pharmacological effects of alcohol can also decrease attention to potential risk cues (e.g., a promiscuous partner), leading to riskier sexual decision-making. Results of potential gender differences related to the effects of alcohol were mixed.

Davis et al. (2007) examined the effect of alcohol and individual perceptions of unprotected sex consequences on risky sexual decision-making across individuals using unblinded placebo and alcohol conditions (resulting BAC = 0.10%). After consuming their randomly assigned beverage, participants watched two 3-minute clips of explicit heterosexual intercourse. Participants then read a hypothetical sexual vignette with themselves as the protagonist and involving a first time acquaintance. Participants answered questions about risky sexual decisions, including intentions of engaging in unsafe sex with the partner. Participants then responded to seven arousal (e.g., “having sex would feel really good”) and seven risk (e.g., “we don't have a condom”) cues by indicating whether or not each cue had been considered during sexual decision-making. If so, they provided a quantitative rating of the cue's impact ranging from much less likely to have sex, to much more likely to have sex. Analyses indicated that men reported greater intentions for unsafe sex, and, alcohol compared to placebo caused increased consideration for arousal cues, a greater proportional consideration of arousal relative to risk cues, and greater intentions for unsafe sex. The effects of intoxication on estimated likelihood of unsafe sex were fully mediated by the proportion of arousal versus risk cues endorsed by participants. In a separate study using similar unblinded methods in a between-subjects design, Davis et al. (2009) found that alcohol intoxication (resulting BAC 0.08%) caused increased sexual risk taking intentions (including unprotected sex intentions) through increased perceived intoxication and increased sexual arousal. These results were strongest while experiencing an increase in BAC levels, relative to experiencing a decrease in BAC levels.

Prause et al. (2011), using a within-subjects unblinded design, studied the effect of intoxication (resulting BAC 0.08%) and arousal on sexual risk behavior. Specifically, the authors examined genital sexual responses (radial penis rigidity and circumference in men, and light reflection as an indirect measure of the amount of blood in vaginal blood vessels in women), self-reported arousal, and intentions to have intercourse with a new partner following erotic vs. neutral film viewing. Alcohol caused greater self-reported (subjective) sexual arousal in men and women in response to both types of films, even the neutral film. However alcohol did not significantly influence genital response in men or women. The authors concluded that alcohol causes increased intentions to have intercourse with a new partner. These effects, however, were not direct causal effects, but alcohol increased arousal, and increased arousal was responsible for the increase in sexual risk behavior (see also George et al., 2009 for a similar design and similar results).

Abbey et al. (2006) also randomly assigned individuals to either double-blind alcohol (resulting BAC 0.08%), placebo, or explicitly sober groups, and investigated the role of intoxication, gender, “cognitive reserve” (measured at baseline by reading subset of the Wide Range Achievement Test 3 [WRAT3]), and partner risk (low or high, e.g., character in video portrayed as having a small or larger number of previous sexual partners) on sexual decision-making. There was no effect of cognitive reserve on participants within the sober or placebo conditions, however, intoxicated participants with lower cognitive reserve were significantly more likely to report they would have sex without a condom. Additionally, sober participants distinguished between high and low risk partners (i.e., less likely to have unprotected sex with high risk partners), but intoxicated individuals did not. Those who were intoxicated, relative to those who were sober, were significantly more sexually aroused by the sexual scenario video that they watched. Men were more likely to report having sex without a condom, although men and women were not differentially affected by alcohol.

Abbey et al. (2005) investigated the role of alcohol consumption on likelihood of engaging in unprotected sex in individuals randomly assigned between-subjects to double-blinded alcohol (resulting BAC 0.08%), placebo, or explicitly sober groups. Analyses showed that intoxication was significantly and positively related to likelihood of sex without a condom. Perceived negative consequences, worry about

negative consequences, and becoming mad at oneself for having sex in the hypothetical sexual scenario were all significantly negatively associated with reported likelihood of sex without a condom. The effects of beverage condition on the likelihood of engaging in unprotected sex did not differ by alcohol expectancies, or by gender.

Fromme et al. (1999) examined expectancy versus impairment explanations in linking alcohol intoxication with risky sexual decision-making using a between-subjects blinded design. Across two experiments, participants drank either alcohol (resulting BAC 0.08%), placebo or water and then rated potential consequences of risky sexual behaviors (e.g., having sex with an unknown partner, Study 1) or negative consequences that could result from having sex without a condom (Study 2). A revised version of the CARE (CARE-Revised) was used in both studies to assess risky sexual decision-making. The authors found that those participants in the alcohol condition reported fewer perceived negative consequences resulting from risky sex. Those participants who expected sexual disinhibition from alcohol relative to those who did not indicated that they were more likely to engage in risky sex. These data suggest that both alcohol impairment regarding personal risk perception and alcohol expectancies influence risky sexual decision-making. In separate studies using similar methods and measurements, Fromme et al. (1997) investigated the effects of alcohol (resulting BAC 0.10%) versus a control condition on the perceptions of risk resulting from sexual decision-making (measured by the CARE conglomerate scale) among both men and women using a within-subject design. Analyses revealed that participants rated negative consequences of risky sex (e.g., sex without a condom) as less likely, as well as a greater likelihood of engaging in risky sex, when they were intoxicated relative to when they were sober. Alcohol effects did not differ by gender.

