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Effects of integrated interventions on transmission risk and care continuum outcomes in persons living with HIV: Meta-analysis, 1996-2014

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Abstract

Background—Reducing HIV infection and improving outcomes along the continuum of HIV care are high priorities of the U.S. National HIV/AIDS Strategy. Interventions that target multiple problem behaviors simultaneously in an integrated approach (referred to as integrated interventions) may improve prevention and care outcomes of persons living with HIV (PLWH). This systematic review and meta-analysis examines the effects of integrated interventions.

Methods—A systematic review, including both electronic and hand searches, was conducted to identify randomized controlled trials (RCTs) published between 1996 and 2014 that were designed to target at least two of the following behaviors among PLWH: HIV transmission risk behaviors, HIV care engagement, and medication adherence. Effect sizes (ESs) were meta-analyzed using random-effects models.

Results—Fifteen RCTs met the inclusion criteria. Integrated interventions significantly reduced sex without condoms (odds ratio [OR] = 0.74, 95% CI = 0.59, 0.94, p = .013, 13 ESs) and had marginally significant effects on improving medication adherence behaviors (OR = 1.35, 95% CI = 0.98, 1.85, p = .063, 12 ESs) and undetectable viral load (OR = 1.46, 95% CI= 0.93, 2.27, p = .098, 7 ESs). Significant intervention effects on at least two outcomes were seen in RCTs tailored to individual needs, delivered one-on-one, or in settings where PLWH received services or care.

Conclusions—Integrated interventions produced some favorable prevention and care continuum outcomes in PLWH. How to incorporate integrated interventions with other Combination HIV Prevention strategies to reach the optimal impact requires further research.

Keywords

People living with HIV; HIV transmission risk; medication adherence; retention in HIV care; integrated HIV interventions

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INTRODUCTION

The National HIV/AIDS Strategy (NHAS)[1] outlines several goals for ending the domestic HIV epidemic, including use of evidence-based prevention strategies to reduce HIV transmission, increase access to care, and optimize health outcomes for persons living with HIV (PLWH). The most up-to-date estimates show that 1.2 million persons were living with HIV infection in the United States (U.S.) in 2012. Among these PLWH, 39% were engaged in HIV medical care, 36% were prescribed antiretroviral therapy (ART), and 30% achieved viral suppression [2]. These figures call for further improvements across the HIV care continuum in order to reach NHAS' prevention and care goals.

Engaging in HIV medical care shortly after HIV diagnosis and sustaining routine care with high adherence to ART can improve health outcomes of PLWH and prevent HIV transmission [3]. Non-engagement in HIV care, non-adherence to ART, and non-adherence to safer sex can each have adverse health consequences for PLWH and their partners. Evidence also suggests these behaviors are associated with each other. Sexual risk among PLWH was found to be associated with not being engaged in HIV care [4] or not adhering to ART [5]. Non-engagement in HIV care was found to be associated with poor medication adherence and detectable viral load [6]. These associations suggest the need for interventions that target multiple behaviors to reduce HIV transmission and improve health outcomes of PLWH.

Intervening on multiple behaviors at one time strengthens the connection between prevention and care and is consistent with Combination HIV Prevention [3, 7]. Integrated interventions are defined here as interventions that target multiple behaviors of PLWH. By simultaneously addressing problem behaviors caused by similar influencing factors (e.g., motivation, knowledge, skills, stigma, mental health, homelessness), integrated interventions may be more practical and economical than interventions that target one behavior at a time (single-target interventions). However, addressing multiple behavioral targets may potentially dilute the intervention effects on any single outcome.

Before considering integrated interventions as part of Combination HIV Prevention, it is important to examine whether integrated interventions are effective in improving prevention and care outcomes. Several systematic reviews and meta-analyses have examined the effects of interventions that reduce behavioral risk of transmitting HIV [8-12], promote HIV care engagement and utilization [13, 14], and improve adherence to HIV medication and viral suppression [15-17] among PLWH. To our knowledge, there is no systematic review or meta-analysis that evaluates the effects of integrated interventions. In this meta-analysis, we systematically reviewed U.S.-based randomized controlled trials (RCTs) that evaluated integrated interventions specifically designed for PLWH and addressed at least two of the following behaviors: transmission risk behaviors, HIV care engagement, and medication adherence. Our goals are to describe the characteristics of currently available integrated interventions, assess intervention effects on prevention and care continuum outcomes, and identify research gaps to inform prevention and treatment efforts.

