

Meta-Analysis of Interventions for Reducing Number of Sexual Partners and Drug and Alcohol Abuse among People Living with HIV/AIDS

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Abstract

Objective: To perform a systematic review and meta-analysis of the efficacy of risk reduction interventions on HIV-related risk behaviors among people living with HIV/AIDS (PLWHA)

Methods: Studies included in the meta-analysis were randomized clinical trials (RCTs) of risk reduction interventions, which targeted PLWHA aged 18 year or older and assessed the changes of number of sexual partners, drug use, needle sharing, and/or alcohol abuse between pre- and post-intervention. The standardized mean differences (SMD) between study arms as well as between baseline and post-intervention, defined as the effect sizes (ES), were calculated in random effects models. Heterogeneity of studies was estimated by the I^2 statistic.

Results: Twelve RCTs involving 3993 PLWHA were included in our analysis: seven reported impacts on the number of sexual partners, and three reported impacts on drug use, needle sharing, and alcohol abuse, respectively. There were no statistically significant impacts of risk reduction interventions on the number of total sexual partners (mean ES, -0.10; 95% confidence interval [CI], -0.26, 0.06; $P=0.22$) or on the subset of HIV-negative or unknown-status sexual partners (mean ES, 0.003; 95% CI, -0.54, 0.54; $P=0.99$). Overall, risk reduction intervention studies documented a reduction of drug abuse (mean ES: -0.26; 95% CI: -0.51, -0.01; $P=0.04$) among HIV-infected drug users, but this impact was mainly attributable to one study. Risk reduction interventions did not show a reduction of needle sharing (mean ES, -0.15; 95% CI, -0.43, 0.13; $P=0.29$) or of alcohol abuse (mean ES, -0.10; 95% CI, -0.36, 0.17; $P=0.47$). No heterogeneity or publication bias was found across individual studies.

Conclusions: Our meta-analysis did not find a positive impacts of risk reduction interventions on number of sexual partners, drug use, needle sharing, or alcohol abuse among PLWHA, but the small number of studies meeting our review criteria limits these findings.

Keywords: People living with HIV/AIDS (PLWHA); Randomized clinical trial (RCT); Sexual partners; Positive prevention; Drug use; Alcohol abuse; Meta-analysis

Introduction

Over 33 million people are living with HIV/AIDS (PLWHA) around the world [1]. As HIV-infected individuals live longer on average, due to the use of combination antiretroviral therapy (cART) [2,3], the global number of PLWHA is unlikely to decline dramatically in the near future [1]. The large number of prevalent cases poses a major public health challenge: PLWHA may continue to transmit HIV through unprotected sex or sharing of contaminated needles. Even after knowing their HIV-positive serostatus, PLWHA may practice unprotected sex [4-6], have multiple sexual partners [7-9], use illicit drugs, share needles, and abuse alcohol [7,10-12].

“Positive prevention”, which targets HIV-infected individuals, is considered a key strategy for preventing new infections. An emerging biomedical approach is HIV treatment as prevention: both observational studies and a definitive randomized controlled trial (HIV Prevention Trials Network [HPTN] 052 study) have shown that antiretroviral therapy (ART) can reduce heterosexual HIV transmission in HIV-discordant couples [13-17]. There is no direct evidence that risk reduction interventions alone reduce HIV transmission among PLWHA; however, risk reduction intervention studies have shown efficacy in reducing risky behaviors [9,18-20]. These studies commonly

assessed the impact on unprotected intercourse [8,9,20,21]; some evaluated the impact on actions other than unprotected sex that could lead to an increased risk of transmitting HIV, including multiple sexual partners and substance and alcohol abuse [9,20,22,23]. Multiple meta-analytic reviews have evaluated the efficacy on unprotected intercourse or condom use among PLWHA [24,25]; but few on number of sexual partners [25] and drug or alcohol use [24]. PLWHA with multiple sex partners may be less likely to disclose their HIV status to their sexual partners [26]. Substance abuse and needle sharing among PLWHA could facilitate HIV transmission [27]; Alcohol use is also associated

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with unprotected sex among PLWHA [12]. Therefore, it is interesting to know the efficacy of risk reduction interventions on these outcomes. We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs), evaluating the efficacy of risk reduction interventions on number of sexual behaviors and drug and alcohol use among PLWHA.