Stoner et al. (2007) investigated the dose response relationship of alcohol (low dose resulting BAC 0.04%; high dose resulting BAC 0.08%), across subjects on sexual fears (measured by the Sexual Aversion Scale, which measures e.g., sexual fears, avoidance, disgust, revulsion, lack of desire for sex on a Likert-type scale), and likelihood of unprotected sex. Analyses revealed that women were more likely to report not engaging in unprotected sex. Participants in the high dose condition only rated their likelihood of unprotected sex significantly higher than controls. The authors found that those who had heightened sexual fears and who drank the control or low alcohol dose beverage were less likely to engage in unprotected sex. Conversely, those who had heightened sexual fears who drank the high dose of alcohol were more likely to report engaging in unprotected sex.

Cho and Span (2010) investigated the effects of alcohol (resulting BAC 0.08%), placebo, or explicitly sober conditions, and gender on the intentions of engaging in sexual risk decision-making using a between-subjects design. Analyses revealed that gender significantly predicted sexual intentions with men expressing stronger intentions of engaging in casual sex. Moreover, women who thought they drank alcohol (whether they did or not) expressed stronger intentions to engage in sex compared to sober women, although this relationship was not revealed among men. In a counterintuitive finding that does not necessarily align with previous research, sober men expressed greater intentions to engage in sex. As hypothesized by the authors of the original study, it is possible that men in the alcohol or placebo conditions overcompensated to guard against risky sexual behavior, and this compensation may arise from expectancy effects (e.g., believing that alcohol leads to risky sexual behavior). Neither alcohol intoxication nor alcohol expectancy was a significant predictor of intentions to engage in sex or condom use when past condom use frequency was controlled for.

Johnson et al. (2016), using a double-blind design, examined the within-subject effects of alcohol (resulting BAC 0.093%) relative to placebo on reported condom use likelihood in response to a casual sexual encounter vignette. Like other alcohol studies, this study examined condom use likelihood when there was no stated delay for protected sex. However, unlike other studies, this study also examined

condom use likelihood when the choice to use a condom was only available after a stated delay, which was parametrically manipulated. There was no significant difference across alcohol and placebo administration with likelihood of engaging in condom-protected sex when no delay was involved. However, alcohol significantly decreased condom use as a function of increasing delay to condom availability for most of the hypothetical sexual partners examined. The study also administered a similar task examining condom use while parametrically manipulating the stated risk of sexually transmitted infection (STI) contraction. There was no difference across alcohol and placebo administration on likelihood of condom use when there was a 100% chance of STI contraction. However, alcohol significantly decreased condom use as a function of decreasing chances of STI contraction, but only when the task involved a more desirable partner. Overall these results suggest that if a condom is not immediately available, or the perceived likelihood of contracting an STI is somewhat low, alcohol consumption might increase the likelihood of HIV sexual risk decisions, specifically in the form of unprotected sex.

3.4.2. Alcohol administration studies among heterosexual women

Seventeen different studies assessed the effects of alcohol relative to control beverage conditions on HIV sexual risk behavior among heterosexual women. Many of these studies were focused on separating the pharmacological effects of alcohol, and alcohol expectancies on HIV sexual risk decision-making, as well as the influence of relationship expectancies women may have within a given sexual encounter. Results showed that alcohol combined with alcohol expectancies increased the likelihood of risky sexual decision-making and decreased perceptions of risk with a risky partner. Alcohol expectancies alone also contributed to decreased perceptions of risk. A woman's desire to be in a relationship also increased the likelihood of risky sexual decision-making. Alcohol intoxication among victims of childhood sexual abuse increased the likelihood of risky sexual decision-making and sexual abidation.

Using a between-subjects randomized design, Maisto et al. (2002) investigated the effects of alcohol (resulting BAC 0.06%) placebo, or explicitly sober control beverage consumption and expectancies on risk perception and 'safer sex behavioral skills' among heterosexual women. Following beverage consumption, participants responded to a sexual risk decision-making questionnaire (CARE, including questions assessing risks and benefits of unprotected sex). Safer sex behavioral skills (measured through audio-video role-play scenarios requiring participants to verbally negotiate condom-use) were also measured. Analyses revealed that alcohol expectancies and the perception of intoxication contributed independently to both higher ratings of positive consequences of risky sex (including unprotected sex) and lower safer sex behavioral skills, while actual alcohol consumption had little influence.

Maisto et al. (2004a) investigated the dose effects of alcohol (low dose resulting BAC 0.04% and high dose resulting BAC 0.07%), placebo, or control beverage consumption on HIV sexual risk decision-making. After consuming their randomly assigned beverage, women participated in an audiovisual role-play scenario to measure "condom use negotiation skills", and also answered questions about sexual risk decision-making (measured by the CARE questionnaire, with focus on likelihood of positive and negative consequences of engaging in sex with a new partner). The authors showed that higher alcohol doses (compared to moderate doses) and stronger alcohol expectancies were associated with greater motivation to engage in risky sexual behavior (more positive ratings for sex with a new partner). Perceived intoxication, however, was the strongest predictor of lack of condom use negotiation skills.

