

Regular article

Behavioral HIV risk reduction among people who inject drugs: Meta-analytic evidence of efficacy

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Received 5 January 2006; received in revised form 24 March 2006; accepted 17 April 2006

Abstract

We conducted a meta-analysis of randomized controlled trials (RCTs) to evaluate behavioral HIV risk reduction interventions targeting people who inject drugs. We included 37 RCTs evaluating 49 independent HIV risk reduction interventions with 10,190 participants. Compared to controls, intervention participants reduced injection drug use (IDU) and non-IDU, increased drug treatment entry, increased condom use, and decreased trading sex for drugs. Interventions were more successful at reducing IDU when participants were non-Caucasians, when content focused equivalently on drug-related and sex-related risks, and when content included interpersonal skills training specific for safer needle use. Condom use outcomes improved when two intervention facilitators were used instead of one. IDU outcomes did not decay, but condom use outcomes did. Behavioral interventions reduce risk behaviors among people who inject drugs, especially when interventions target both drug risk and sexual risk behaviors, and when they include certain behavioral skills components. Implications for future interventions are presented. © 2006 Elsevier Inc. All rights reserved.

Keywords: HIV prevention; Risk reduction; Behavioral intervention; Injection drug use; Meta-analysis; Substance abuse

1. Introduction

Despite a wide array of HIV prevention approaches and related research, there has been a decade-long trend of 40,000 new HIV infections per year in the United States (Centers for Disease Control and Prevention, 2004). Injection drug use (IDU) remains an important vector for the transmission of new HIV infections (Avants, Margolin, Usubiaga, & Doebrick, 2004; Margolin, Avants, Warburton, Hawkins, & Shi, 2003), and people who inject drugs

experience increased risk through both drug and sexual behaviors. Because people who inject drugs exhibit diverse risk behaviors, this group presents a formidable prevention challenge. Specifically, investigators report considerable variability over time in the risk profiles of people who inject drugs, owing predominantly to their current amount of HIV risk behavior, their HIV serostatus, and the recency of their exposure to HIV risk reduction interventions. For example, investigators have observed different individuals who inject drugs as circulating in and out of risky behavior states over time rather than as exhibiting steady HIV risk behavior states (Celantano, Muñoz, Cohn, & Vlahov, 2001).

A number of HIV prevention interventions have now been identified as demonstrating evidence of effectiveness (Semaan et al., 2002; Strathdee et al., 1998; Vlahov et al., 1997). Researchers have also begun to evaluate strategies to

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facilitate the integration of evidence-based interventions into clinical settings (Fisher et al., 2004; Kalichman et al., 2001). Even so, individual studies have yielded little evidence about the intervention components that are most helpful for risk reduction interventions for people who inject drugs. Therefore, we conducted a meta-analysis of randomized controlled trials (RCTs) of behavior change interventions targeting people who inject drugs. We strove to specify the intervention components that could be used for the future development and deployment of more effective strategies for reducing drug-related and sex-related HIV risks among those who inject drugs.

2. Materials and methods

2.1. Sample of studies

Reports were gathered using four overlapping strategies: (1) search for terms such as “HIV,” “AIDS,” “human and immun* and virus,” “acquired and immun* and syndrome” and “interven* and prevent* paired with (needle* or inject*, or idu or IDU, or IVDU or ivdu)” in electronic databases MEDLINE, PsycINFO, AIDSLINE, CINAHL, Dissertation Abstracts Online, and ERIC; (2) requests for articles sent to

authors and e-mail list servers; (3) search for reference sections of articles already obtained; and (4) manual search for conference proceedings and professional journals that are not available electronically. Studies that were available as of March 30, 2004, and that matched the selection criteria (discussed below) were included.

2.2. Study selection criteria

To qualify for this meta-analysis, a study had to: (1) evaluate group or individual behavioral HIV prevention interventions; (2) include a sample of at least 50% of people who report injecting drugs; (3) include IDU-related behavioral outcomes; (4) use an RCT design; and (5) provide statistical information for the calculation of effect size(s) (ES; Fig. 1). After reviewing 713 abstracts that contained one or more keywords, we identified 129 studies that reported evaluating behavioral interventions with IDU-related outcomes. Studies were excluded if they did not implement a control group ($k = 41$), or if data reported in one study overlapped with data reported in another study, or when a study presented follow-up data that were included in another analysis ($k = 20$). The primary instance was the public domain report that included individual site data from the National AIDS Demonstration Research (NADR)