Methods

Search strategy and study selection

A systematic literature search was conducted to identify RCTs that studied risk reduction intervention impacts on various outcomes among PLWHA. Because of the limitation of manuscript length, unprotected sex/condom use will be presented elsewhere (unpublished). In this manuscript, the interest outcomes for analysis included number of sexual partners, drug use, needle sharing, and alcohol abuse. Twelve electronic databases were searched for studies published as of February 2012, including AMED, British Library Direct, British Nursing Index, Centre for Reviews and Dissemination databases, Cochrane Library, EMBASE, EconLit, ERIC, Ovid Medline, PsycINFO, Scopus, and Web of Science. Keywords used in the database search included: (HIV-infected or HIV infections, HIV-positive, HIV seropositive, or people living with HIV or AIDS or acquired immunodeficiency syndrome) AND (behavior therapy or behavioral intervention or risk reduction intervention or clinical trial or intervention study) AND (sexual partners or drug use or needle sharing or alcohol abuse). Each title and abstract was reviewed to determine whether the paper was potentially relevant to the topic.

Study criteria and selection

Studies were selected if they met the following criteria: (1) original randomized clinical trials among PLWHA; (2) using risk reduction intervention; (3) targeting PLWHA aged 18 or older; (4) reporting outcomes of number of sexual partners, drug use, needle sharing, and/or alcohol abuse at baseline and at follow-up.

All abstracts were independently reviewed by two authors, and full-text papers were reviewed for determining the eligibility if abstracts missed key information. Papers that did not meet the above-mentioned criteria were excluded. The disagreements between the two reviewers were less than 10%, and were resolved by further discussion involving two other authors. The references from each eligible paper were also examined to supplement the literature search described above, termed cross-referencing.

Data extraction

Two authors independently extracted the following data from eligible studies in the same standardized manner: authors, publication year, study country, description of interventions in study arms, participant recruitment, population characteristics and sample sizes at baseline and follow-up assessments, duration of follow-ups, retention at the last follow-up, as well as the proportions and mean frequencies of number of sexual partners (any sexual partners and HIV-negative or unknown-status sexual partners), drug use, needle sharing and alcohol abuse in each study arm at the baseline and follow-ups [28]. Any disagreements were reviewed and discussed between two data extractors and/or two quality controllers until a consensus was reached.

Rigor scores

The quality of study design of the included studies was assessed using rigor scores, which included an 8-point scale adopted by other

systematic review [29] plus an additional item of sample size >100 (as an indicator for good statistical power). The scale is additive, with 1 point awarded for each of 9 items. Therefore, the rigor score for an article may range from 0 to 9, with a higher value representing a higher rigor of study design.

Statistical methods

The primary outcomes of interest in this meta-analysis were number of sexual partners, drug use, needle sharing, and alcohol abuse. These outcome variables were typically measured at baseline and follow-up in each study arm (e.g., intervention and comparison arm), and some studies might have multiple measurements at different follow-up time points. In the latter case, the last follow-up measurement was used for estimating the overall effect size of intervention, while each follow-up measurement was compared with baseline measurement in subgroup analyses. As the measurements were either expressed as proportion differences or as mean differences we converted estimates to a common metric of standard mean differences (SMD) using a Cox transformation [30,31]. SMD in each study arm was calculated as a fraction of difference of means between follow-up and baseline in each study arm divided by pooled standard deviation (SD) of these two means. We attempted to contact authors when published articles did not provide sufficient information to make the calculations. As the study arms might not be comparable at baseline, even in RCT, Becker's strategy was used to adjust for any differences between arms at baseline [32]. The difference of SMDs between study arms, defined as effect sizes (ES), were calculated for each study and then pooled across studies using meta-analysis with a random effects model [33,34]. A negative value of SMD difference indicates reduction of outcomes in the intervention arm compared to the comparison arm. When multiple intervention arms in the same study were available [35], we calculated individual effect sizes in each of the separate intervention arms with the same comparison group. Random effect estimates allows for variation of true effects across studies [36], and random effect estimates in our analyses were derived using the DerSimonian-Laird method [33, 37]. The meta-analysis results were displayed with forest plots.

Heterogeneities were assessed by I^2 statistics [38], and standardized deleted residual analyses were performed to identify outliers. The funnel plot, Begg and Mazumdar rank correlation test, and Egger's test of the intercept were employed to assess indications of publication bias [39].

The subgroup analyses were performed to examine change of durations of follow-ups (immediately after intervention, 3, 6, 9, 12, or 18 months). Meta-regression was also used to examine the relationship of between-group effects, except for duration of follow-ups (because outcomes at multiple follow-ups were often reported in individual studies). No subgroup analyses and meta-regressions were performed for drug use, needle sharing, and alcohol abuse due to the small number of studies. Sensitivity analyses were conducted to determine the stability of intervention effects by evaluating whether the overall effect size was sensitive to inclusion of any individual study [34]. All meta-analyses were performed in the R/S plus Software version 2.15.1.