Gilmore et al. (2013) investigated the influence of alcohol intoxication (resulting BAC 0.10% or control) and alcohol expectancies on desire to have sex using a between-subjects design. Results showed that alcohol interacted with sexual alcohol expectancies, indicating that stronger expectancy endorsement was associated with greater desire for sex with a hypothetical partner and greater self-reported arousal in the

alcohol condition, but not in the placebo condition.

Using a between-subjects design, [Murphy et al. \(1998\)](#) investigated the effects of alcohol (resulting BAC 0.054%) or control beverage consumption, expectancy, and conflicting affective (attractiveness of partner) and inhibitory (suggesting the partner is risky) cues during videos of sexual risk scenarios. The primary dependent variable of interest for the present review was answers to sexual decision-making questions such as “How receptive do you think this person would be to wearing a condom during sex?” Sexual decision-making was unchanged by alcohol consumption. Alcohol expectancy, however, did influence sexual decision-making, in that those who believed they had consumed alcohol (whether they did or not), were more likely to judge the highly attractive partner, but also the highly risky partner, as significantly less risky compared to those who did not believe they consumed alcohol.

[Zawacki \(2011\)](#) examined the effects of alcohol intoxication on heterosexual women's sexual decision-making within a social interaction with a potential dating partner (a confederate in the experiment) across three between-subject beverage conditions (alcohol [resulting BAC of 0.08%], placebo or explicitly sober control condition). Participants drank the randomly assigned beverage, interacted with the confederate on designated topics (i.e., school and work, relationships and friends), and then completed sexual decision-making questions assessing relationship interest, risk (e.g., “if you were to have sex with this person, how likely would it be that you get an STD?”) and likelihood of unprotected sex with the partner (which were embedded into broader surveys to disguise the purpose of the study). Analyses showed alcohol consumption and stronger sex-related alcohol expectancies significantly increased relationship interest in the partner and led to a lower perception of partner risk, which in turn resulted in a higher likelihood of unprotected sex.

Other research has shown that alcohol intoxication directly decreased the intention to use condoms in a hypothetical sexual scenario ([Davis et al., 2014](#)). Participants were assigned to one of two unblinded beverage conditions (resulting BAC 0.10%, or control). Analyses revealed that alcohol intoxication directly decreased the intention to use condoms in the future with the partner in the sexual scenario. Somewhat counterintuitively, women with greater condom use self-efficacy (measured by a subset of questions on the Condom Use Self-Efficacy Scale, [[Braftford and Beck, 1991](#)]) had stronger intentions to engage in condom negotiation (measured by the Condom Influence Strategy Questionnaire; [Noar et al., 2002](#)), and this relationship was stronger for those who were intoxicated relative to those who were sober.

[Purdie et al. \(2011\)](#) examined intoxicated initial desire in sexual encounters and likelihood of unprotected sex. Female social drinkers were randomized to 1 of 4 alcohol and control beverage administration conditions (control, placebo, low dose resulting BAC 0.04%, high dose resulting BAC 0.08%) and 1 of 3 partner risk level conditions (unknown, low, high: information about the sexual history of the male was embedded and manipulated within the hypothetical sexual meeting scenario to create three levels of risk). Participants provided ratings of likelihood of having unprotected sex. Women in the alcohol and placebo conditions endorsed stronger initial desire (e.g., “how much do you want to have sex with Nick?”) than those in the control conditions in the low or unknown risk conditions, which led to reported decreases in likelihood of condom use. Importantly, in the high risk partner condition, *only* those women who consumed alcohol (although no differences in low dose or high dose were reported) endorsed stronger initial desires, which led to reported decreases in likelihood of condom use.

[Norris et al. \(2009a\)](#) examined sexual risk decision-making processes across women who were randomly assigned to either control, placebo, low-dose (resulting BAC 0.04%), or high dose (resulting BAC 0.08) beverage groups. Analyses showed that only at the high dose of alcohol was arousal increased. Higher arousal in turn had an indirect significant effect on both decreased condom insistence (e.g., “tell him I would be more comfortable using a condom”) and increased

endorsement of unprotected sex.

[Stoner et al. \(2008\)](#) examined causal relationships between alcohol intoxication and sexual risk decision-making across social drinking females using several beverage conditions: low dose resulting BAC 0.04%, high dose resulting BAC 0.08%, placebo and control conditions. The authors found that alcohol consumption compared to placebo consumption reduced perceived adverse health consequences of engaging in unprotected sex, and thereby increased the likelihood of engaging in unprotected sex. The less sexually assertive a woman was, the less she intended to insist on condom use with the hypothetical sexual partner, regardless of beverage consumed. Additional direct comparisons between effects of low versus high dose alcohol were not made.

