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SUBSTANTIVE REVIEW

A Review of the Literature on Event-Level Substance Use and Sexual Risk Behavior Among Men Who Have Sex with Men

H. Waverly Vosburgh · Gordon Mansergh · Patrick S. Sullivan · David W. Purcell

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Abstract In the United States, there continues to be high incidence of HIV infection among men who have sex with men (MSM), who represent 57% of new infections in 2009. While many studies report associations between non-injection substance use and sexual risk behavior among MSM, overall results are mixed. Summarizing these studies is difficult because researchers have used a variety of assessment periods for substance use and sexual behavior. We review the scientific literature on event-level measures, which assess substance use and sexual risk behavior immediately before or during a sexual encounter and provide the most precise link between these two behaviors. From January 2009 through March 2010, we searched four databases: Ovid (MEDLINE and PsycINFO), Web of Knowledge, and Sociofile. Across studies, results varied by substance with little within substance consistency or a lack of research except for two notable exceptions: methamphetamine and binge alcohol use. The findings underscore the importance of providing HIV risk-reduction interventions for substance-using MSM.

Keywords MSM · Substance · Sexual risk · HIV

Resumen En los Estados Unidos, incidencia alta de la infección por VIH entre los hombres que tienen sexo con hombres (HSH) sigue, y HSH representaron 57% de las infecciones nuevas en 2009. Estudios múltiples han demostrado que asociaciones existe entre el uso de drogas no inyectables y el comportamiento sexual riesgoso entre HSH. Estudios del uso de drogas y del comportamiento sexual han usado tres tipos de evaluacíon (global, circunstancial y nivel del acontecimiento) y han proporcionado resultados variados. Las medidas al nivel del acontecimiento sexual determinan uso de sustancias y comportamiento sexual riesgoso de inmediato antes de o durante el encuentro sexual. Se revsamos la literatura científica acerca de la conexión más precisa entre el uso de drogas y el comportamiento sexual riesgoso, lo cual es evaluacíon al nivel del acontecimiento. Desde enero de 2009 hasta marzo de 2010, buscamos en cuatro bases de datos repetidamente: Ovid (MEDLINE y PsycINFO), Web of Knowledge, y Sociofile. Resumimos la investigación cuantitativa acerca de nivel del acontecimiento, discutimos la consistencia de la evidencia, y recomendamos las direcciones para las investigaciónes futuras. Los resultados subrayan la importancia de proporcionar las intervenciones para la reducción del riesgo por el VIH para HSH que usan drogas.

H. W. Vosburgh (✉) · G. Mansergh · D. W. Purcell
Division of HIV/AIDS Prevention, Mailstop E37, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, Atlanta, GA 30333, USA
e-mail: HWVosburgh@cdc.gov; irx3@cdc.gov

H. W. Vosburgh · P. S. Sullivan
Rollins School of Public Health, Emory University, Atlanta, GA, USA

Introduction

In the United States, men who have sex with men (MSM) continue to have the highest incidence of HIV infection, representing 57% of new infections in 2009 in the 40 states reporting HIV infection [1]. Although diagnoses among other groups have been stable or have declined since 2000 [2], the recent incidence estimates of the Centers for Disease Control and Prevention (CDC) show an increase in new HIV diagnoses among MSM beginning in the early 1990s. Similar trends among MSM have been shown in other countries [2–6]. A model based on annual HIV

incidence data since the introduction of highly active antiretroviral therapy in 1995 predicted that among a cohort of HIV-negative MSM aged 18 today, 41% would be infected by the time they reached 40 years of age [7].

Substance use is one factor that has been explored as a potential factor in high rates of HIV incidence among MSM. Research suggests that the rates of illicit substance use are higher among MSM compared to the general US population and heterosexual counterparts [8, 9]. Despite associations between non-injection substance use and sexual risk behavior among MSM [10–12], the results of research from various measurement approaches [13] have not been consistent.

Leigh and Stall [13] outlined methodological issues related to assessing the association of substance use and sexual behaviors and identified three measurement approaches: global, situational, and event-level. *Global assessments* measure substance use and sexual behavior during a specified broad period of time (e.g., past 3 months)—the drug use and sexual behaviors do not necessarily occur together; however, they take place during the same recall period. *Situational assessments* measure substance use and sexual behavior occurring together within a specified time period (e.g., past 3 months) but given a broad recall period, this assessment may measure any number of events where sex and substance use occurred together. *Event-level assessments* measure the specific substances used and sexual behaviors surrounding a specific sexual encounter (e.g. most recent sexual encounter). Event-level measurement can capture important contextual details (e.g., substance used, sexual position, partner and environmental characteristics) [13].

To date, there have been summary reviews of the research on the association of substance use and sexual risk behavior among MSM [11, 14–16] including summaries specific to alcohol [17, 18], methamphetamine [19, 20], and erectile dysfunction drugs [21, 22]. Only three systematic reviews that thoroughly addressed literature on the association of substance use and sexual risk behavior of MSM have included event-level behavioral measurement [17, 23, 24]. Drumright and colleagues conducted a systematic review of substances limited to specific "club drugs" [23]. Since that 2006 review, a considerable number of event-level studies [10, 25–41] have been published on a full range of MSM substance use. Another systematic review [24] focused on MSM over 50 years of age, and only two event-level studies were included. A third systematic review [17] focused solely on MSM alcohol use.

The purpose of this article is to review the scientific literature on the association between substance use and sexual behavior among MSM at the event-level and expand on the prior systematic reviews by examining all substances, focusing on event-level literature, and not limiting the samples of MSM [17, 23, 24]. The growing body of event-level research may provide an expanded understanding of the link between substance use and sexual risk among MSM. In the current review, event-level associations are subdivided into two categories: single episode event-level analysis (i.e., a specific sexual episode), and multiday event-level analysis (i.e., sexual behavior that occurred over a specified several-day timeframe, as in a circuit party).