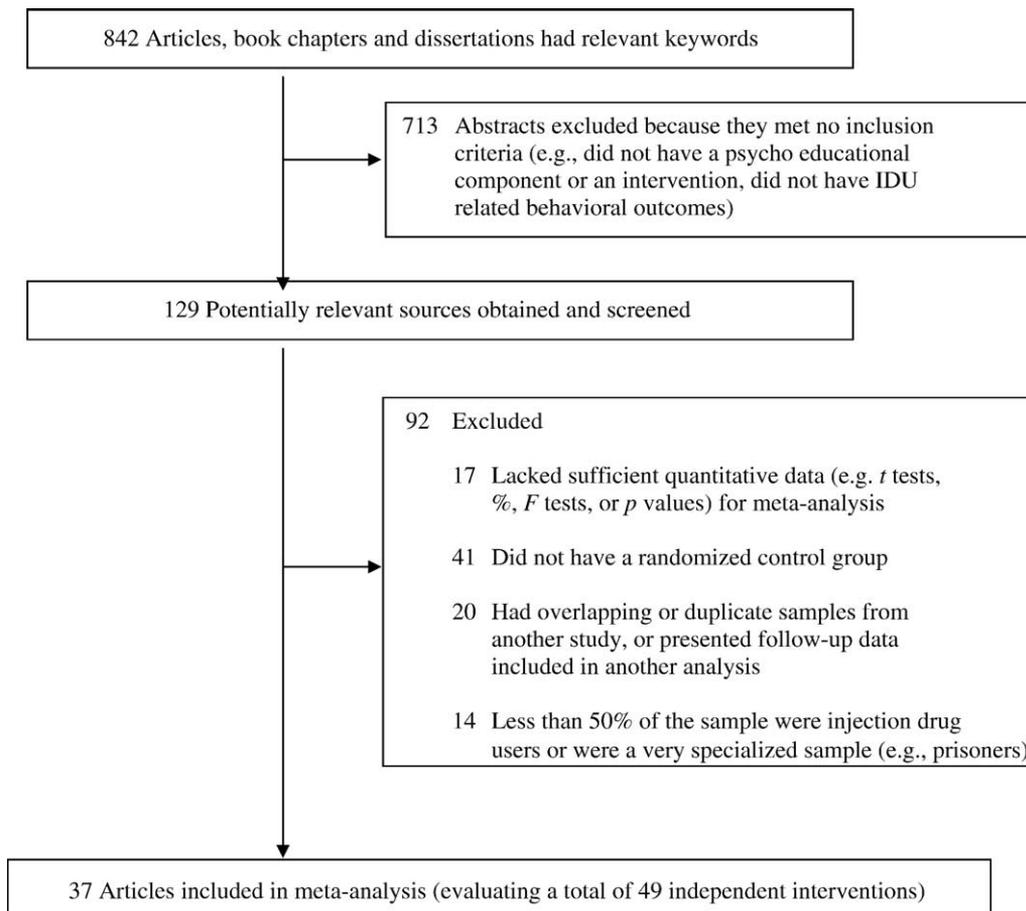


Fig. 1. Selection process for study inclusion in the meta-analysis.

project. Seventeen other studies were excluded because they had insufficient statistics, and 14 studies were excluded because less than 50% of their samples were characterized as people who inject drugs or because they included a specialized sample (e.g., prisoners). Studies reporting behavioral measures were included even if measures were indirectly or distally related to HIV risk reduction (e.g., communication skills pertaining to needle sharing and discussing safer sex with a partner). Thirty-seven studies ultimately qualified based on our selection criteria; of these, 26 studies evaluated a single intervention, 10 evaluated two interventions, and one evaluated three interventions. In total, there were 49 independent interventions using 10,190 participants following attrition, representing a retention rate of approximately 65% ($SD = 25%$) of participants.

2.3. Extraction of ES information

A minimum of two trained raters independently coded each study to describe the studies and to determine in stratified analyses whether variations in ES could be linked to the features of the study. Across study-level and intervention-level categorical dimensions, coders agreed on 82–100% of judgments, resulting in an average Cohen's κ value of .80. Disagreements were resolved through discussion. Effective reliability for continuous variables was calculated with the Spearman–Brown result, which takes into account the mean interrater correlation and the number of raters, and ranged from .85 to 1.00 ($M = .99$).