Using a between-subjects design, [Zawacki et al. \(2009\)](#) examined the relationships between alcohol (high dose resulting BAC 0.08%; low dose resulting BAC 0.04%), placebo, or control beverage consumption, women's relationship motivation, and partnership familiarity (low [not very familiar with the partner], high [familiar with the partner]) on sexual decision-making (including unprotected sex intentions). The authors found that intoxication and greater interest in a long-term relationship with the story character positively mediated the effects of women's relationship motivation (higher), and partner familiarity (more familiar), to increase the likelihood of unprotected sex intentions (see also [Norris et al., 2009b](#) for similar results, in which alcohol intoxication increased women's thoughts that the potential to have sex was high, which led to increased unprotected sex intentions). [Jacques-Tiura et al. \(2015\)](#), using a between subjects design, investigated the influence of randomly assigned alcohol (high dose resulting BAC 0.08%; low dose resulting BAC 0.04%) or control beverage consumption on unprotected sex intentions. Analyses revealed stronger interests in a long-term relationship and belief that sex would facilitate that relationship were strengthened by increased alcohol intoxication and predicted an increase in unprotected sex intentions.

[Norris et al. \(2013\)](#) investigated the between-subject effects of alcohol or control beverage consumption (control, low dose resulting BAC 0.04%, high dose resulting BAC 0.08%) and relationship type (on-again off-again relationship versus new) on women's judgments of a male partner of varying risk (unknown, low, high). The authors found that in all risk conditions alcohol intoxication, as well as an on-again off-again relationship, increased women's ratings of the partner's sexual potential, which was a conglomerate measure assessing desire, and likelihood of having sex (e.g., “How likely are you to have sex with Nick right now?”).

Previous sexual assault may also interact with alcohol to influence HIV sexual risk decision-making in women. [George et al. \(2014\)](#) assigned participants to either the alcohol (resulting BAC 0.10%) or control conditions. Following beverage consumption, women were presented with an erotic story. Number of adolescent/adult sexual assault experiences and alcohol intoxication were positively and significantly related to heightened risky sexual decision-making, including sex without a condom (assessed by a composite measure similar to that used by [Purdie et al., 2011](#); e.g., “How likely are you to have vaginal sex without a condom?”). Alcohol intoxication also led to a heightened positive mood, which led to a decreased likelihood of condom use. Relatedly, [Schacht et al. \(2010\)](#), showed that intoxicated women who were victims of childhood sexual abuse (CSA) reported a significantly higher likelihood of unprotected sex compared to sober CSA women, as well as compared to intoxicated women who were victims of adult sexual abuse or those never abused.

Using a between-subjects design, [Staples et al. \(2015\)](#) investigated the effects of alcohol intoxication (resulting BAC 0.10%) or control beverage consumption, and “inhibition conflict” (high conflict = condom was available in scenario, low conflict = no condom was available) on women's sexual abdication among individuals who experienced child sexual abuse (CSA) and those who did not experience abuse (NSA). Analyses revealed that with high inhibition conflict intoxicated CSA women were more likely to abdicate than sober CSA

women, although no difference was revealed between intoxicated and sober NSA women. When there was low inhibition conflict, however, CSA history and alcohol intoxication had no influence on abdication.

George et al. (2016) used a between-subjects design to examine the effects of alcohol (resulting BAC 0.07%) versus control beverage consumption on women's sexual decision-making processes and the causal influence of partner pressure (high/low), history of sexual victimization, mood and anticipated negative reaction from partner (e.g., angry as a result of woman's insistence on condom use) on condom-decision abdication. The authors found that in the control and alcohol condition alike, high pressure increased anticipated negative partner reactions, and positive elevated mood was correlated with increased abdication. Only when intoxicated did a previous victimization experience predicted increased abdication via stronger anticipated negative partner reaction.

3.4.3. Alcohol administration studies among heterosexual men

Ten studies assessed the effects of alcohol relative to control beverage conditions on HIV sexual risk behavior among heterosexual men. These studies focused on interactions of alcohol and arousal, condom use negotiation skills, as well as aggressive tendencies and coercion in HIV sexual risk decision-making models. Alcohol intoxication led to diminished attention to risk cues, increased likelihood of engaging in unprotected sex, and poorer condom use negotiation skills. Alcohol intoxication combined with sexual arousal also led to greater unprotected sex intentions, and alcohol intoxication also led to greater aggressive tendencies and coercion.

Using a between-subjects design, Maisto et al. (2004b) examined the effects of three beverage conditions (alcohol resulting BAC 0.06%, control, placebo), on risky sexual decision-making (e.g., intentions to engage in risky sex, the Multidimensional Condom Attitudes Scale [MCAS; Helweg-Larsen and Collins, 1994]; condom use negotiations skills adapted from Gordon et al., 1997) in a sample of heterosexual males using interactive role-play scenarios. Results showed that those who drank alcohol relative to those who did not, showed poorer condom use negotiation skills and greater intentions to engage in risky sex. Alcohol, however, did not influence attitudes about condoms.

Gordon et al. (1997) also investigated condom use negotiation skills and attitudes towards condoms among mostly heavy drinking men. Participants drank either control, placebo, or an alcoholic (resulting BAC = 0.065%) beverage. The authors showed that participants who consumed alcohol relative to placebo and control conditions showed poorer condom use negotiation skills. Participants who had stronger sex-related alcohol expectancies (and especially when these expectancies were triggered by subjective intoxication) had more negative attitudes towards condom use.