Results

Results from literature searches

The initial searches in twelve individual electronic databases yielded 7181 entries. After excluding 2597 duplicates and 4492 irrelevant ones (not meeting above-mentioned inclusion criteria), 92 full-text papers were further reviewed, and 80 were excluded for the following reasons: not an original article but rather an editorial, comment, or review

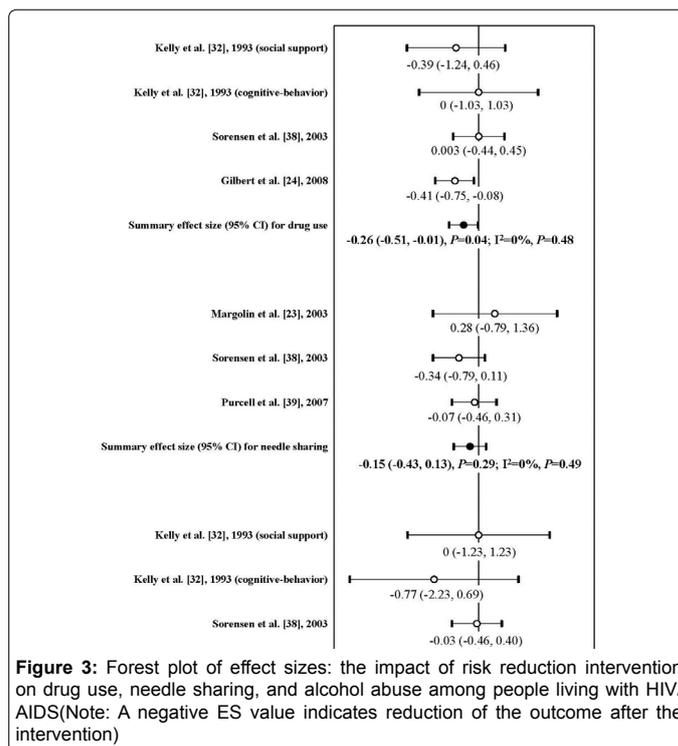
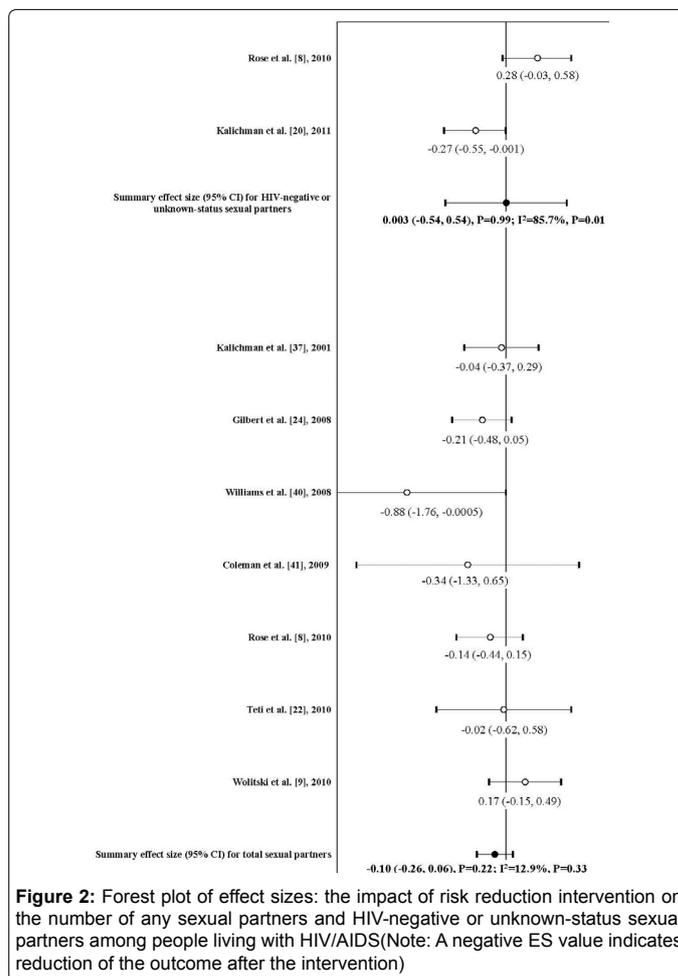
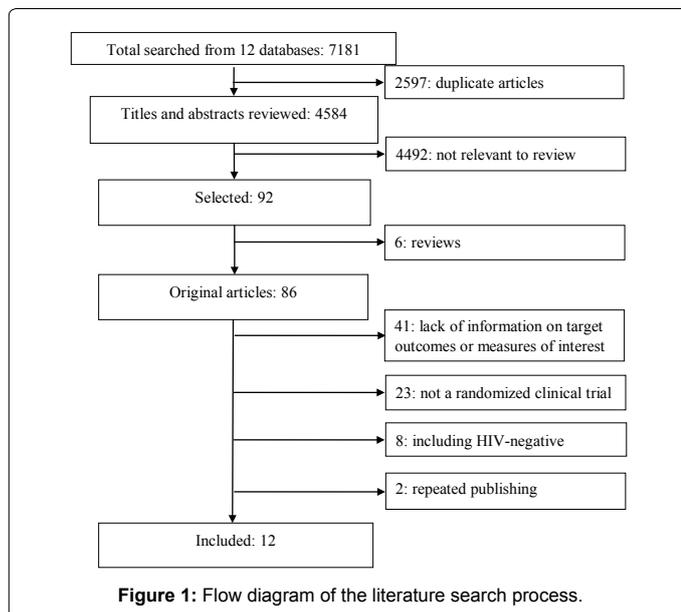
(k=6), lack of information on outcomes of interests (k=41), not a randomized clinical trial (k=23), including HIV-negative participants (k=8), and repeated publishing (k=2) (Figure 1). These 80 studies are listed in the Appendix. Finally, 12 studies were included in our review [8,9,20-23,35,40-44].