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METHODS

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [18] to report our systematic review and meta-analysis. Supplementary Material A provides the PRISMA checklist. A study protocol is not available for this review.

Search Strategy

We used the CDC's Prevention Research Synthesis (PRS) project's cumulative HIV/AIDS/STD research database for identifying relevant reports. The PRS database is updated annually following a well-established systematic search protocol, which consists of automated and manual searches [19]. Each year, four comprehensive searches are conducted to locate citations related to HIV risk reduction (RR), medication adherence (MA), linkage to and retention and re-engagement in HIV care (LRC), and systematic reviews of HIV prevention. All four searches include the electronic databases (and platforms): EMBASE (OVID), MEDLINE (OVID), and PsycINFO (OVID). Additional electronic databases (e.g., Sociological Abstracts, CINAHL, CAB Global Health) are included for some searches (see Supplementary Material B for detailed information).

Each comprehensive, automated search combines keywords and index terms used to describe concepts within a domain. For example, the RR search consists of three domains: (1) HIV, AIDS or STD index terms; (2) prevention, intervention or evaluation terms; and (3) behavior or outcome terms. The Boolean operator ‘OR’ is used to consolidate each domain with an ‘AND’ operator used to cross-reference each domain. No language restriction was applied to the automated search. The full search strategy of the MEDLINE database for each of the four comprehensive searches is provided as Supplementary Material C. The searches of the other databases are available from the corresponding author.

The manual search included three components: (a) quarterly searches of all reports published in the previous 3 months of 60 journals (see Supplementary Material D) to identify potentially relevant citations not yet indexed in electronic databases, (b) review of the reference lists of pertinent articles; and (c) searches of HIV/AIDS Internet listservs and other research databases (e.g., ISI Web of Knowledge, RePORTER, Cochrane Library).

Citations identified through automated and manual searches were downloaded and de-duplicated in the PRS database before conducting title/abstract screening and full-report coding. The last date we searched the PRS database was January 2, 2015.

Inclusion Criteria

Inclusion criteria were randomized controlled trials that: (1) evaluated interventions specifically designed for PLWH; (2) were conducted in the U.S.; (3) were published or in press between 1996 and 2014; (5) tested interventions that addressed at least two of the behaviors: HIV transmission risk behaviors, HIV care engagement, or medication adherence; and (6) reported at least two of the following relevant outcomes:

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- Behaviors (i.e., sex without condoms, number of sex partners, needle sharing, injection drug use) or biological outcomes (i.e., STD) that increase HIV transmission risk,
- HIV care engagement (i.e., retention in HIV care measured by the number of missed or kept HIV care appointments or having 2 HIV medical visits within past 6 months), and
- HIV medication adherence (i.e., being on ART, behavioral measures of adherence by medication event monitoring system [MEMS], electronic drug monitoring [EDM], pill count, pharmacy refill, or self-report; viral load level measured by self-report or medical records).

Data Abstraction

Pairs of trained coders independently coded each eligible intervention using standardized coding forms for the following: study characteristics (e.g., study date, location, study design, sample size, data collection method), participant characteristics (e.g., target population, gender, race/ethnicity, sexual orientation), intervention characteristics (e.g., components, delivery method, duration, time span), outcomes, and risk of bias. Linked citations, defined as publications offering additional information on the same study, were included if they provided relevant intervention and evaluation information. The overall percentage agreement among trained coders is 96% with a kappa rate of 80%, indicating a high inter-rater reliability. We contacted the primary study investigator to obtain additional information as needed. The response rate was 90%.

Because studies differ in reporting outcomes and findings, we applied the following rules for guiding data abstraction for analyses. For studies that reported multiple outcomes of interest, separate analyses were conducted for sex without condoms, number of sex partners, STD, needle sharing, injection drug use, taking ART, HIV care engagement, medication adherence and viral load suppression. This approach allowed us to examine intervention effects on different outcomes as the prevention literature showed some outcomes (e.g., number of sex partners, STD) were more difficult to change than other outcomes (e.g., sex without condoms) [9].