MacDonald et al. (2000b) tested the role of arousal and alcohol intoxication on unprotected sex intentions across sober, placebo, or alcohol (resulting BAC 0.08%) conditions. Analyses revealed that after viewing a hypothetical video in the alcohol condition, those who felt sexually aroused, as opposed to those who did not feel aroused, reported more favorable attitudes towards unprotected sex and greater unprotected sex intentions. These effects of attitudes and intentions regarding unprotected sex were not observed in the sober or placebo conditions. Using similar methods, MacDonald et al. (1996) also conducted laboratory studies that showed intoxicated males relative to sober males (alcohol resulting BAC 0.084%, placebo and control conditions) reported more positive intentions regarding having unprotected sex. The authors hypothesized these results were due to alcohol enhanced focus on salient stimulating cues, rather than focus on potential negative consequences of not using condoms.

Ebel-Lam et al. (2009) investigated the effects of intoxicated versus sober sexual decision-making. Men were assigned to either the alcohol (resulting BAC 0.08%), placebo or sober conditions, and either read an explicit vignette (arousal condition) or read about space (neutral condition). Participants then watched a video and answered sexual

decision-making questions (including likelihood of having unprotected sex) regarding how they would respond in a similar situation. The authors found that participants who were intoxicated and also in the arousing condition (as opposed to the neutral condition) reported that they were more likely to have unprotected sex.

Using a between-subjects design, Wray et al. (2015) investigated the effects of alcohol (alcohol resulting BAC 0.08%), placebo, or control) and exercise induced high or low autonomic arousal (participants pedaled a bike or rested, respectively) on ratings of sexual arousal and unprotected sexual intentions among mostly heavy drinkers. Autonomic arousal had little effect on unprotected sex intentions, although intoxication showed a positive trend with unprotected sex intentions. Sexual arousal was also heightened with alcohol consumption, suggesting alcohol may interact with arousal to increase risky sexual decision-making.

Kruse and Fromme (2005) investigated partner physical attractiveness and alcohol intoxication on male perception of potential sexual partners and sexual intentions. Participants were randomized to one of two groups (either alcohol [resulting BAC 0.06%] or placebo). Analyses revealed that the dose of alcohol used did not influence perceptions of desirability of a hypothetical potential partner, intentions to have sex, discuss risks, or use condoms. Alcohol, however, did significantly moderate the relations between perceived risk (e.g., endorsement on a 0–100% scale for items such as “In terms of overall risk for STDs besides AIDS, how risky do you think this person is”) and intentions to have sex (“How likely is it that you would have sex in the first 6 months of dating this person?”). Specifically, men who consumed alcohol had a stronger relationship between risk perceptions and sex intentions in which higher risk perceptions led to lower sex intentions (although this was only the case in the ascending alcohol absorption limb in Study 1, but not the descending limb of alcohol absorption in Study 2).

In separate laboratory studies using between subject designs, MacDonald et al. (2000a) investigated the effects of control, placebo or alcohol (resulting BAC 0.08%) beverage consumption and “cue type” (impelling versus inhibiting cues) on sexual risk decision-making. The impelling cue condition included questions (all answered on a Likert-type scale) that assessed the likelihood that the participant and hypothetical partner would *engage in intercourse*. Conversely, the inhibiting cue condition included questions that assessed the likelihood that the participant would *engage in unprotected intercourse*. The authors found an interaction between intoxication and “cue type” (impelling versus inhibiting cues). Males who were intoxicated as opposed to those who were sober reported stronger intentions to have sex when impelling cues were present. No significant difference in intentions to have sex were found between intoxicated and sober participants, however, with inhibitory cues present. In a replication and extension of the first laboratory study, the authors found that when inhibitory cues were present intoxicated individuals were actually less likely to report intentions to engage in sex than sober individuals.

Davis (2010) examined the relation between men's alcohol intoxication (either alcohol resulting BAC 0.08%, or control; unblinded) on aggressive unprotected sex intentions among males. Intoxicated participants who had stronger alcohol-aggression expectancies (more endorsements for items such as “When I am drunk, I am likely to hit or slap”) reported greater sexual aggression congruent emotions/motivations (e.g., responses to Likert scale regarding questions of how “angry”, “powerful”, etc. they felt) than did intoxicated participants with weaker alcohol-aggression expectancies. Alternatively, alcohol-aggression expectancies did not influence sober participants sexual aggression emotions/motivations. In a similar vein of research, Abbey et al. (2009) used a between-subjects design to examine the role of alcohol (resulting BAC 0.080%), placebo, or control beverage consumption on college men's use of coercive strategies (e.g., endorsement for statements indicating they will spread rumors about their partner if she does not have unprotected sex with him) to obtain unprotected sex from women. Men who had previously committed sexual assault (measured by the

Sexual Experiences Survey [SES]) relative to those who had not, felt more justified in using coercive methods to obtain unprotected sex – and this relationship was increased by alcohol intoxication. That is, individuals who consumed alcohol prior to watching the hypothetical sexual scenario video and who also had higher levels of general hostility or had previously misperceived women's sexual intentions, felt the most strongly justified in the use of coercion for unprotected sex.