Description of studies

All included randomized clinical trials were conducted in the United States (Table 1). Study rigor scores ranged from 7 to 9 (mean 8.4), and six studies had a full score of 9 [8,9,20,23,42,43] (Table 2). The sample sizes at baseline ranged from 60 to 966. Ten studies recruited participants by AIDS-service-organization-based sampling (ASOB), such as hospitals, clinics, or detoxification centers [8,9,20-23,40,41,43-46], and less frequently used approaches, either combining with ASOB or not, included community-based sampling [35,42,44], paper-advertisement-based sampling [40,43], and peer-driven referrals [21]. The follow-up period of intervention ranged from 3 to 18 months, and retention rates varied from 30% to 100%.

Impact on number of sexual partners

Table 3 presents the findings in changes of the number of sexual partners due to intervention. Most studies reported a mean number of any sexual partners while two studies presented a proportion of multiple sexual partners [9,44]. All outcomes, either measured in mean or in proportion, were transferred to SMD between baseline and follow-up in each study arm, and the difference of SMD between intervention and comparison groups was used for meta-analysis. Figure 2 shows the overall efficacy. Of seven studies reporting the number of any sexual partners in post-intervention assessment, only one was statistically significant [43]. The combined efficacy from these studies was not statistically significant (mean ES: -0.10; 95% CI: -0.26, 0.06; $P=0.22$). Small heterogeneity was shown among these seven interventions ($I^2=12.9%$; $P=0.33$). Funnel plot analysis showed no evidence of publication bias (Kendall tau=0.14, $P=0.77$; Egger's t value=-1.09; $P=0.27$). Further subgroup analyses were performed, but no significant effect was detected in any duration of follow-up ($P>0.05$). With the above noted, it is important to point out that in meta-regression, no factor statistically modified the overall effect size of the number of