ES estimates were based on information provided in a report or from data provided by the authors. ES estimates were calculated in standard deviation units because the selected studies typically used parametric statistical tests with continuous measures of intervention outcomes (odds ratios are the ES of choice when the outcomes are dichotomous in nature; Lipsey & Wilson, 2001). Specifically, the ES was calculated as the difference on risk measures between the means of the intervention group and the comparison group divided by pooled standard deviation; ES were corrected for sample size bias. Signs of ES were set so that positive values indicated improvement (i.e., reduced risk). If more than one comparison group was included in a given study, which occurred in a minority of cases ($k = 6$), we used the comparison group that was most similar to the modal comparison group in the literature, typically a brief HIV intervention or HIV/AIDS education.

Multiple ES estimates were calculated from individual studies when more than one behavioral measure was reported, including these behavioral outcomes: (1) frequency of IDU, (2) frequency of non-IDU, (3) frequency of sharing needles/equipment, (4) frequency of bleaching needles/equipment, (5) entry into drug treatment, (6) frequency of condom use, (7) frequency of sex-related HIV risk behavior, and (8) frequency of trading sex for drugs. No studies provided data on HIV incidence, precluding examination of this outcome. Due to sample size constraints, ES

were calculated using only data reported at baseline and postintervention measurement points, although a minority of the studies reported data at follow-up points beyond post intervention. ES were corrected for any significant between-group differences on behavioral outcomes at baseline.

We calculated weighted mean ES and 95% confidence intervals (CIs) around mean ES using conventional fixed-effects meta-analytic procedures and estimated the homogeneity (Q) of the ES that comprise each mean. To avoid violating the assumption of independent observations, analyses proceeded by examining the study outcomes in separate analyses. For the two outcomes with significant overall Q values (i.e., IDU and condom use), we determined whether coded features of studies related significantly to the variability in the magnitude of the ES. The IDU set of ES outcomes was large enough to apply more than one feature at a time, but condom use set was not. In these models, we controlled for type I error by using the Bonferroni correction for each set of ES (effectively, .0008 for IDU outcomes and .0009 for condom use outcomes). Study dimensions that were significantly related to IDU variability were further pursued in a series of multiple regression models that controlled for intercorrelations among study dimensions that were maintained. Such models determined whether variation attributed to one study dimension would be better attributed to another study dimension. The number of studies was too small to permit all study dimensions to be included simultaneously, but did permit model testing with three predictors at one time. The univariate predictor with the best fit was paired sequentially against other univariate predictors. The end result was that the final multiple regression model with the remaining significant study dimensions was correctly specified, meaning that the variation remaining unexplained was within the limits of sampling error and that there was no need to incorporate random effects in this analysis, consistent with meta-analytic convention (e.g., Johnson, Carey, Marsh, Levin, & Scott-Sheldon, 2003; Johnson & Eagly, 2000; Lipsey & Wilson, 2001). Supporting this conclusion, an analysis incorporating random-effects assumptions did not change the pattern of results on regression analysis. To maintain cases in these models, we used the multiple-imputation method to estimate missing values because it has been proven superior for this purpose (Pigott, 2001; Sinharay, Stern, & Russell, 2001). Of variables pertaining to methodology, sample characteristics, and control group characteristics, 32% of the variables had missing values; these were estimated by the multiple-imputation method using NORM 2.03 (Schafer & Graham, 2002), whereas 68% of those variables required no imputation. NORM assigns a value from a set of multiple-imputation values created from conceptually meaningful variables provided by each study under an unstructured normal model. Imputation was not used if less than 50% of the observations were available.

3. Results

3.1. Description of studies and their interventions

Seventy-eight percent of the studies were published in peer-reviewed journals; 20% were studies from individual sites that were published in the public domain report of the NADR project; and 2% were obtained from unpublished documents. Approximately 49% of the studies advocated a specific behavioral theory (or a blend of theoretical perspectives) in their approach to risk reduction, whereas the remainder (about 51%) did not. The majority of investigations (88%) were performed in the United States and involved participants within medium to large cities. Slightly less than half of the studies (47%) recruited community participants who were not enrolled in drug treatment, whereas the remainder recruited participants who were enrolled in treatment (e.g., methadone maintenance, outpatient drug treatment, inpatient drug treatment, and detoxification).