Method

A systematic literature search was conducted to identify studies that quantitatively assessed the event-level association between substance use and sexual risk behavior of MSM. We searched four databases for all studies that collected data from 1996 to the present: OVID (MEDLINE and PsycINFO), Web of Knowledge, and Sociological Abstracts. Searches were conducted in 2009 and again in early 2010 to ensure that no relevant studies were missed due to the delay between publication and database indexing. Search terms were determined after reviewing combinations of frequently used indexing and keyword terms from the literature. We searched combinations of the following terms:

- MSM, gay, homosexual, men who have sex with men
- Substance, substance use, drugs, drug use
- HIV, HIV risk, condom use, unprotected

Literature searches were conducted in two phases. First, we selected studies assessing substance use and sexual risk behavior among MSM. Second, we reviewed the content of the studies to determine the focus of assessment and eliminate studies that did not provide event-level analyses. We also reviewed the reference lists of the selected studies to locate other studies that met our criteria for inclusion:

- Research published in peer-reviewed journals
- Research conducted in North America, Western Europe, or Australia—countries where the HIV epidemic continues to be majority MSM [6]
- Data collection completed from January 1996—a period when highly active antiretroviral therapy was available
- Quantitative assessments of the association of non-injection substance use and
  - (a) sexual risk behavior
  - (b) recent HIV infection
  - (c) other sexually transmitted infection [STI])
- At least one analysis of event-level association between substance use and measures of sexual risk behavior

We eliminated studies that included populations other than MSM (e.g., women or transgender persons), as well as, injection drug users. Studies assessing the association of sexual risk behavior and substance use typically separate injection drug use and non-injection drug use because injection drug use introduces additional risk opportunity (i.e., sharing needles) [42]; thus, we excluded studies of injection drug-using MSM.

The first phase of the search identified 1,608 articles. Following thorough screening of these abstracts, 151 full reports were reviewed to identify studies using event-level assessment. We excluded 60 studies in which only global measures were assessed and 59 studies in which only situational measures were assessed. Two reviewers independently coded the content of the remaining 32 studies to ensure the appropriateness of inclusion and to summarize the findings. Of the 32 remaining studies, nine did not fit the criteria and were excluded as follows: six because the data had been collected before 1996 [43–48], one because the referent group was not comparable (i.e., the study compared protected and unprotected anal sex to "no anal intercourse") [49], one because no associational analyses were presented [50], and one because a sub-analysis of the data (from another publication) [51] had already been included in the review. Ultimately, our review included 23 independent samples.

Definitions of Substance Use and Sexual Risk Behavior

The measurement of substance use was highly variable from study to study. To address the inconsistent use of terms and allow for qualitative comparison, we created a terminology list (Table 1) and applied it to the studies as appropriate. Similarly, the definitions of sexual risk behavior varied (Table 2). A few studies used recent STI or HIV infection as the outcome measure; most assessed unprotected anal sex (UA). Among studies whose outcome was UA, many were stratified by position (i.e., insertive or receptive), HIV status (i.e., positive, negative, or unknown), and partner type (e.g., primary or casual). Due to the heterogeneity of the substance use measures and the varied definitions of the sexual risk behavior measures, we determined that a meta-analysis was not the most appropriate approach.

Results

Table 2 presents descriptive statistics of the 23 studies. Across the studies, results varied by substance with little within substance consistency except for two notable exceptions. Out of 15 substance categories measured, only methamphetamine use and binge drinking (i.e., five or more alcoholic drinks on one occasion) were consistently associated with event-level sexual risk behavior among MSM.

Characteristics of Studies

Of the 23 included studies, 18 were conducted in North America [26–32, 35–40, 46, 52–55] with the remaining studies conducted in Australia [25, 28, 33, 34] and Scotland [56]. Fifteen of the studies were single event-level analyses (Table 3), and eight included event-level analysis of sexual behavior during multi-day events (Table 4). A majority of the studies ($n = 18$) were cross-sectional in nature [10, 25–33, 36, 39–41, 52, 54–56], including all of the North American studies. The other five studies represent case–control approaches [34, 38] or a prospective daily diary assessment [35, 37, 53]. Sample sizes of all studies ranged from $n = 78$ to $n = 4{,}295$. Although most of the studies defined sexual risk behavior as sex without a condom, specification of the measure was highly variable. Some of the studies analyzed by partner type (i.e., primary or casual partner) or only analyzed a specific partner type [25, 32, 54], including sexual behavior with a casual partner [10, 28, 33, 39]. Another difference across studies was sub-analysis by insertive or receptive anal sex [26, 29, 38, 54], HIV-discordance or concordance between the respondent and his partner [29, 37, 40, 41, 52, 55, 56], and single vs. multiple partners during the sexual event [31]. Three studies investigated recent STIs (i.e., Chlamydia, gonorrhea, syphilis, urethritis, other STI) [10] or recent HIV infection [34, 38]; one study created a composite HIV risk score [35]. Across the studies, a variety of substances were examined with measures representing 15 different substance categories (i.e., four broad substance categories, 11 specific substances).

Specific Substance Use Measures

Across the 11 specific substances measured, only methamphetamine use and binge alcohol drinking were associated with sexual risk behavior in at least one analysis in each of the studies that examined those substances (Fig. 1). Methamphetamine use before sex was evaluated in eight [27, 29, 31, 32, 38, 40, 41, 52] and binge drinking was assessed in six [26, 30, 34, 39, 41, 55] of the 23 studies. Methamphetamine use was particularly associated with unprotected receptive anal sex [29, 38]. Several of the analytic models that did not find methamphetamine use to be significantly associated with sexual risk behavior either addressed small subsamples [31] or had unique variables (e.g., unprotected insertive anal sex) that could account for the lack of independent statistical significance [38]. Every analysis of the association of binge alcohol use and sexual

Table 1 Substance use definitions of the reviewed studies ($n = 23$)

Substance use category[a]	Substance use review category	Study citations	Original substance use definition of cited study
Alcohol or drug	Any measure of combined generic drug and alcohol use	Stueve et al. [54]	Being high—any use of drugs or alcohol
		Holtgrave et al. [28]	Being high or drunk
Alcohol	Any generic alcohol measure or any measure of <4 drinks of alcohol; if more than one amount, <4 is included then this is specified in the table	Clutterbuck et al. [56]	Alcohol
		Colfax et al. [55]	1–2 alcoholic drinks
		Prestage et al. [25]	Alcohol
		Chiasson et al. [31]	Alcohol
		Read et al. [46]	<30 g, >30 g of alcohol
		Mansergh et al. [10]	Alcohol
		Prestage et al. [41]	Less than 5 alcoholic drinks
		Gillmore et al. [53]	Alcohol
		Benotsch et al. [26]	Alcohol
		Mustanski [35]	Number of drinks
Binge alcohol	Any measure of "excessive" alcohol use or ≥4 alcohol drinks on one occasion	Colfax et al. [55]	≥6 alcoholic drinks
		Read et al. [34]	>60 g and >100 g of alcohol
		Prestage et al. [41]	≥5 alcoholic drinks
		Benotsch et al. [26]	Alcohol used to the point of intoxication—'anal sex after having too much to drink'
		Benotsch et al. [30]	Alcohol used to the point of intoxication—'anal sex after having too much to drink'
		Lambert et al. [39]	≥5 alcoholic drinks at last sex event
Drug	Any measure that did not define specific drug use and assessed drug use as a single measure	Colfax et al. [55]	Poppers (amyl nitrites), snorted or cocaine or amphetamines
		Prestage et al. [33]	Recreational drug use (aside from Viagra measured separately)
		Mansergh et al. [10]	Drug use includes marijuana, methamphetamine, poppers, crack, cocaine, Viagra and other drugs
		Wilson et al. [37]	Any drug use
		Gillmore et al. [53]	Drug use
		Benotsch et al. [26]	Anal sex after using drugs
		Benotsch et al. [30]	Anal sex after using drugs
		Wilson et al. [36]	Use of any drugs by self, partner or both self and partner
		Drumright et al. [27]	Use of any drugs other than erectile dysfunction drugs
		Drumright et al. [38]	Any drug use
		Lambert et al. [39]	Cocaine with or without other substances