Publication	Country (trial period)	Study participants					Study participants		Follow-up (months)	Retention rate (%)
		Recruitment methods	Population	Sex (%)	No. of participants (age at baseline: mean and range)		IG	CG		
					IG	CG				
Kelly et al. [32]	USA (1991-1992)	CBS	94% MSM	100% Male	Pre-intervention 51 ^A or 26 ^B Post-intervention 27 ^A or 14 ^B (34, N/A)	Pre-intervention 38 Post-intervention 27 (34, N/A)	A: 8-week cognitive-behavioral group intervention B: 8-week social support group intervention	No	3	59
Kalichman et al. [37]	USA (N/A)	ABS, MOBS	61% MSM	70% Male	Pre-intervention 185 Post-intervention 150 ^{F3} or 146 ^{F6} (40, N/A)	Pre-intervention 143 Post-intervention 121 ^{F3} or 110 ^{F6} (40, N/A)	5-session group intervention focused on strategies for practicing safer sexual behavior	5-session contact-matched, health-maintenance support group	6	78
Margolin et al. [23]	USA (1997-2001)	MOBS	IDU	70% Male	Pre-intervention 45 Post-intervention 32 ^{F0} or 34 ^{F3} (41, N/A)	Pre-intervention 45 Post-intervention 32 ^{F0} or 29 ^{F3} (41, N/A)	Manual-Guided HIV+ harm reduction program	Enhanced methadone maintenance program	3	70
Sorensen et al. [38]	USA (1994-1998)	MOBS	DU	73% Male	Pre-intervention 92 Post-intervention 77 ^{F6} , 76 ^{F12} , 71 ^{F18} (39, N/A)	Pre-intervention 98 Post-intervention 83 ^{F6} , 74 ^{F12} , 80 ^{F18} (38, N/A)	Case management delivered by paraprofessionals	A brief contact condition	18	79
Purcell et al. [39]	USA (2001-2005)	CBS	IDU	61% Male	Pre-intervention 486 Post-intervention 419 ^{F3} , 402 ^{F6} , 417 ^{F12} (42, 22-60)	Pre-intervention 480 Post-intervention 421 ^{F3} , 404 ^{F6} , 404 ^{F12} (42, 22-60)	10-session peer mentoring intervention	8-session video discussion intervention	12	85
Gilbert et al. [24]	USA (2003-2006)	MOBS	51% MSM	79% Male	Pre-intervention 240 Post-intervention 182 ^{F3} , 200 ^{F6} (43, ≥18)	Pre-intervention 231 Post-intervention 188 ^{F3} , 193 ^{F6} (44, ≥18)	Tailored risk-Reduction counseling via "Video Doctor" on laptop computer & printed Educational Worksheet	Usual care	6	83
Williams et al. [40]	USA (2003-2006)	ABS, MOBS	Male	MSM	Pre-intervention 75 Post-intervention 75 (43, ≥18)	Pre-intervention 62 Post-intervention 62 (43, ≥18)	Sexual health intervention for men guided by cognitive-behavioral approaches	Attention- control standard health promotion comparison	6	100
Coleman et al. [41]	USA (2006-2007)	MOBS, CBS	Male	MSM	Pre-intervention 30 Post-intervention 30 (51, 50-59)	Pre-intervention 30 Post-intervention 30 (51, 50-72)	Four 120-min sessions HIV risk reduction intervention	Four 120-min sessions (health condition)	3	100
Rose et al. [8]	USA (2004-2006)	MOBS	69% Male	SAA	Pre-intervention 181 Post-intervention 161 (43, N/A)	Pre-intervention 205 Post-intervention 167 (43, N/A)	Clinician-delivered HIV risk-reduction intervention	Standard care	6	85
Teti et al. [22]	USA (2004-2007)	MOBS, PRS, ABS	Female	86% Black	Pre-intervention 92 Post-intervention 61 ^{F6} , 46 ^{F12} , 28 ^{F18} (40, 20-70)	Pre-intervention 92 Post-intervention 70 ^{F6} , 52 ^{F12} , 27 ^{F18} (38, 20-70)	Received messages, group-level, peer-led support intervention;	Received brief messages	18	30
Wolitski et al. [9]	USA (2004-2007)	MOBS	70% Male	Homeless and unstably housed adults	Pre-intervention 315 Post-intervention 301 ^{F6} , 284 ^{F12} , 274 ^{F18} (N/A, 18-50+)	Pre-intervention 315 Post-intervention 275 ^{F6} , 266 ^{F12} , 259 ^{F18} (N/A, 18-50+)	Immediate housing opportunities for people with AIDS rental assistance	Customary housing service	18	85
Kalichman et al. [20]	USA (2005-2009)	MOBS	78% Male	91% African American	Pre-intervention 217 Post-intervention 201 ^{F3} , 193 ^{F6} , 192 ^{F9} (44, ≥18)	Pre-intervention 219 Post-intervention 201 ^{F3} , 202 ^{F6} , 210 ^{F9} (44, ≥18)	Theory-based integrated behavioral intervention	Attention control	9	92

Note: IG: intervention group; CG: control group; ABS: advertisement-based sampling; CBS: community-based sampling; MOBS: medical-organization-based sampling; PRS: peer-referral sampling; MSM: men who have sex with men; DU: drug users; IDU: injection drug users; SAA: sexually active adults; N/A: not available; ^{F0}Immediately after intervention; ^{F3}At 3-month follow-up; ^{F6}At 6-month follow-up; ^{F9}At 9-month follow-up; ^{F12}At 12-month follow-up; ^{F18}At 18-month follow-up.

Table 1: Randomized clinical trials of HIV risk reduction intervention among people living with HIV/AIDS.

Publication	Cohort (a)	With control group (b)	Pre/post intervention (c)	Random assignment (d)	Random selection for assessment (e)	Sample size >100 (f)	Follow-up ≥80% (g)	Comparable socio-demographics between study groups (h)	Comparable outcome measures at baseline (i)	Total
Kelly et al. [32]	1	1	1	1	1	1	0	1	1	8
Kalichman et al.[37]	1	1	1	1	1	1	0	1	1	8
Margolin et al. [23]	1	1	1	1	1	0	0	1	1	7
Sorensen et al. [38]	1	1	1	1	1	1	0	1	1	8
Purcell et al. [39]	1	1	1	1	1	1	1	1	1	9
Gilbert et al. [24]	1	1	1	1	1	1	1	1	1	9
Williams et al. [40]	1	1	1	1	1	1	1	1	1	9
Coleman et al. [41]	1	1	1	1	1	0	1	1	1	8
Rose et al. [8]	1	1	1	1	1	1	1	1	1	9
Teti et al. [22]	1	1	1	1	1	1	0	1	1	8
Wolitski et al. [9]	1	1	1	1	1	1	1	1	1	9
Kalichman et al. [20]	1	1	1	1	1	1	1	1	1	9