Study participants tended to be middle-aged men ($M = 35$ years; range, 26–41 years; 61% male). The samples were ethnically diverse, with 51% African American, 29% Caucasian, and 20% Latino. The vast majority (88%) reported recent IDU (i.e., within the past 3 months), 46% reported recent needle sharing or borrowing, and 29% reported recent sex trading. Those who reported current IDU were most likely to report heroine (54%) and cocaine (54%) use. Approximately 82% reported being sexually active, 50% reported having had sex with another person who injects drugs, and 28% reported being aware that they were HIV-infected.

All studies adopted RCTs. Among them, 51% of the studies implemented a brief HIV risk reduction intervention as control condition, whereas 22% used HIV/AIDS education only, 20% adopted a wait-list treatment/no treatment, 4% used substance abuse treatment only, and 2% used an intervention with non-HIV content as control. All studies used a pretest/posttest design in which data were obtained

from the same participants at distinct time points. Outcomes were assessed at baseline and posttest for 49% of studies; at baseline, posttest, and one follow-up for 45%; and at baseline, posttest, and two follow-ups for 6% of studies.

Group interventions were the most common (51%), with individual interventions used in 44% of studies; the remaining 5% used a combination of group and individual modes. On average, interventions consisted of eight sessions of approximately 87 minutes each (range, 33–300 minutes) for the course of 29 days (range, 1–113 days). Studies evaluating group-level intervention included approximately four participants per group and were most commonly facilitated by either one or two group leaders. Group facilitators included individuals described as paraprofessionals (without an advanced degree or license; 63% of studies), professionals (with an advanced degree or license; 27% of studies), both paraprofessionals and professionals (8% of studies), and neither paraprofessionals nor professionals (e.g., peers; 2% of studies).

Most interventions included the following components: HIV/AIDS education (90% of interventions), condom use skills (69%), self-management skills (e.g., coping with drug cravings; 57%), and both drug-related and sex-related risk reduction (70%). Less commonly, interventions contained drug treatment (35%), provided bleach (35%), and provided condoms (35%). No intervention included the provision of clean syringes to participants.

3.2. How efficacious were HIV risk reduction interventions?

First, we evaluated how successful interventions were relative to control conditions on risk reduction outcomes (see Table 1). The outcomes included IDU (30 studies), condom use (16), non-IDU (11), and entry into drug treatment (6). Using data from the first available assessment point following the completion of the intervention, participants significantly: (1) reduced IDU ($d = 0.08$; 95% CI = 0.03, 0.13); (2) decreased non-IDU ($d = 0.18$; 95% CI = 0.06, 0.30); (3) increased entry into drug treatment

Table 1

Summary of intervention efficacy outcomes (ES), grouped as to whether the outcome measure was primarily drug-risk-related or sexual-risk-related

Outcome (ES)	<i>k</i> of studies	Weighted mean ES (95% CI)	Homogeneity of ES	
			<i>Q</i>	<i>p</i> ^a
Drug-risk-related outcomes				
Decrease in IDU	30	0.078 (0.028, 0.127)	83.95	.000
Decrease in non-IDU	11	0.181 (0.063, 0.299)	12.12	.280
Entry into drug treatment	6	0.114 (0.020, 0.209)	8.45	.130
Frequency of sharing needles/equipment	16	0.033 (−0.037, 0.104)	24.22	.062
Frequency of bleaching needles/equipment	10	0.052 (−0.028, 0.132)	14.42	.108
Sexual-risk-related outcomes				
Increase in condom use	16	0.186 (0.115, 0.258)	28.91	.017
Frequency of trading sex for drugs	4	0.334 (0.097, 0.570)	2.26	.520
Frequency of unprotected sex	15	0.042 (−0.041, 0.124)	18.87	.170

Notes. ES are positive for differences of lowered risk in the treatment group relative to the control group; all measures were from the first follow-up assessments available in each study.

^a Significance implies rejection of the hypothesis of homogeneity. Significant ES outcomes appear in **bold**.

($d = 0.11$; 95% CI = 0.02, 0.21); (4) increased condom use ($d = 0.19$; 95% CI = 0.11, 0.26); and (5) reduced the frequency of trading sex for drugs ($d = 0.33$; 95% CI = 0.10,

0.57). Although the ES for trading sex was statistically significant, it was based on only four studies and thus should be interpreted cautiously.