Table 1 continued

Substance use category[a]	Substance use review category	Study citations	Original substance use definition of cited study
Marijuana	Any measure of marijuana use	Clutterbuck et al. [56]	Marijuana
		Benotsch et al. [26]	Marijuana
		Drumright et al. [48]	Marijuana
		Prestage et al. [41]	Cannabis
		Drumright et al. [38]	Marijuana
Poppers	Any measure of amyl nitrates/nitrites use	Clutterbuck et al. [56]	Nitrites
		Prestage et al. [25]	Amyl nitrites
		Read et al. [34]	Amyl nitrite
		Prestage et al. [41]	Amyl
		Colfax et al. [52]	Amyl nitrites
		Benotsch et al. [26]	Poppers
		Drumright et al. [27]	Volatile Nitrites
		Drumright et al. [38]	Volatile Nitrites
Erectile dysfunction drug	Any combined measure of erectile dysfunction drug use; if multiple ED drugs were assessed individually, then the name of the drug is used in the tables	Colfax et al. [52]	Sildenafil
		Benotsch et al. [26]	PDE5 Inhibitor use—any use of Viagra, Levitra or Cialis (also measured individually)
		Drumright et al. [27]	Erectile Dysfunction Medications including Viagra/sildenafil citrate, Levitra/vardenafil HCL, Cialis/tadalafil
		Drumright et al. [38]	Any use of sildenafil citrate (Viagra1, Pfizer), tadalafil (Cialis1, Eli Lilly), and vardenafil hydrochloride (Levitra1, Bayer Pharmaceuticals, GlaxoSmithKlein, and Schering-Plough).
		Prestage et al. [25]	Viagra
		Mansergh et al. [29]	Sildenafil (Viagra)
		Chiasson et al. [31]	Sildenafil
		Prestage et al. [41]	Orally-administered Erectile Medications (specified Viagra and Cialis)
Methamphet-amine	Any measure of methamphetamine or amphetamine use	Mansergh et al. [29]	Methamphetamines
		Chiasson et al. [31]	Crystal methamphetamine
		Koblin et al. [32]	Non-injection use of "amphetamines, meth, speed, crystal, crank, ice"
		Ober et al. [40]	Methamphetamines
		Prestage et al. [41]	Methamphetamines
		Colfax et al. [52]	Crystal methamphetamine
		Drumright et al. [27]	Methamphetamines
		Drumright et al. [38]	Methamphetamines

Table 1 continued

Substance use category[a]	Substance use review category	Study citations	Original substance use definition of cited study
Other drug	Any measure of additional drugs after some specific substances were assessed individually	Clutterbuck et al. [56]	Party drugs—any use of LSD, ecstasy, amphetamines and cocaine
		Colfax et al. [55]	Partner's use of other drugs
		Prestage et al. [25]	Other recreational drugs
		Mansergh et al. [29]	Use of other substances including alcohol, marijuana, cocaine, crack, LSD/mushrooms, heroin, ecstasy/MDMA, ketamine, GHB, amyl nitrite/poppers)
		Lambert et al. [39]	Use of any other substances than cocaine
		Read et al. [34]	Amphetamine and/or ecstasy
Multidrug	Any measure of multiple substance use during a specific occasion	Drumright et al. [27]	Use of more than one drug other than erectile dysfunction drugs
		Drumright et al. [38]	Use of more than one drug

ED erectile dysfunction, *GHB* gamma-hydroxybutyric acid, *STI* sexually transmitted infection, *LSD* Lysergic acid diethylamide, *MDMA* Methylenedioxymethamphetamine

[a] Substances measured individually that do not fit in the above categories are labeled by their name

Table 2 Descriptive characteristics of the reviewed studies ($n = 23$)

Characteristic/measure	*n* (%) of all studies
Study location	
North America	18 (78)
Outside North America	5 (22)
Type of analysis	
Bivariate analysis only	5 (22)
Multivariate analysis	18 (78)
Type of event-level measure	
Single episode event	15 (65)
Multi-day event	8 (35)
Specific substance use measured[a]	
Alcohol	10 (44)
Binge alcohol	6 (26)
Cocaine	4 (17)
Crack	1 (4)
Ecstasy	2 (9)
Erectile dysfunction drugs	8 (35)
GHB	3 (13)
Ketamine	3 (13)
Marijuana	5 (22)
Methamphetamine	8 (35)
Poppers (amyl nitrates)	8 (35)
Broad substance use measured[a]	
Alcohol or drug use	2 (9)
Drug use	11 (48)
Multi-drug use	2 (9)
Other drug use	7 (30)
Type and number of substance use measured[a]	
Broad substance use only	5 (22)
Specific substances only	5 (22)
1–3 specific substances measures	13 (57)
4–5 specific substances measures	1 (4)
≥6 specific substances measures	4 (17)
Sexual risk behaviors measured[a]	
Unprotected anal sex	16 (70)
HIV-discordant unprotected anal sex	7 (30)
Unprotected insertive anal sex	4 (17)
HIV-discordant unprotected insertive anal sex	1 (4)
Unprotected receptive anal sex	4 (17)
HIV-discordant unprotected receptive anal sex	1 (4)
Case: recent HIV infection (past year)	2 (9)
Recent sexually transmitted infection (past year)	1 (4)
Composite HIV risk score	1 (4)

GHB gamma-hydroxybutyric acid

[a] Measures are not mutually exclusive across studies

Table 3 Single episode event-level studies of substance use and HIV risk among MSM reviewed