* One point score for meeting each of the following items: (a) was a prospective cohort, (b) used a comparison arm, (c) collected pre and post intervention data, (d) used random assignment of participants to study arms, (e) did random sampling for assessments, (f) sample size > 100, (g) follow-up rate ≥ 80%, (h) had a comparison group with comparable socio-demographics such as age, education, race, employment, income, marital status and others [score "1" if > 50% variables were comparable between study arms, and '0' if not], and (i) had a comparison arm with comparable outcome measures at baseline between study arms.

Table 2: Quality assessment of study design for 12 randomized clinical trials (rigor scores).

sexual partners ($P > 0.05$).

In standardized deleted residual analysis, no individual study was identified as an outlier. Sensitivity analyses were used to evaluate the stability of the summary effect size in meta-analysis by excluding the study by Gilbert et al. [23], because it only reported number of casual sexual partners, but the summary effect size did not change correspondingly (mean ES: -0.06; 95% CI: -0.25, 0.13; $P = 0.53$).

Two randomized clinical trials were included in the meta-analysis of the efficacy on number of HIV-negative or unknown-status sexual partners [8,20], and the combined effect was null (mean ES: 0.003; 95% CI: -0.54, 0.54; $P = 0.99$). Large heterogeneity was observed in these two studies ($I^2 = 85.7\%$; $P = 0.01$) (Figure 2).

Impact on drug use

Among three studies reported the outcome of drug use, one showed a significant impact [23]. Meta-analysis found that there was statistically significant association between risk reduction intervention and reduction of drug use (mean ES: -0.26; 95% CI: -0.51, -0.01; $P = 0.04$), which was largely attributable to one study [23] (Figure 3). Null heterogeneity was shown across these three studies ($I^2 = 0\%$; $P = 0.48$). The funnel plot did not detect publication bias (Kendall tau=0.33, $P = 0.75$; Egger's t value=0.47, $P = 0.64$).

Impact on needle sharing

Of three studies assessing the outcome of needle sharing among HIV-positive drug users, two showed a positive impact [41,42] while the other one did not [22]; however, no difference was statistically significant, nor was the pooled effect size (mean ES: -0.15; 95% CI: -0.43, 0.13; $P = 0.29$) (Figure 3). Neither heterogeneity ($I^2 = 0\%$; $P = 0.49$) nor publication bias were detected (Kendall tau=0.33; $P = 1$; Egger's t value=0.65). Further sensitivity analysis by removing the study assessing needle sharing with HIV-negative or unknown-status sexual partners did not change the conclusion [42] (mean ES: -0.23; 95% CI: -0.69, 0.23; $P = 0.33$).

Impact on alcohol abuse

Of three studies measuring the outcome of alcohol abuse among

HIV-infected persons [23,35,41], none showed a significant impact. Their pooled effect size was also non-significant (mean ES: -0.10; 95% CI: -0.36, 0.17; $P = 0.47$) (Figure 3). There was no heterogeneity across these studies ($I^2 = 0\%$; $P = 0.82$). Publication bias was not found (Kendall tau=-0.33, $P = 0.75$; Egger's t value=-0.53, $P = 0.59$).

Discussion

Our meta-analysis of 12-risk reduction intervention RCTs involving 3993 PLWHA failed to show significant impacts on reduction of sexual partners, drug use, needle sharing, or alcohol abuse among PLWHA. A previous meta-analytic review also did not show efficacy in reducing the number of sexual partners, but it included studies involving both HIV-positive and negative participants [25]. Our study focused on well-designed RCTs in which all participants were HIV-positive.

HIV-infected individuals may reduce their sexual partners or practice partner serosorting after knowing their HIV status in order to reduce the risk of transmission to others [47-50]. However, it is difficult to detect a significant reduction of sexual partners between study arms if the average number of sexual partners at recruitment is low. Participants in RCTs, even in the comparison arm, may also modify their sexual behaviors during the trial as trial participants are typically offered education and risk reduction counseling for ethical reasons; this could lead to reduction in the magnitude of the intervention effect in individual studies. These are among the possible explanation of the null synthesized efficacy found in this meta-analysis.

Only two studies measured the impact on number of HIV-negative or unknown-status sexual partners; they had contradictory results [8,20]. Subgroup and sensitivity analyses did not find a significant effect on the number of any sexual partners in any subgroup.