3.4.4. Alcohol administration studies among MSM

In the only study found that examined sexual risk decision-making in MSM, [Maisto et al. \(2012\)](#) examined between-subject effects of alcohol (resulting BAC 0.07%), placebo, or control administration expectancies, and sexual arousal (low or high), which was manipulated by viewing either non erotic or mildly erotic movie clips. Each interactive movie clip contained a “risk exposure element” (in which participants were scored based on the number of progressively risky choices made (e.g., do you go with John to his apartment? Do you accept a drink?)). A “behavioral skills element” was also assessed (which included condom use negotiation; e.g., statement of intentions for safer sex). A participant rating of the video was also obtained to evaluate the likelihood that the participant would have engaged in unprotected anal intercourse. These scores were combined to result in a single sexual risk metric. Analyses showed that alcohol administration and greater alcohol sex expectancies led to increased sexual risk on the conglomerate metric, which included unprotected anal intercourse.

3.5. Cocaine self-administration and HIV sexual risk decision-making

[Johnson et al. \(2017\)](#), using a double-blind within-subject design, examined the role of cocaine compared to placebo (orally ingested capsule containing either 0 [placebo], 125, or 250 mg/70 kg of cocaine HCl in capsule form) on reported condom use likelihood in response to a casual sexual encounter vignette using the Sexual Delay Discounting Task ([Johnson and Bruner, 2012](#)). Results showed that participants reported the least sexual desire in the placebo condition, more sexual desire in the low dose condition, and the highest levels of arousal in the high dose condition. There was no significant difference across cocaine and placebo administration with likelihood of engaging in condom-protected sex when no delay was involved. However, cocaine significantly decreased condom use likelihood as a function of increasing delay to condom availability (i.e., participants reported the highest likelihood of condom-use in the placebo condition, and the lowest likelihood of condom use in the highest dose condition). The study also administered a similar task that parametrically manipulated the stated risk of STI contraction using the Sexual Probability Discounting Task ([Johnson et al., 2015](#)). There was no difference across cocaine and placebo administration on likelihood of condom use when there was 100% chance of STI contraction. However, significantly greater effect of delay in terms of reducing condom use in the 250 mg/70 kg as well as 125 mg/70 kg relative to placebo was observed. These results suggest cocaine administration increases the likelihood of engaging in unprotected sex when a condom is not immediately available or perceived risk of STI contraction is low.

3.6. Cannabis self-administration and HIV sexual risk decision-making

[Metrik et al. \(2012\)](#) investigated the role of expectancy in HIV sexual risk decision-making between subjects in a two by two randomized factorial design crossing drug administration (2.8% THC or 0% THC; one cannabis or placebo cigarette from the National Institute on Drug Abuse, smoked until the ash reached 10 mm from the end) with instructed condition (told THC or told placebo). Participants in each condition were matched on demographic characteristics and tobacco smoking. Cannabis cigarettes (2.8% or placebo) were smoked according to a standardized puffing procedure. After smoking, risky sexual decision-making was assessed with a non-exclusive partner, as part of the

CARE-Revised (in which the likelihood of benefits and harms of unprotected sex were also assessed). Results revealed that relative to the placebo group, those who received THC rated benefits of risky sexual decisions with a non-exclusive partner as significantly *less likely*. Additionally, no expectancy effects were revealed.

3.7. Buspirone and HIV sexual risk decision-making

The majority of research reviewed here has been designed to test the effects of substances with abuse liability potential on increased HIV sexual risk decision-making. Very little research however, has tested potential antidotes to risky sexual decision-making, as [Bolin et al. \(2016\)](#) have done. Using a within-subject placebo-controlled design, [Bolin et al. \(2016\)](#) tested the effects of buspirone maintenance (30 mg/day) versus placebo on HIV sexual risk decision-making, as measured by condom use likelihood within the Sexual Delay Discounting Task ([Johnson and Bruner, 2012](#)). Buspirone is an anxiolytic medication that might improve cognitive and behavioral processes associated with impulsive decision-making underlying sexual risk behavior. At the beginning of the first and fourth experimental sessions (following three days of buspirone or placebo maintenance), the authors assessed the difference in the likelihood of using an immediately available condom and the likelihood of using a condom available after stated delays. Each participant answered the condom use likelihood assessments for several partner conditions (i.e., high/low desirability partners, and risky/safe partners).

Results showed that when there was no delay until condom availability, buspirone relative to placebo maintenance increased the likelihood of condom use for less desirable and more risky partners. Although delay to condom availability decreased condom use likelihood, this did not differ between buspirone and placebo maintenance conditions (although for highly desirable partners a trend towards higher likelihood of condom use as opposed to unprotected sex was observed in the buspirone condition). Higher doses of buspirone, longer maintenance periods, and a counseling component may also help to maximize these initial promising findings ([Bolin et al., 2016](#)). Indeed, [Strickland et al. \(2017\)](#) tested the effects of acute (rather than maintenance) buspirone using the Sexual Delay Discounting Task as described above, and found little effect on condom-protected versus unprotected sex.