If sex behavior data for different types of partners were reported, the analysis focused on sex with at-risk partners (i.e., HIV-negative or status-unknown partners) rather than HIV-positive or all partners. For studies that reported medication adherence outcomes based on self-report or MEMS data, the latter was used in the analysis. For studies that reported multiple follow-up assessments, we selected the time point closest to 3 months post completion of the intervention for interventions that are clearly discrete (i.e., all the sessions are thought to be necessary and sufficient for yielding the desired change) and the last assessment point for interventions that are designed to be on-going (i.e., receiving the intervention at each clinic visit). To reduce the impact of group differences at baseline on the outcome, we calculated effect sizes for the follow-up outcome data by adjusting for baseline differences.

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Risk of Bias Assessment

Study quality was assessed using adapted Cochrane risk-of-bias variables [20]. Each intervention was evaluated for participant selection (sequence generation, allocation concealment), blinding (personnel, outcome assessors), and attrition bias (intent to treat [ITT], differences between those lost and retained, overall retention [≥ 80% vs. <80%], differential attrition [≤ 10% vs. >10%]). Each item was scored as either high or unclear risk of bias (0) or low risk of bias (1). Overall study quality was scored from 0 to 8, with a higher score indicating a lower risk of bias.

Data Analysis

Standard meta-analytical methods were used [21, 22]. Effect sizes were estimated using odds ratios (OR) because the majority of the studies reported dichotomous outcomes. For studies reporting means and standard deviation (SD) values on continuous outcomes, standardized mean differences were calculated and converted into OR values [21, 22]. Random-effects models with two-tailed tests were used to calculate aggregated effects for all outcomes of interest [23]. For HIV transmission risk outcomes, an OR < 1 indicates a greater reduction in odds of reporting sex without condoms, multiple sex partners, STD, needle sharing, or injection drug use in the intervention group, relative to the comparison group. For HIV engagement and medication adherence outcomes, an OR > 1 indicates a greater increase in odds of being retained in HIV care, being on ART, adhering to HIV medication, or having an undetectable viral load in the intervention group, relative to the comparison group.

The magnitude of heterogeneity of the effect sizes was tested using the Q statistic, for which a significant result indicates the existence of heterogeneity, and I^2 statistic, which quantifies the percentage of variation across studies that was due to heterogeneity [24]. For outcomes that had a significant Q statistic or moderate to high levels of heterogeneity ($I^2 \geq 50$), we conducted stratified analyses to assess the impact of intervention as well as study design characteristics on the outcomes to further explore the heterogeneity when there were sufficient numbers of studies (> 6). Specifically, we assessed between-group differences (Q_B) using the mixed-effects model [22] to determine whether intervention and study design characteristics were associated with effect sizes. There were a limited number of studies for specific subgroups of PLWH and thus stratified analyses were not conducted by participant characteristics. All the analyses were carried out using the Comprehensive Meta-Analysis software (version 2) [25]. Meta-regression was considered, but not used due to a small number of stratified variables with significant between-group differences.

Sensitivity analyses were conducted to test the robustness of the findings. We removed one study at a time from each set of aggregated analyses to determine if any one study affected the aggregated effect size. Additionally, we re-did the analyses with the longest follow-up time point available from each study to determine if the findings were stable at time points farther removed from the intervention. Publication bias was ascertained by inspection of a funnel plot of standard error estimates versus effect-size estimates and by a linear regression test [22, 26].

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RESULTS

The study selection process is summarized in Figure 1. Among 148 intervention studies that were specifically designed for PLWH in the U.S., 15 RCTs, consisting of 4,487 PLWH, met the inclusion criteria (see Supplementary Materials F for excluded studies).

Overall Characteristics of Integrated Interventions for PLWH in the United States

Table 1 provides brief descriptive characteristics of the 15 integrated interventions. Interventions targeted a variety of PLWH subgroups, including (not mutually exclusive) clinic patients [27-32], youth or young adults [31-33], persons who use/inject drugs [30, 33, 34], women [35, 36], inmates reentering the community [37, 38], women with histories of sexual abuse [36], persons who were homeless or at risk of homelessness [39] and other high-risk PLWH (e.g., persons who engaged in unprotected sex with HIV-negative/status unknown partners or had medication/visit adherence problems) [28, 31, 40].