We also analyzed the impact on reduction of drug use among HIV-infected drug users, but only three individual clinical trials were available in our analysis [23,35,41]. The synthesized efficacy was statistically significant, primarily due to one study [23]. Though risk reduction interventions studies among drug users have shown reduction of drug injection [51] as well as risky sexual behaviors [52,53], the evidence available from studies among HIV-infected drug users was too sparse for drawing a conclusion of efficacy of interventions to reduce drug use.

Publication	No. of sexual partners (Mean(SD)) or proportion of multiple sexual partners (%)		Drug use or needle sharing (% or Mean(SD))		Alcohol abuse * (% or Mean(SD))	
	IG	CG	IG	CG	IG	CG
Kelly et al. [32]	N/A	N/A	Drug use I1: 70.4→55.6 ^{PM3,F3} I2: 64.3→64.3 ^{PM3,F3}	Drug use 63.0→63.0 ^{PM3,F3}	I1: 88.9→88.9 ^{PM3,F3} I2: 92.9→78.6 ^{PM3,F3}	85.2→85.2 ^{PM3,F3}
Kalichman et al. [37]	AP ^{PM3} 1.6(2.4)→1.3(2.3) ^{PM3,F3} 1.6(2.4)→1.2(1.9) ^{PM3,F6}	AP ^{PM3} 1.7(3.3)→1.2(1.5) ^{PM3,F3} 1.7(3.3)→1.3(1.9) ^{PM3,F6}	N/A	N/A	N/A	N/A
Margolin et al. [23]	N/A	N/A	Needle sharing 44.4→12.9 ^{PM1,F0} 44.4→11.8 ^{PM1,F3}	Needle sharing 53.3→22.6 ^{PM1,F0} 53.3→10.7 ^{PM1,F3}	N/A	N/A
Sorensen et al. [38]	N/A	N/A	Drug use 0.2(0.13)→0.2(0.14) ^{PM1,F6} 0.2(0.13)→0.2(0.13) ^{PM1,F12} 0.2(0.13)→0.1(0.10) ^{PM1,F18} Needle sharing 1.2(0.99)→0.6(0.84) ^{PM1,F6} 1.2(0.99)→0.7(0.90) ^{PM1,F12} 1.2(0.99)→0.3(0.65) ^{PM1,F18}	Drug use 0.2(0.13)→0.2(0.13) ^{PM1,F6} 0.2(0.13)→0.1(0.12) ^{PM1,F12} 0.2(0.13)→0.1(0.10) ^{PM1,F18} Needle sharing 1.2(1.06)→0.7(0.98) ^{PM1,F6} 1.2(1.06)→0.8(1.04) ^{PM1,F12} 1.2(1.06)→0.5(0.89) ^{M1,F18}	0.2(0.25)→0.2(0.22) ^{PM1,F6} 0.2(0.25)→0.1(0.18) ^{PM1,F12} 0.2(0.25)→0.1(0.16) ^{PM1,F18}	0.2(0.26)→0.2(0.22) ^{PM1,F6} 0.2(0.26)→0.2(0.23) ^{PM1,F12} 0.2(0.26)→0.1(0.19) ^{PM1,F18}
Purcell et al. [39]	N/A	N/A	Needle sharing for HNUP 28.6→9.7 ^{PM3,F3} 28.6→7.3 ^{PM3,F6} 28.6→5.8 ^{PM3,F12}	Needle sharing for HNUP 28.9→12.0 ^{PM3,F3} 28.9→10.6 ^{PM3,F6} 28.9→6.6 ^{PM3,F12}	N/A	N/A
Gilbert et al. [24]	CP ^{PM3} -2.3(9.2) ^{F3} -2.7(8.4) ^{F6}	CP ^{PM3} -1.4(7.9) ^{F3} -0.6(5.6) ^{F6}	Drug use 43.8→38.5 ^{PM3,F3} 43.8→29.5 ^{PM3,F6}	Drug use 41.1→41.5 ^{PM3,F3} 41.1→42.5 ^{PM3,F6}	Any risk drinking ² 38.3→26.4 ^{PM3,F3} 38.3→23.5 ^{PM3,F6}	Any risk drinking ² 39.0→29.8 ^{PM3,F3} 39.0→27.5 ^{PM3,F6}
Williams et al. [40]	AP ^{PM6} 6.69(1.43)→3.46(0.51) ^{F0} 6.69(1.43)→2.34(0.47) ^{F3} 6.69(1.43)→1.69(0.19) ^{F6}	AP ^{PM6} 5.49(1.32)→3.49(0.47) ^{F0} 5.49(1.32)→3.12(0.43) ^{F3} 5.49(1.32)→1.71(0.17) ^{F6}	N/A	N/A	N/A	N/A
Coleman et al. [41]	AP ^{PM3} 81.8→45.0 ^{F3}	AP ^{PM3} 78.6→53.9 ^{F3}	N/A	N/A	N/A	N/A
Rose et al. [8]	AP ^{PM6} 5.2(16.3)→4.3(9.9) ^{F6} HNUP ^{PM6} 3.1(3.8)→1.5(2.0) ^{F6}	AP ^{PM6} 4.6(16.0)→8.1(67.3) ^{F6} HNUP ^{PM6} 2.3(2.3)→0.8(1.2) ^{F6}	N/A	N/A	N/A	N/A
Teti et al. [22]	AP ^{PM6} 2.50(4.36)→4.57(16.66) ^{F6} 2.50(4.36)→1.50(0.81) ^{F12} 2.50(4.36)→1.40(0.84) ^{F18}	AP ^{PM6} 2.24(3.52)→5.15(15.91) ^{F6} 2.24(3.52)→2.77(4.39) ^{F12} 2.24(3.52)→1.40(1.30) ^{F18}	N/A	N/A	N/A	N/A
Wolitski et al. [9]	AP ^{PM3} 27.2→22.6 ^{F6} 27.2→20.6 ^{F12} 27.2→24.3 ^{F18}	AP ^{PM3} 29.2→20.9 ^{F6} 29.2→21.1 ^{F12} 29.2→21.1 ^{F18}	N/A	N/A	N/A	N/A
Kalichman et al. [20]	HNUP ^{PM3} 0.6(1.8)→0.5(1.4) ^{F3} 0.6(1.8)→0.6(1.1) ^{F6} 0.6(1.8)→0.04(0.6) ^{F9}	HNUP ^{PM3} 0.7(3.1)→0.6(1.3) ^{F3} 0.7(3.1)→0.9(5.1) ^{F6} 0.7(3.1)→0.4(0.6) ^{F9}	N/A	N/A	N/A	N/A