Reference	Location	Research design and analytic sample (*n*)	Sexual risk behavior or other HIV-related risk variables measured[a]	Substance use variables measured[b]	Bivariate analysis results (significant in bold)[c]	Multivariate analysis results (significant in bold)[c]
Clutterbuck et al. [56]	Edinburgh, Scotland	Cross-sectional (critical incidents interview); $n = 506$	DUA at last sex; separate analysis- most recent DUA in past 3 months compared to last protected anal sex of those that did not have any DUA in past 3 months	Use <2 h before sex at last sex: Alcohol, Marijuana, Poppers, Other drug use	*DUA at last sex*: alcohol, **marijuana (OR = 4.50, CI = 1.90–10.09), poppers (OR = 2.40, CI = 1.40–4.05),** "other drug use". *Most recent DUA*: alcohol, **marijuana (OR = 2.60, CI = 1.20–5.45), poppers (OR = 3.60, CI = 1.80–7.10), "other drug use" (OR = 2.90, CI = 1.20–7.30)**	No multivariate analysis
Stueve et al. [54]	Multiple cities in the following states: AL; CA; GA; IL; MI; MN; NY; NY; WA; WI	Cross-sectional survey (baseline interview of CITY project); $n = 2{,}624$	UA, URA, UIA at last sexual encounter separately for main and casual partner	Alcohol or drug use	Not reported	*UA* with nonmain partner—**alcohol or drug use (OR = 1.55, CI = 1.09–2.20),** *UA* with main partner—alcohol or drug use; *URA* with nonmain partner**—alcohol or drug use (OR = 1.66, CI = 1.08–2.56);** URA with main partner: alcohol or drug use; UIA with nonmain partner—alcohol or drug use; UIA with main partner—alcohol or drug use
Colfax et al. [55]	San Francisco, CA; Denver, CO; Chicago, IL; Boston, MA; New York City, NY	Randomized behavioral intervention (baseline interview); $n = 4{,}295$	DUA	Alcohol use, binge alcohol, alcohol use by partner (any amount), drug use, other drug use by partner, drug use by partner unknown	Alcohol use; b**inge alcohol (OR = 3.30, CI = 2.30–4.70); alcohol use by partner (OR = 1.80, CI = 1.50–2.10); drug use (OR = 1.90, CI = 1.40–2.50); other drug use by partner (OR = 2.00, CI = 1.60–2.40); drug use by partner unknown (OR = 1.80, CI = 1.40–2.10)**	Alcohol use—1–2 drinks; **binge alcohol (OR = 2.40, CI = 1.60–3.70); alcohol use by partner (OR = 1.30, CI = 1.00–1.70), $P = 0.03$; drug use (OR = 1.50, CI = 1.10–2.00); other drug use by partner (OR = 1.50, CI = 1.20–2.00); drug use by partner unknown (OR = 1.60, CI = 1.20–2.00)**
Prestage et al. [25]	Sydney, Australia	Cross-sectional (baseline of longitudinal study); $n = 471$	UA vs. protected anal sex at last encounter by partner type	Alcohol, poppers, ED drugs, other drug use	*Regular partner*: Alcohol, poppers, ED drugs, other drug use; *casual partner*: alcohol, poppers, ED drugs, other drug use	No multivariate analysis

Table 3 continued

Reference	Location	Research design and analytic sample (*n*)	Sexual risk behavior or other HIV-related risk variables measured[a]	Substance use variables measured[b]	Bivariate analysis results (significant in bold)[c]	Multivariate analysis results (significant in bold)[c]
Holtgrave et al. [28]	Atlanta, GA	Cross-sectional survey, $n = 391$	UA: last anal sex event with non-primary partner (had to have occurred in past 12 months)	During last sex: alcohol or drug use	*UA*: **alcohol or drug use (OR = 1.60, CI = 1.10–2.20)**	*UA*: **alcohol or drug use (OR = 1.80, CI = 1.15–3.00)**
Mansergh et al. [29]	San Francisco, CA	Cross sectional survey, $n = 388$	UA, UIA, URA, DUA, DUIA, DURA	Before or during most recent sexual encounter: ED drugs, meth/amphetamine, other drug use	*UA*: **ED Drugs: ($P < 0.05$); Meth/Amphetamine: $P < 0.05$,** *UIA*: **ED Drugs: $P < 0.01$;** Meth/Amphetamine, Other drugs *URA*: ED Drugs; **Meth/Amphetamine $P < 0.01$**, Other drugs, *DUA*: **ED Drugs: $P < 0.01$**; Meth/Ampetamine; *DUIA*: **ED Drugs: $P < 0.01$;** Meth/Amphetamine, Other drugs *DURA*: ED Drugs (Sildenafil); **Meth/Amphetamine $P < 0.01$**, Other drugs	*UA*: ED Drugs; Meth/Amphetmaine, Other drugs; ***UIA*: ED Drugs: (OR = 6.56, CI = 2.47–17.40)**; Meth/Amphetamine; Other drugs; *URA*: ED Drugs; **Methamphetamine (OR = 2.04, CI = 1.10–3.81);** Other drugs; *DUA*: **ED Drugs: (OR = 4.35, CI = 1.63–11.59);** Meth/Amphetamine; Other drugs; *DUIA*: **ED Drugs: (OR = 29.24, CI = 7.9–108.26);** Meth/Amphetamines; Other drugs; *DURA*: ED Drugs; **Methamphetamine (OR = 2.15, CI = 1.02–4.50);** Other drugs
Chiasson et al. [31]	US; Canada	Cross-sectional survey (internet study), $n = 1,683$	UA at last sexual encounter	Use before sex—alcohol, ED drugs, meth/amphetamine	*UA*: Single partner encounter ($n = 638$): alcohol; **ED drugs: (OR = 2.10, CI = 1.20–3.90); meth/amphetamine (OR = 6.70, CI = 2.50–17.90)**; multiple partner encounter ($n = 243$): alcohol; **ED drugs: (OR = 3.00, CI = 1.30–6.50); meth/amphetamine (OR = 4.10, CI = 1.70–10.00)**	*UA*: Single partner encounter ($n = 638$): alcohol; ED drugs; **meth/amphetamine (OR = 5.70, CI = 2.00–15.90)**; multiple partner encounter ($n = 243$): alcohol; ED drugs; meth/amphetamine
Koblin et al. [32]	New York City, NY	Cross-sectional survey (Wave 1 of NHBS[d]), $n = 243$	UA: Within-subject comparison of last UA and protected anal sex	Meth/amphetamines	*UA*: **meth/amphetamines (OR = 4.50, CI = 1.00–20.80), $P < 0.05$**	*UA*: **meth/amphetamines (OR = 4.90, CI = 1.10–34.30)**
Prestage et al. [33]	Sydney, Australia	Cross sectional survey; $n = 103$	UA with casual partners at most recent encounter	Drug use: (alcohol mentioned in discussion but not results)	*UA*: Drug use	No multivariate analysis