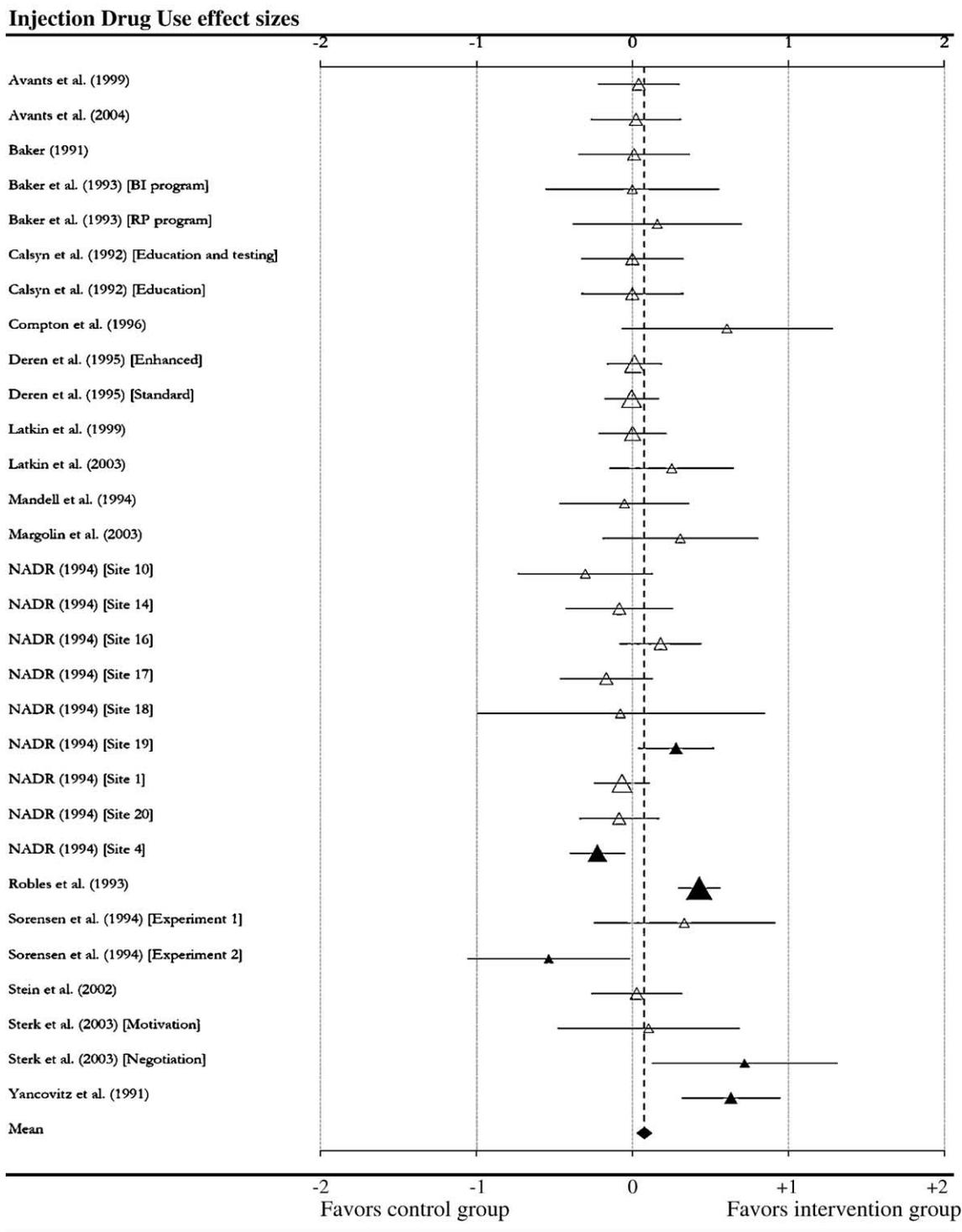


Fig. 2. Forest plots for IDU (upper panel) and condom use (lower panel) ES, in which delta points to the right of zero reflect risk reduction and those to the left reflect risk increase, relative to the control group. Zero values indicate exactly no difference between the two groups. The symbols for statistically significant effects are filled, whereas those that are not significant are open. The size of the delta symbol for each ES reflects its weight in the analyses. The CI for the mean ES is displayed by the width of its diamond.