Note: IG: intervention group; CG: control groups; SD: standard deviation; AP: any partners; HNUP: HIV-negative or unknown partners; IDU: injection drug use; DU: drug users; I1: cognitive-behavioral group intervention; I2: social support group intervention; N/A: not available;

*Alcohol abuse was defined as exceeding the US National Institute on Alcoholism and Alcohol Abuse's recommended numbers of drinks per week (14 or fewer for men; 7 or fewer for women) and/or 3 or more binge drinking episodes (5 or more drinks on 1 occasion for men; 4 or more drinks on 1 occasion for women).

PM1: In the past month; PM3: In the past 3 months; PM6: In the past 6 months;

F0: Immediately after intervention; F3: At 3-month follow-up; F6: At 6-month follow-up; F9: At 9-month follow-up; F12: At 12-month follow-up; F18: At 18-month follow-up.

Table 3: Efficacy of risk reduction interventions on number of sexual partners and drug and alcohol abuse among persons living with HIV/AIDS.

Sharing of contaminated needles is the primary driver of the HIV epidemic among injection drug users. There were only three RCTs estimating the efficacy of interventions on needle sharing among HIV-positive drug users [22,41,42]. Compared to a previous meta-analysis, our review added one recent RCT [42], but excluded a quasi-experimental study [54]. Both our meta-analysis and the previous one found no significant effect of interventions on needle sharing.

A previous systematic review of 27 observational studies found that any alcohol consumption was significantly associated with an increase of unprotected sex among PLWHA [12]. None of three risk reduction intervention RCTs among PLWHA showed a significant intervention effect in reducing alcohol abuse, though all demonstrated statistically significant reduction of unprotected sex [23,35,41]. The synthesized result in our meta-analysis failed to show a relationship between risk reduction interventions and reduction of alcohol abuse. As alcohol abuse among PLWHA may increase risky sexual behaviors and reduce adherence to HIV antiretroviral therapy [55,56], effective interventions for alcohol abuse among HIV-infected individuals are needed.

Our meta-analysis has several limitations. Firstly, outcomes were based on self-report and might be subject to social desirability bias. For example, if participants in the intervention arm underreported a risk activity post-intervention in order to please the researchers, this may bias the study conclusion towards the null hypothesis. Secondly, the number of RCT studies was small. Thirdly, we found English-language publications only; studies published in other languages, if any, may have different study findings. Thirdly, even though twelve international databases were explored, all included RCTs were conducted in the USA; three RCTs in Africa were excluded because no target outcomes were reported or there were not enough data available for calculation. Therefore, more trials are needed from regions other than the United States. Finally, although twelve databases were searched for, the reviews and we deployed extensive checks for completeness by cross-referencing; we cannot exclude having missed a relevant study.

In conclusion, our meta-analysis suggested that the available RCTs for risk reduction among PLWHA did not have significant impacts on reducing number of sexual partners, and substance and alcohol abuse. Studies of more promising behavioral, community, or structural interventions are needed, properly designed and powered that target "positive prevention" strategies for PLWHA.

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