Table 3 continued

Reference	Location	Research design and analytic sample (*n*)	Sexual risk behavior or other HIV-related risk variables measured[a]	Substance use variables measured[b]	Bivariate analysis results (significant in bold)[c]	Multivariate analysis results (significant in bold)[c]
Read et al. [34]	Victoria, Australia	Case–control; $n = 78$	Case: recent HIV infection	Alcohol; binge alcohol; poppers; other drug use	Case: Alcohol (<30 g); Alcohol (>30 g); **Binge alcohol (>60 g) (OR = 2.30, CI = 1.50–30.60)**; Binge alcohol (>100 g); ***P* = 0.01 for trend in alcohol;** Poppers; Other drug use	No multivariate analysis
Mansergh et al. [10]	Los Angeles, CA; San Francisco, CA; Chicago, IL; New York City, NY	Cross-sectional survey, $n = 1{,}540$	In the past year: any STI, Chlamydia, Gonorrhea, Syphilis, Urethritis, Other STI (includes undetermined)	During most recent anal sex encounter with non-primary partner: alcohol; drug use	*Any STI*: **drug use—OR = not reported, *P* < 0.05, alcohol use inversely associated with any recent STI, *P* < 0.05**	*Any STI*: **alcohol use (OR = 0.80, CI = 0.60–1.00), *P* < 0.05; drug use (OR = 1.30, CI = 1.00–1.60), *P* < 0.05;** *Syphilis*: **alcohol use (OR = 0.60, CI = 0.40–0.80); drug use— (OR = 1.50, CI = 1.00–2.10) *P* < .05;** *Other STI*: alcohol use**, drug use-(OR = 1.60, CI = 1.10–2.40);** *Gonorrhea*: alcohol use, drug use; *Chlamydia*: alcohol use, drug use; *Urethritis*: alcohol use, drug use
Wilson et al. [36]	Los Angeles, CA; Miami, FL; New York City, NY (Subsample from Nuestras Voces Latino Gay Men's Study)	Cross sectional survey (within-subjects comparison); $n = 270$	UA	During sexual episode: drug use—"drug use" not further defined; analyzed by self use, partner use, or self and partner use	*UA*: drug use; **drug use by partner (OR = 1.69, CI = 1.07–2.67);** drug use by both self & partner	*UA*: **drug use by partner (OR = 1.82, CI = 1.10–3.03)**
Ober et al. [40]	Los Angeles, CA	Cross-sectional (2 phases); $n = 779$	UA, DUA, UA if HIV+, UA with HIV+ partner	Use during encounter: Meth/amphetamine; crack	*UA*: **meth/amphetamine use (OR = 2.10, CI = 1.20–3.70)**; crack; *DUA*: meth/amphetamine, **crack (OR = 0.29, CI = 0.11–0.80);** *UA if HIV* + : meth/amphetamine, **crack (OR = 0.21, CI = 0.10–0.47);** *UA if partner HIV* + **:** meth/amphetamine, **crack (OR = 0.08, CI = 0.02–0.36)**	*UA*: **meth/amphetamine (OR = 2.80, CI = 1.50–5.30);** crack**;** *DUA*: Meth/Amphetamine, **crack (OR = 0.34, CI = 0.12–0.92);** *UA if HIV* + : meth/amphetamine, crack**;** *UA if partner HIV* + **:** meth/amphetamine, **crack (OR = 0.12, CI = 0.03–0.53)**

Table 3 continued

Reference	Location	Research design and analytic sample (*n*)	Sexual risk behavior or other HIV-related risk variables measured[a]	Substance use variables measured[b]	Bivariate analysis results (significant in bold)[c]	Multivariate analysis results (significant in bold)[c]
Prestage et al. [41]	Australia	Cross-sectional survey; $n = 746$	DUA	Use during the most recent group sex event: alcohol, binge alcohol, marijuana, poppers, ED drugs, meth/amphetamine, cocaine, GHB, ketamine, heroin, "psychedelic" drugs, other drug use	*DUA:* alcohol, **binge alcohol: $P < 0.01$, marijuana: $P < 0.01$, poppers: $P < 0.01$, ED drugs: $P < 0.01$, meth/amphetamine: $P < 0.01$, cocaine: $P < 0.01$, GHB: $P < 0.01$, ketamine: $P < 0.01$, heroin: $P < 0.01$, "psychedelic" drugs: $P < 0.01$**	*DUA*: alcohol, **binge alcohol (OR = 2.41, CI = 1.34–4.33),** marijuana, poppers, ED drugs, **meth/amphetamine (OR = 1.74, CI = 1.06–2.88),** cocaine, GHB, ketamine, heroin, "psychedelic" drugs
Lambert et al. [39]	Montreal, Canada	Cross-sectional survey; $n = 965$	UA at last sexual episode	At last sexual episode: binge alcohol, other drug use (than cocaine), cocaine use with or without other drugs	*UA*: b**inge alcohol (OR = 1.78, CI = 1.13–2.80), other drug use (OR = 1.76, CI = 1.10–2.8), cocaine use (OR = 3.01, CI = 1.65–5.49)**	*UA*: **binge alcohol (OR = 1.78, CI = 1.06–3.0),** other drug use**, cocaine use (OR = 2.49, CI = 1.23–5.04)**

OR odds ratio, *CI* 95% confidence interval, *ED* erectile dysfunction; *GHB* gamma-hydroxybutyric acid, *STI* sexually transmitted infection

[a] The sexual risk variables are abbreviated as follows: unprotected anal intercourse (UA); HIV sero-discordant unprotected anal intercourse (DUA); unprotected receptive anal intercourse (URA); unprotected insertive anal intercourse (UIA), HIV sero-discordant unprotected receptive anal intercourse (DURA); HIV sero-discordant unprotected insertive anal intercourse (DUIA)

[b] Actual substance use variables can be found in Table I. Erectile dysfunction drugs are abbreviated as ED Drugs

[c] All results significant at $P < 0.05$ are in **BOLD**

[d] Survey was part of the National HIV Behaviorally Surveillance survey in New York City

Table 4 Multi-day event level studies of substance use and HIV-related risk behavior among men who have sex with men