Condom Use effect sizes

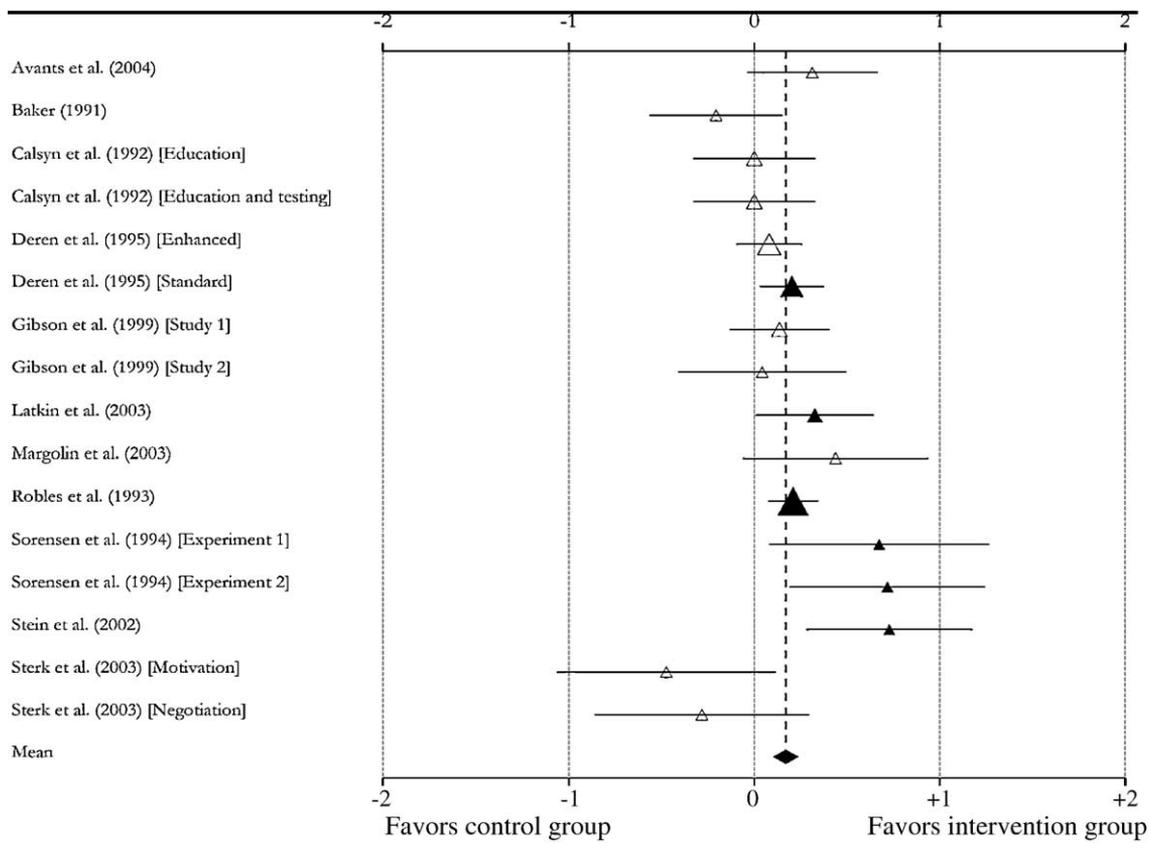


Fig. 2. (continued).

Results were similar with fixed-effects or random-effects assumptions. Outcomes associated with treatment entry, non-IDU, and trading sex for drugs showed a high degree of homogeneity; thus, they were well characterized by their respective means (Table 1), and further (moderator) analyses were not warranted. ES arrays for condom use and IDU were *not* well-characterized by their mean ES, $Q(15) = 28.91$ and $Q(29) = 83.95$, respectively, $P < .05$ (Fig. 2), but further analyses explained these heterogeneous effects. Finally, no difference between HIV risk reduction and conditions was observed for three outcomes: (1) frequency of sharing needles/equipment; (2) frequency of bleaching needles/equipment; and (3) frequency of unprotected sex (Table 1).

3.3. Intervention features that influenced IDU and condom use outcomes

3.3.1. Reduced IDU

Considered individually, nine sample and intervention features were associated with reduced IDU: (1) more non-Caucasian participants; (2) more Latina/Latino participants; (3) more participants who reported recent cocaine use; (4) more participants who reported recently injecting “speedball” (a mixture of heroin and cocaine); (5) participants recruited through self-selection in the community or through

clinical contact; (6) use of an individual intervention approach; (7) no provision of bleach; (8) provision of interpersonal skills training specific for safer needle use; and (9) provision of equivalent intervention content on drug-related and sexual-related HIV risks. Follow-up multiple predictor models indicated that six of these associations became nonsignificant when controlling for other features. IDU ES were modeled successfully based on the remaining three features, included simultaneously: (1) more non-Caucasian participants; (2) dedication of equivalent intervention content to drug-related and sexual-related HIV risks; and (3) provision of interpersonal skills training specific for safer needle use (Table 2). This model explained 63% of the variation in ES and had good model fit, $Q_E(26) = 31.21$, $p = .22$.