4. Discussion

This systematic review is the first to evaluate the effects of acute substance administration (including alcohol, cocaine, THC, buspirone) on sexual HIV risk decision-making within controlled laboratory settings (see also [Rehm et al., 2012](#) for a recent meta-analysis limited to only 12 experimental alcohol studies meeting strict criteria regarding statistical reporting, and requiring participants blinded to all conditions and unable to detect differences between conditions). Several themes emerged from the present review. First, despite some variability across studies, the pharmacological effects of alcohol appear to causally increase HIV sexual risk decision-making, particularly in the form of unprotected sex. Second, cocaine is the only non-alcohol substance that has been shown in the laboratory to increase HIV sexual risk decision-making. In contrast, limited evidence suggests that acute cannabis and buspirone maintenance might decrease HIV sexual risk behavior, and acute buspirone might have no impact on HIV sexual risk behavior. Third, comparisons across similar studies revealed cocaine led to greater self-reported sexual arousal than alcohol, suggesting a differential risk profile. Other substantial gaps in the literature were also observed, such as little experimental research investigating acute substance intoxication in populations at very high risk for HIV transmission. Each of these themes will be discussed in turn, followed by consideration as to why laboratory studies offer unique benefits to complement other approaches.

4.1. Alcohol administration and HIV sexual risk decision-making

The majority of studies that qualified for this review addressed the acute effects of alcohol on HIV sexual risk decision-making. These studies, however, are still relatively rare. Although the majority of studies did establish a direct or indirect causal connection between alcohol administration and increased sexual risk decision-making processes, some did not. Additionally, although men tended to report higher baseline levels of HIV sexual risk decision-making than women, acute alcohol intoxication did not seem to influence HIV sexual risk decision-making processes differently across men and women.

One common theme among some studies reviewed was the attempt to separate the influence of alcohol expectancy effects from the intoxicating pharmacological effects of alcohol on sexual risk. Most studies investigating this issue showed that the intoxicating pharmacological effects of alcohol in addition to strong alcohol expectancy significantly increased HIV sexual risk decision-making (e.g., Fromme et al., 1999; Gilmore et al., 2013; Maisto et al., 2004a, b; Maisto et al., 2012; Zawacki, 2011). A minority of studies found effects of alcohol expectancies on sexual risk outcomes but no pharmacological effect of alcohol itself (e.g., Maisto et al., 2002; Murphy et al., 1998). Only one study reported that neither alcohol nor alcohol expectancies had any effect on sexual risk outcomes (Cho and Span, 2010). Further, mediation analyses indicated that those who were intoxicated paid more “attention” to cues indicating an arousing situation than cues indicating a risky situation, and this led to increased HIV sexual risk decision-making (Davis et al., 2007).

Many alcohol studies covered in this review did not differentiate between an *immediately* available condom or a condom that was *not immediately* available. Johnson et al. (2016) demonstrated that when a condom was immediately available, there were no differences in likelihood of condom use across placebo versus alcohol conditions. However, alcohol significantly decreased condom use when there was a delay associated with obtaining a condom. In other words, alcohol only seemed to increase risk in less than ideal conditions. These data suggest that immediately available condoms could increase condom use for some individuals, regardless of alcohol intoxication. Similarly, acute alcohol intoxication also decreased condom use likelihood at lower levels of STI contraction risk, but not when there was a 100% chance of STI contraction. The ability of alcohol to reduce condom use may be consistent with the known effects of alcohol on nonhuman avoidance behavior. Studies in nonhumans suggest that high doses of alcohol (with mixed evidence at lower doses) decrease active responses that are required to prevent future punishment (Galizio et al., 1984; Reynolds and van Sommers, 1960; Heise and Boff, 1962; Katz and Barrett, 1978). This is consistent with the effect of alcohol on human condom use, because condom use is an active, effortful (particularly when postponement of sex is required) response, the purpose of which is to prevent future unwanted consequences, including HIV or other STI contraction.

Taken together, the results of this review suggest that acute alcohol intoxication causes heightened arousal and less attention to risky sexual cues, leading to riskier sexual decision-making and reduced likelihood of condom use. These detrimental effects of alcohol intoxication are exacerbated by stronger alcohol expectancies (which are not decoupled from alcohol intoxication in real world sexual situations), and delay to condom availability, which further reduces the likelihood of condom use during sex.

4.2. Cocaine, THC, or bupirone administration and HIV sexual risk decision-making

Only one study tested the acute effects of cocaine on sexual risk behavior. Johnson et al. (2017) showed that cocaine relative to placebo administration dose dependently increased sexual desire, as well as dose dependently decreased the likelihood of condom use *only* when a

condom was not immediately available. In other words, like the alcohol effects of Johnson et al. (2016) cocaine only seemed to increase risk in less than ideal conditions. However, such suboptimal circumstances without immediately available condoms likely reflects many real life sexual risk scenarios. A similar pattern of results was found with regard to risk of STI contraction, with cocaine only decreasing condom use when STI contraction from unprotected sex was uncertain, not when it was certain. Overall, these results suggest the public health benefits of making condoms freely and readily accessible. These benefits may be maximized in contexts in which substance use occurs and sexual interactions are initiated (e.g., bars, night clubs).