Citation	Location	Research design and analytic sample (*n*)	Sexual risk behavior or other HIV-related risk variables measured[a]	Substance use variables measured[b]	Bivariate analyses results (significant in bold)[c]	Multivariate analyses results (significant in bold)[c]
Colfax et al. [52]	San Francisco, CA	Cross-sectional survey; $n = 295$	DUA	Poppers, ED drugs, meth/amphetamines, Number of drugs used at specific venue	No bivariate analysis	*DUA*: **poppers (OR = 2.20, CI = 1.30–4.00); ED drugs (OR = 3.80, CI = 2.00–7.30); meth/amphetamines (OR = 2.40, CI = 1.10–4.90);** number of drugs used
Gillmore et al. [53]	Unspecified NW US City	Prospective daily diary over 8 weeks; $n = 104$	UA, up to 3 episodes/day over 8 weeks	Within 4 h of sex: alcohol, number of drinks, drug use	*UA*: alcohol; drug use	*UA*: alcohol; drug use
Benotsch et al. [26]	Rehoboth Beach, DE; Key West, FL	Cross-sectional survey; $n = 268$	On current trip (mean = 3.6 days): UA, # of UIA acts, # of URA acts	On current trip (mean = 3.6 days): binge alcohol, marijuana, Poppers, Viagra, Levitra, Cialis, ED drugs (all combined), cocaine, ecstasy, ketamine, anal sex after using drugs	*UA*: binge alcohol, marijuana, **poppers: $P < 0.01$, 20% vs 6%, Viagra: $P < 0.05$, 14% vs. 5%, Levitra: $P < 0.01$, 11% vs. 2%, Cialis: $P < 0.01$, 8% vs 1%,** cocaine, **ecstasy: $P < 0.05$, 8% vs 2%, ketamine: $P < 0.05$, 3% vs 0%,** # of UIAI acts: **drug use with sex: $P < 0.01$, binge alcohol: $P < 0.001$**, *# of URA acts*: Drug use with sex, **binge alcohol: $P < 0.001$**, *ED drugs*: **# UIA acts: $P < 0.01$**, # URA acts	***UA*: binge alcohol (OR = 2.00, CI = 1.30–3.20);** anal sex after using drugs; **ED drugs (OR = 2.90, CI = 1.10–7.30)**
Drumright et al. [27]	Los Angeles, CA; San Diego, CA	Cross-sectional; $n = 194$ ($n = 116$ within subjects analysis)	UA with last 3 partners: 0, 1–2, all	Substance use just before or during sex—marijuana, poppers, ED drugs, meth/amphetamines, GHB, multidrug use, any drug use, ED drug use with main partner	Within-subjects analysis ($n = 116$), *UA*: **marijuana (OR = 5.70, CI = 2.10–15.50), poppers (OR = 2.60, CI = 1.10–5.70),** ED Drugs, **meth/amphetamines (OR = 5.30, CI = 1.90–14.60),** GHB, **multidrug use (OR = 4.20, CI = 1.80–10.00), any drug use (OR = 3.80, CI = 1.90–7.80).** Within- and between-subjects analysis ($n = 194$), UA: **marijuana (OR = 3.97, CI = 1.90–8.00), poppers (OR = 2.70, CI = 1.50–4.70),** ED Drugs, **meth/amphetamines (OR = 4.00, CI = 2.20–7.00), GHB (OR = 5.40, CI = 2.10–13.70), multidrug use (OR = 4.30, CI = 2.40–7.70), any drug use (OR = 2.70, CI = 1.70–4.40)**	Within-subjects analysis ($n = 116$), *UA*: **marijuana (OR = 4.00, CI = 1.40–11.90),** poppers, ED drug use with main partner interaction, **meth/amphetamines (OR = 4.90, CI = 1.40–17.40,** within- and between-subjects analysis ($n = 194$), *UA*: **marijuana (OR = 2.20, CI = 1.00–4.50),** poppers, **ED drug use with main partner interaction (OR = 11.60, CI = 1.00–130.50), meth/amphetamines (OR = 3.50, CI = 1.90–6.70)**
Benotsch et al. [30]	New Orleans, LA	Cross-sectional survey; $n = 132$	On current trip (mean = 3.7 days): UA	Having sex after use on current trip (mean = 3.7 days): binge alcohol, drug use	*UA*: **binge alcohol (OR = 1.40, CI = 1.02–1.91); drug use (OR = 2.34, CI = 1.02–5.40)**	No Multivariate Analysis
Mustanski [35]	Not reported	Prospective daily diaries; $n = 155$	On the prior day: UA, HIV risk composite score	On the prior day: alcohol	No bivariate analysis	*UA*: alcohol, *HIV risk composite score*: **alcohol (coefficient = 0.29, SE = 0.09, $P < 0.01$)**
Wilson et al. [37]	Not reported	Aggregate cross sectional analysis (6-week prospective diary, internet-based study); $n = 100$	UA & DUA	Drug use:analyzed by self use, partner use, or self & partner use	*UA*: **Drug use—(OR = 2.30, CI = 1.10–4.70), $P < 0.05$, Drug use by partner—(OR = 2.80, CI = 1.30–6.40), $P \leq 0.01$, Drug use by both self & partner—(OR = 2.40, CI = 1.10–5.10)**; *DUA*: Drug use, Drug use by partner, Drug use by self & partner	*UA*: Drug use, Drug use by partner, Drug use by both self & partner, DUA: Drug use, Drug use by partner, Drug use by self & partner

Table 4 continued

Citation	Location	Research design and analytic sample (*n*)	Sexual risk behavior or other HIV-related risk variables measured[a]	Substance use variables measured[b]	Bivariate analyses results (significant in bold)[c]	Multivariate analyses results (significant in bold)[c]
Drumright et al. [38]	San Diego, CA	Case–control study, $n = 145$; 86 cases & 59 controls	UA, UIA, URA, & case: recent HIV infection	Marijuana, poppers, ED drugs, meth/amphetamine, GHB, multidrug use (not including ED drugs), any substance use (not including ED drugs), drug use during sex with any of last 3 partners	*Case*: marijuana, **poppers: (OR = 2.75, CI = 1.37–5.52), *P* < 0.01**, ED drugs, meth/amphetamine, cocaine, ecstasy, GHB, **multidrug use: (OR = 2.18, CI = 1.10–4.31), *P* = 0.03, any drug use: (OR = 2.10, CI = 1.01–4.37), *P* = 0.05**	*UA*: **poppers—(OR = 1.80, CI = 1.10–2.90), *P* = 0.01**, ED drugs, **meth/amphetamines—(OR = 3.10, CI = 1.90–5.00), *P* < 0.01,** *URA*: **poppers—OR = 1.90, *P* = 0.01,** ED drugs, **meth/amphetamines—OR = 2.40, *P* < 0.01,** *UIA*: poppers, ED drugs, **meth/amphetamines—OR = 1.80, *P* = 0.02**, *Case-substance use as a single variable controlling for covariates*: marijuana, **poppers: (OR = 2.71, CI = 1.20–6.20), *P* = 0.02**, ED drugs, **meth/amphetamine: (OR = 2.77, CI = 1.20–6.60), *P* = 0.02,** cocaine, ecstasy, ketamine, GHB, *Case-substance use as a single variable w/new multilevel substance use comparison variable*: poppers use only, meth/amphetamine use only, **combined meth/amphetamine & poppers use—(OR = 3.23, CI = 1.12–9.34), *P* = 0.03,** Other substance use