Because decay of intervention effects is an important concern, we also examined whether IDU ES related to the time that elapsed between the end of the intervention and the posttest and follow-up measurement points. Based on all 30 interventions, no decay was found in IDU outcomes following the intervention to the posttest point, $\beta = .08$, $p = .46$. Based on six of the interventions that gathered both posttest *and* follow-up data, no decay was found in the IDU outcome up to 52 weeks following the intervention, $\beta = -.06$, $p = .77$.

Table 2
Final models of study dimensions that are significantly related to the efficacy of interventions

Study dimension	Patterns	Weighted mean (95% CI)	<i>k</i>	β alone ^a	Model statistics	
	Level				β^b	<i>p</i>
Reduced IDU						
Percentage of Caucasian intervention participants	0	0.213 (0.138, 0.286)	30	−.397	−0.299	<.01
	30	0.133 (0.076, 0.189)				
	60	0.053 (−0.037, 0.144)				
Equality of emphasis on injection risk behavior and emphasis on sexual risk behavior	Equal emphasis	0.298 (0.203, 0.393)	30	.649	0.626	<.001
	Unequal emphasis	−0.027 (−0.087, 0.032)				
Intervention with interpersonal skills training on safer needle use	Present	0.196 (0.119, 0.273)	30	.396	0.261	<.05
	Absent	0.074 (−0.026, 0.151)				
Increased condom use						
Number of intervention facilitators	1	−0.005 (−0.197, 0.186)	10 ^c	.834	.834	<.001
	2	0.344 (0.172, 0.516)				

Notes. Analyses follow fixed-effects assumptions with each ES (*d*) weighted by the inverse of its variance. The results for injection drug risk outcomes result from one model with the 30 IDU studies, following fixed-effects assumptions in which all three study dimensions appeared. Each displayed mean is adjusted for the presence of the other study dimension, with that dimension held constant at zero. The full regression equation, with each study dimension contrast-coded (+1, −1), was: $ES = 0.2118 - 0.2643 (\% \text{ Caucasian}) + 0.0608 (\text{interpersonal skills}) + 0.1626 (\text{equal emphasis})$; multiple $R^2 = .628$. Analyses on the increase of condom use are a series of models for each of the study dimensions based on fixed-effects assumptions, where each ES (*d*) was weighted by the inverse of its variance.

k = number of studies; *p* = probability; β = standardized regression coefficient; Q_E = model specification statistic (distributed as χ^2 with $k - 2df$); when statistically significant, the variation that remains unexplained exceeds that expected by sampling error alone.

^a Without controlling for the other study dimension (i.e., univariate analysis).

^b Controlling for the other study dimensions within drug use ES.

^c The number of studies was reduced to 10 due to missing data.

3.3.2. Increased condom use

Only one study feature was associated with variability in the magnitude of condom use ES (Table 2): Interventions were more successful when they included two facilitators, as evidenced by a model that fit the data correctly, $Q_E=4.90$, $p = .77$. No evidence that facilitators' qualifications (e.g., professionals vs. nonprofessionals) played a role in this outcome, $Q_B(1) = 0.01$, $p = .91$, was found.

Finally, exploratory analysis revealed that condom use ES tended to decrease as the interval between the end of the intervention and the measurement point increased, $\beta = -.51$, $p = .006$. Seven of the interventions gathered both posttest and follow-up data pertaining to condom use; a similar trend of decay appeared, but it did not reach conventional levels of significance, $\beta = -.30$, $p = .19$.

4. Discussion

This meta-analysis examined both sexual-related and drug-related HIV risk reduction outcomes in studies that included persons who inject street drugs, evaluating only the strongest evidence, RCTs. The sample of 37 studies included data from both participants who were already enrolled in drug treatment and persons who were "out of treatment" and living in the community. Thus, we could evaluate the extent to which interventions were successful at prompting out-of-treatment drug users to enroll in treatment.