Cross-study comparisons of subjective arousal across alcohol (Johnson et al., 2016) and cocaine (Johnson et al., 2017) suggest that arousal might be substantially higher with cocaine administration compared to alcohol administration. Using similar but slightly differing scales (e.g., using terms “desire” vs. “arousal”), the difference between high dose cocaine and placebo administration on peak arousal ratings was equivalent to roughly 56% of the scale maximum. However, the difference between alcohol and placebo administration on peak arousal ratings was equivalent to only roughly 16% of the scale maximum (see Johnson et al., 2017; Johnson et al., 2016). These data suggest that intoxicated arousal effects observed for alcohol that lead to increased HIV sexual risk behavior, might be more extreme for cocaine. The non-human animal literature also points to intense sexual responses with exposure to dopaminergic stimulants including cocaine (Afonso et al., 2009; Holder et al., 2010; Levens and Akins, 2004). This may constitute a difference in the mechanisms driving increased HIV sexual risk decision-making processes across various substances.

In contrast to a number of the alcohol studies reviewed and the single cocaine study reviewed, researchers investigating the effects of cannabis relative to placebo found that perceptions of benefits of sex with a non-exclusive partner were *less likely* (Metrik et al., 2012), and observed no evidence of expectancy effects. Naturalistic self-report research incorporating event-level analyses among adolescents at high risk for HIV, however, has shown a decreased likelihood of condom use while under the influence of cannabis while controlling for alcohol consumption (Hendershot et al., 2010), although this relation was in part influenced by expectancy effects and behavioral intentions. The lack of laboratory data support for a causal effect of cannabis on sexual risk suggests that the naturalistic research results might be due to other factors (e.g., specialized population, unaccounted environmental risk cues, limitations of self-report). This possibility highlights the need for more experimental studies designed to determine the potential causal role of cannabis use in sexual risk behavior.

Strickland et al. (2017) and Bolin et al. (2016) have tested bupirone in a novel approach examining a drug that may *reduce* HIV sexual risk decision-making. The initial results of bupirone maintenance treatment on HIV sexual risk decision-making are promising. Anecdotal reports of bupirone effects have indicated decreased libido, however, this is a relatively rare side effect (U.S. Food and Drug Administration, 2010). It is therefore unknown whether decreased libido may be driving the increase in condom use observed in the research of Strickland and colleagues. More innovative research of this kind is needed to determine factors that *reduce* HIV sexual risk decision-making within at risk populations.

4.3. Notable literature gaps

The literature is substantially lacking in several areas. Experimental investigation needed to establish a causal link between substance intoxication and HIV sexual risk decision-making is nearly non-existent outside of alcohol. This is surprising, given the extraordinarily high rates of HIV in specific substance using populations (e.g., cocaine, methamphetamine) compared to the general public (CDC, 2016a). There is also very little investigation (only one alcohol study) into a high-risk population for HIV transmission, MSM, despite broad

associations between MSM, drug use and HIV sexual risk decision-making. Many studies only examined a single drug dose. As dose-response relations may potentially be complex (e.g., absence of an adverse effect until some threshold dose is reached; inverted “U” shaped relations), researchers should strive to incorporate multiple active substance doses in addition to placebo when feasible. Very few studies in this review incorporated within-subject designs. Within-subject designs are ideal when examining reversible or temporary effects as is typically the case with drug administration, and may therefore reduce the variability associated with individual differences, especially regarding how substances affect individuals.

4.4. Limitations

Laboratory experiments offer substantial methodological benefits (e.g., ability to determine pharmacological causality, controlled doses, and data collection does not rely on participant memory), which complement naturalistic data collection. However, limitations exist with experimental laboratory methods as well. First, it is difficult to capture the causal effects of chronic substance use on HIV sexual risk decision-making with most study designs using humans as subjects (with the exception of an extended longitudinal study). This is a relevant concern because general neurocognitive decrements resulting from chronic substance use (Bates et al., 2002; Davis et al., 2002; Rogers and Robbins, 2001) likely also play a role in HIV sexual risk decision-making. Additionally, removal of individuals from a naturalistic context of substance use may nullify important social and situational variables contributing to HIV sexual risk decision-making processes. Experiments also necessarily incorporate hypothetical as opposed to real sexual risk scenarios, although this may represent the best possible way to examine HIV sexual risk decision-making under controlled conditions. These results should also be considered in the context of publication bias. Additional cross-pollination and multi-pronged approaches for fusing naturalistic and experimental attributes (e.g., experiments in the context of social drinking or substance use) may represent the next generation of HIV sexual risk decision-making research.

4.5. Conclusions

Placebo-controlled experimental research designed to determine acute effects of substances other than alcohol on HIV sexual risk decision-making processes is in its infancy. This is unfortunate, as sexually active substance using populations (e.g., cocaine and methamphetamine users) are at a significantly heightened risk for HIV infection compared to the general population (CDC, 2016a, b). Although substance administration experiments investigating HIV sexual risk decision-making can be costly and time-consuming, researchers with facilities and personnel equipped to run administration experiments should consider adding HIV sexual risk decision-making metrics to their existing studies. Such efforts have the potential to considerably inform the direction of public health initiatives designed to reduce HIV transmission. The results of this review suggest a causal role of acute substance intoxication and HIV sexual risk decision-making processes (with the exception of THC administration), and thus targeting substance use education and reduction as a means to reduce HIV risk decision-making may lead to more effective HIV prevention measures. Making condoms freely available for community members may also help to attenuate the influence of acute intoxication on HIV sexual risk decision-making.

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