OR odds ratio, *CI* 95% confidence interval, *ED* erectile dysfunction, *GHB* gamma-hydroxybutyric acid, *STI* sexually transmitted infection

[a] The sexual risk variables are abbreviated as follows; unprotected anal intercourse (UA); HIV sero-discordant unprotected anal intercourse (DUA); unprotected receptive anal intercourse (URA); unprotected insertive anal intercourse (UIA), HIV sero-discordant unprotected receptive anal intercourse (DURA); HIV sero-discordant unprotected insertive anal intercourse (DUIA)

[b] Actual substance use variables can be found in Table I. Erectile dysfunction drugs abbreviated as ED Drugs

[c] All results significant at $P < 0.05$ are in **BOLD**

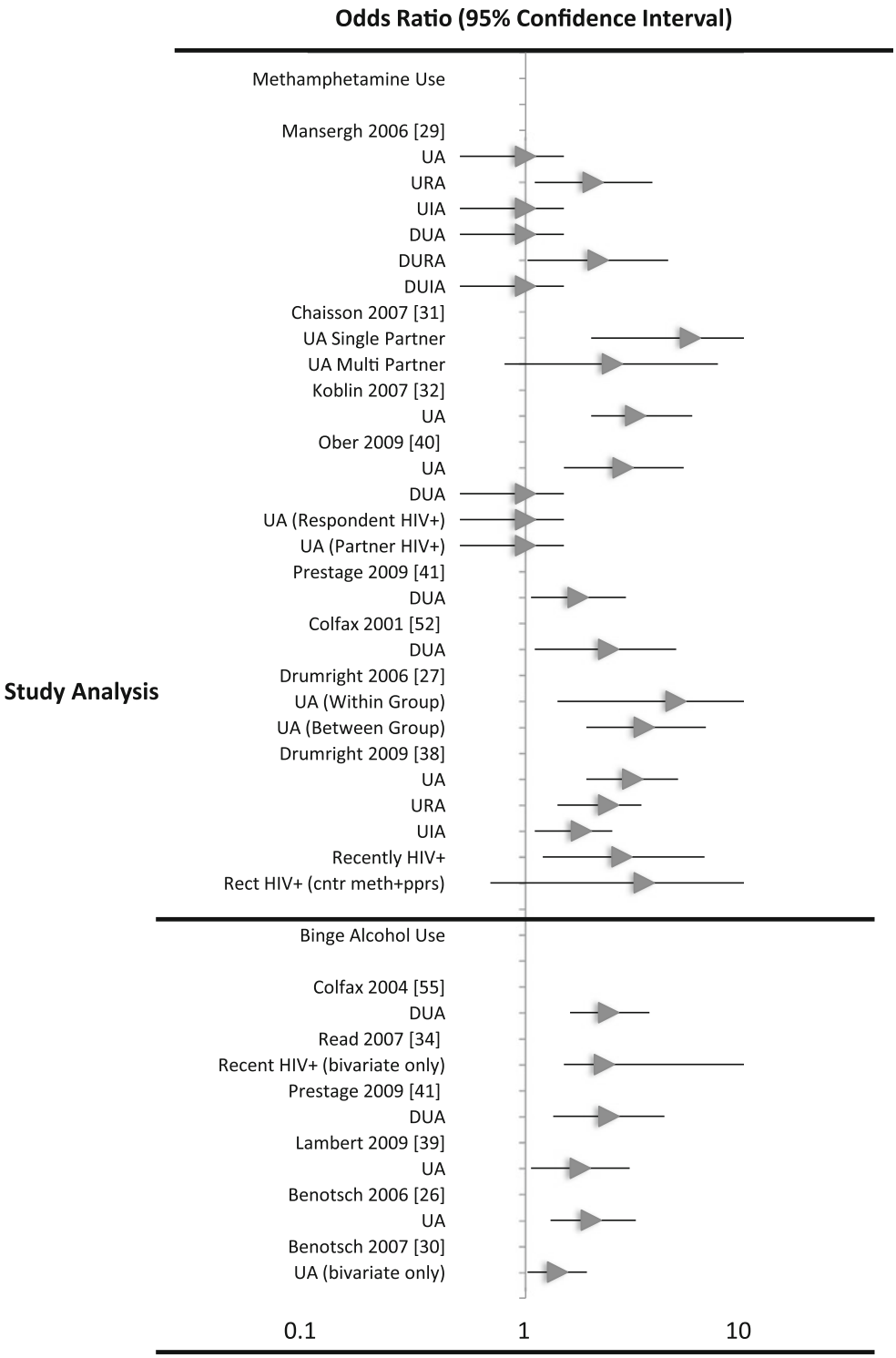

Fig. 1 Associations of event-level methamphetamine, binge alcohol, and HIV-related risk indicators by analysis model within study. For analyses that reported nonsignificant findings but did not include the OR and CI values, we present their results here as OR = 1.0, 95% CI = 0.5–1.5

risk behavior reported was statistically significant. No other individual substance use was associated with sexual risk behavior in each of the studies that tested them.

Of the 10 studies that examined alcohol use that was not than binge use, six [31, 33–35, 53, 56] found no association with sexual risk behavior. Three studies [35, 41, 55] found a bivariate association, but only one [10] was significant in multivariate analysis; "alcohol use" before sex was actually protective when "drug use" before sex was controlled for in a high-risk, substance using sample of alcohol and drug-using MSM.

Poppers (i.e., amyl nitrates) and erectile dysfunction (e.g., sildenafil) drugs were the most commonly assessed substances besides methamphetamine, and results were

mixed for associations with sexual risk behavior. Half [26, 27, 29, 52] of the eight [25–27, 29, 31, 38, 41, 52] studies that included erectile dysfunction drugs found an association in multivariate analysis. Only two [38, 52] of the eight [25–27, 34, 38, 41, 52, 56] studies that included poppers found an association with sexual risk behavior when controlling for other factors.

Other individual substances were examined less often and included ecstasy/MDMA, ketamine, GHB, marijuana, crack, and cocaine. Although three studies [26, 27, 41] found significant bivariate associations with sexual risk behavior, ecstasy/MDMA, ketamine, and GHB were not significant in multivariate analysis. Marijuana use was examined in five studies [26, 27, 38, 41, 56], and only one [27] found an association with UA when controlling for other factors. Cocaine use was examined in four studies [26, 29, 38, 41]; only one [39] found an association with UA in multivariate models. Crack use was examined in one study [40] and MSM who reported UA with an HIV-discordant partner were less likely to report crack use during that sexual episode.