The synthesis relied on 49 independent interventions from 37 studies and supported the conclusion that, overall, the interventions facilitated condom use; promoted entry into drug treatment; and helped reduce IDU, non-IDU, and

sex trading. These effects were consistent with regard to non-IDU, drug treatment entry, and sex trading outcomes (i.e., intervention participants tended to enter drug treatment and to reduce both their use of noninjected drugs and the practice of trading sex for drugs regardless of other interventions or personal characteristics). The enhanced drug treatment entry outcome is a particularly encouraging outcome given the multiple benefits that accrue from successful drug treatment (Metzger, Navaline, & Woody, 1998; National Institutes of Health, 1997; Prendergast, Urada, & Podus, 2001).

The observed effects were *not* consistent for two key outcomes: IDU and condom use. The tendency for the interventions to enhance condom use and to reduce IDU relative to controls was modified by specific features of the interventions and by the characteristics of the participants. Interventions tended to be more successful at reducing IDU for non-Caucasians. With respect to HIV, this result is encouraging because ethnic/racial minorities are disproportionately vulnerable to HIV (Centers for Disease Control and Prevention, 2004).

IDU was reduced to the extent that interventions were characterized by an equivalent focus on drug and sexual behaviors as opposed to an exclusive focus on either type of risk behavior. Furthermore, reduced IDU was more likely when interventions provided interpersonal skills training specific for safer needle use. Importantly, this intervention outcome appeared to be durable; we found no evidence of decay up to a year following the interventions.

Frequency of condom use improved to the extent that the interventions were led by more than a single intervention facilitator. To date, no primary-level study with an IDU

sample has compared the effects of interventions using one facilitator versus the effects of interventions using two facilitators. Future studies could examine whether the use of two facilitators increases intervention fidelity, affords more enriched opportunities for modeling (and shaping) interpersonal skills, improves the ability to manage complex group processes, or enhances facilitator–participant matching (e.g., on sex, race/ethnicity, and sexual orientation).

Of some concern, the interventions' effects on condom use tended to decay over time. Maintaining consistent condom use may require additional strategies (e.g., booster sessions) to address emergent challenges and to maintain behavior change. Considered together, these findings suggest an HIV risk reduction program led by two facilitators that targets a broad range of drug and sexual risk behaviors and provides periodic booster sessions.

Overall, like previous reviews, we observed modest ES on risk behavior outcomes. As previous reviews have noted (Semaan et al., 2002; Prendergast et al., 2001; Strathdee et al., 1998), these effects may reflect the use of control conditions that are *similar* to, although briefer than, the intervention being evaluated. This design feature, which is ethically necessary, inadvertently restricts the range of ES that might be observed from the literature. Moreover, behavior change is generally difficult, as demonstrated in numerous health behavior domains (e.g., smoking, weight loss, and substance abuse; Pigott, 2001). Behavior change interventions, in general, and behavioral HIV risk reduction interventions, in particular, tend to produce small increments of behavior change. Nonetheless, when extrapolated to high-risk populations, the modest changes reported here and in prior reviews have the potential to improve public health (e.g., Glasgow, Vogt, & Boles, 1999; Semaan et al., 2002).

Meta-analyses, like primary-level studies, have limitations that need to be acknowledged so that findings can be interpreted appropriately. One limitation of the current analyses involved the decision to include only RCTs. This decision allowed us to examine the strongest evidence, but it also constrained the range of potential analyses that we could conduct. For example, because only a minority of the included studies reported outcomes assessed at a distant follow-up occasion, our analyses could not provide extensive detail on long-term outcomes. Similarly, the variables that we could analyze were limited by the outcomes reported, most of which were based on self-reported data. Thus, although other outcomes (e.g., sero conversion rates) were of keen interest, such data were not available. Third, the size of the available literature constrained the number of predictors that could be included in the multivariate analyses we conducted. Despite these limitations, this meta-analysis provides a valuable summary of the extant research. Our results provide evidence that behavioral interventions reduce behaviors that place persons injecting drugs at risk for contracting and transmitting HIV. Enhancing the magnitude of HIV risk reduction is facilitated by the identification of specific intervention features associated

with positive outcomes. In addition, these results identify participants who are less likely to profit from behavioral interventions as currently constructed, and point to the need for continued refinement of these interventions so that they benefit all who are in need.

Acknowledgment

Funding to support the design and conduct of this research and the preparation of this manuscript was provided by National Institutes of Health grants (K23-DA017015 to Michael M. Copenhaver; R01-MH58563 to Blair T. Johnson; F31-MH069079 to Jennifer J. Harman; and K02-MH01582 to Michael P. Carey).

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