Broad Substance Use Measures

Lack of consistency in results is particularly true for broad categories of substance use (i.e., "alcohol or drug use", "drug use", "multi-drug use" or "other drug use"). Across the 18 studies that included a broader category of substance use, 13 studies [10, 26–28, 30, 36–39, 41, 54–56] found an association between sexual risk and at least one broad substance use measure; the remaining five studies [25, 29, 33, 34, 53] found no association. Additionally, the results differed based on the context of the measure. For example, Wilson and colleagues [37] found an association for substance use and having UA if the participant reported a partner was "high" before or during anal sex (Odds Ratio [OR] = 1.8, 95% Confidence Interval [CI] = 1.1–3.0); however, UA was not associated with drug use by the participant. Broad substance use measures varied in definition across studies (Table 1), making it difficult to summarize across studies.

"Drug use" was examined in 11 studies [10, 26, 27, 30, 33, 36–39, 53, 55] and only three studies [10, 36, 39] found significance when controlling for other factors. Two studies [28, 54] applied a definition that combined drug or alcohol use, and they found limited association with sexual risk behavior. "Multi-drug use" was examined in two studies [27, 38] and both found bivariate associations with sexual risk behavior. The seven studies [25, 29, 34, 39, 41, 55, 56] that examined drug use broader than specific substances (i.e., other drug use) found mixed results; only one study [55] retained significance in multivariate analysis.

Discussion

Much of the event-level research on substance use among MSM and its association with sexual risk for HIV infection underscores the complexity of human behavior and inconsistencies in behavioral measurement and analysis. In spite of these challenges, this systematic review found several consistent associations, namely temporal behavioral linkages of sexual risk behavior with methamphetamine use and alcohol binge drinking. Binge drinking and methamphetamine use—controlling for other variables in multivariate analysis—were consistently associated with sexual risk behavior. Less consistent results described in earlier reviews of studies of sexual risk and these substances [13, 17, 23] may be at least partially accounted for by a lack of temporal proximity or behavioral complexity in substance use and sexual behavior assessment. Even though some global and situational assessments [57–59] have found similar results to ours for methamphetamine use and alcohol binge drinking, studies of more temporally distant behaviors may not necessarily produce findings consistent with event-level research. Associations identified using broader situational or global level assessments could be more linked to third variables such as general risk-taking or sensation-seeking factors. In addition, even though temporal proximity is clearer for event-level studies, the behavioral linkages still do not signify direct causal links or rule out psychosocial mediators. Further research on potential associational mediators is needed to better understand factors underlying existing temporal associations of substance use and sexual risk. Because of the contextual complexity and specificity that event-level assessment affords, its use has increased in recent years. For a clearer understanding of the strengths and limitations of various assessment approaches, multi-method studies should simultaneously examine behaviors at the event-level and at broader levels to compare findings.

Another methodological factor identified through this review is the importance of clarifying type and perhaps extent of substance use, as exemplified in the tested association of alcohol use and sexual risk behavior. In event-level analysis, alcohol binge drinking is consistently associated with unsafe sex while general alcohol use is not, which is consistent with the conclusions from another study [17]. Given the pervasiveness of alcohol use in society, more research is needed to better understand alcohol use and binge drinking among MSM compared with other populations. For example, although some studies have not found differences in the general alcohol use of MSM and heterosexuals [60–62], other studies have shown higher rates of binge drinking among MSM [60]. Current research suggests that possible factors shaping alcohol use among MSM are socialization to alcohol use, stigma or anxiety

management, socioeconomic issues (e.g., educational attainment, occupation), and the historical importance of bars in gay culture [63, 64].

Methamphetamine use is consistently linked with sexual risk behavior among MSM at the sexual event-level. This association is particularly concerning given that studies have shown a relatively high prevalence of methamphetamine use among urban gay and bisexual men compared to heterosexuals [8, 19, 29, 65, 66]. Desirable characteristics and potential facilitators of methamphetamine use among MSM are both physiological (e.g., increased sensory acuity, decreased fatigue) and psychological (e.g., increased libido, decreased inhibition) in nature [19, 20, 65]. For example, a study examining methamphetamine use among HIV-positive MSM [67] found that almost 90% of the men used the drug to enhance sexual pleasure; the study also found that methamphetamine was used to dull negative feelings about being HIV-positive. Further research is needed to better understand these and other underlying factors associated with methamphetamine use among MSM.

The studies conducted outside of North America highlight methodological issues (e.g., unspecified substance measures, no multivariate analysis) and illustrate that the approach taken to address these issues can influence findings. Results of the most recent study conducted outside of North America [41] were consistent with results of most North American studies, whereas earlier studies that utilized a similar study design [25, 33, 34, 41] reported different findings perhaps due to methodological limitations; the recent study reported significant associations between substance use and sexual risk behavior, whereas earlier studies did not. To help avoid these types of discrepancies, use of standardized and detailed substance use and sexual risk behavior measures and common analytic approaches in future research will allow for quantitative comparison across studies through meta-analysis which provides the ability to estimate the magnitude of the effects.

Like many systematic reviews, this paper is limited to published research and thus possibly biased toward significant findings. The studies relied on respondent self-report; however, most tried to minimize potential reporting bias by providing computer-based or other self-assessment. Most of the studies measured event-level behavior within the past 3–12 months, periods that may be subject to recall bias. The daily diary design, used in three studies [35, 36, 53] may improve recall accuracy. Another limitation of this review, we chose not to conduct a meta-analysis due largely to inconsistencies in measurement definitions.

In sum, methamphetamine use and binge drinking are linked to sexual risk behavior at the event-level, however not enough event-level research has been conducted on other substances, including those that have been anecdotally linked to sexual risk (e.g., amyl nitrates). Although event-level assessments have increased over the past decade, such studies among MSM should further examine demographic factors and specific risk-related details of event-level behavior. Event-level assessment temporally links substance use and sexual behavior and allows for more detailed contextual understanding than do global and situational levels of analysis [13]. Research on psychosocial and other potential mediators and moderators of substance use and sexual risk behavior is still needed to more fully comprehend the temporal link; more prospective research is needed to directly assess causal links. Standardization of substance use and sexual risk behavior measurement will facilitate cross-study comparisons, as will the application of multivariate analysis controlling for potential confounders and other important covariates.

MSM continue to be the population most affected by the HIV epidemic in the Western World. Precision and detail in event-level assessment are critical to better understand the link between substance use and HIV-related risk behavior. In addition, to help reduce HIV among MSM, it is important to provide effective HIV risk-reduction interventions, including substance abuse treatment, for MSM who use methamphetamine and are binge drinkers.

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