Regarding the intervention characteristics, nine studies addressed risk reduction and medication adherence [29-32, 35, 36, 38, 40, 41], four studies examined all three behaviors [33, 34, 37, 39], and two studies focused on HIV care engagement and medication adherence [27, 28]. Almost half of the interventions were tailored to an individual's needs by using less structured sessions [27-29, 31, 32, 35, 38]. The majority of the interventions were delivered oneon-one [27-29, 31-33, 37, 39, 40] and in settings where PLWH receive services or care (e.g., HIV outpatient clinics, community AIDS service centers, methadone treatment clinics) [27-32, 35, 40, 41]. Interventions were delivered by trained facilitators [27, 28, 34, 36, 37, 39-41] or by health care providers or counselors [30-33, 35, 38]. One was a computer-delivered intervention [29]. The number of intervention sessions ranged from 3 to 48 with a median of 8 sessions. The median time per session was 90 minutes (range: 30 to 120 minutes per session) and the median total time of the interventions was 10.5 hours (range: 2 to 96 hours).

Regarding the study design and quality, the sample sizes ranged from 56 to 966 with a median of 175 participants. Five studies [29, 34, 39-41] conducted power analyses to estimate the sample sizes needed for detecting moderate effect sizes. Although all studies were RCTs, the level of risk of bias varied (see Supplementary Material F). Out of 8 risk of bias variables, seven RCTs scored 0 to 4 (higher risk of bias), five scored 5, and three scored 6 to 7 (lower risk of bias). The majority of studies retained > 80% of participants (12 studies) and had differential retention < 10% (12 studies). The most common risk of bias was not clearly reporting blinding, ITT, or allocation concealment.

Efficacy of Integrated Interventions

Figure 2 presents the aggregated effect sizes for the nine outcomes related to HIV transmission risk, HIV care engagement, and medication adherence. Overall, PLWH receiving integrated interventions were significantly less likely than comparison participants to report sex without condoms. The intervention effects on HIV medication adherence behavior and undetectable viral load approached statistical significance. No significant

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intervention effects were observed for number of sex partners, STD, needle sharing, injection drug use, retention in HIV care, and being on ART.

Heterogeneity, Sensitivity Tests, and Publication Bias

As seen in Figure 2, four out of nine outcomes (i.e., sex without condoms, number of sex partners, medication adherence, undetectable viral load) had significant Q statistics or a moderate to high level of heterogeneity across studies ($I^2 > 50$). Sensitivity tests did not reveal any single study that exerted influence on the overall effect size for the majority of outcomes, except for medication adherence behavior. Excluding either one of the two studies [33, 39] made the overall intervention effect on the medication adherence behavior significant (OR = 1.48, 95% CI = 1.11, 1.97, p = 0.007 when removed [39]; OR = 1.44, 95% CI = 1.04, 1.98, p = 0.028 when removed [33]). However, neither study significantly reduced the overall heterogeneity. Additional sensitivity tests using the longest follow-ups when data were available did not significantly change the findings for any of the outcomes reported in Figure 2.

Based on the inspection of funnel plots and the linear regression tests, there was no evidence that our effect-size estimates for sex without condoms, medication adherence behavior, and undetectable viral load were influenced by non-inclusion of studies with non-significant findings.

Stratified Analysis

The results of stratified analyses for sex without condoms, medication adherence behavior, and undetectable viral load are presented in Table 2. When comparing intervention groups to comparison groups, significant intervention effects on at least two of three outcomes were seen in RCTs that were tailored to individual needs (for all three outcomes), delivered one-on-one (for sex without condoms and undetectable viral load), delivered in settings where PLWH receive services or care (for sex without condoms and medication adherence), had more than 4 sessions (for sex without condoms and medication adherence), had lower risk of bias (for sex without condoms and undetectable viral load), and used standard of care or wait list control (for sex without condoms and undetectable viral load). The Q_B statistics showed that several (but not all) intervention and study design characteristics remained statistically significant.

Discussion

This meta-analysis is the first to focus on integrated interventions for PLWH. Our findings show that integrated interventions are effective in reducing sex without condoms and potentially improve medication adherence behavior and undetectable viral load. The overall intervention effects on sex without condoms (OR, 0.74), medication adherence (OR, 1.35), and undetectable viral load (OR, 1.46) observed in this meta-analysis were comparable to the magnitude of effect sizes observed in previously published meta-analyses of RCTs for PLWH (sex without condoms: OR, 0.57 [8]; sex without condoms with at-risk partners: OR, 0.79 [11]; medication adherence: OR, 1.50 [16]; undetectable viral load: OR, 1.25 [16]). Results indicate no evidence that integrated interventions have effects on changing the number of sex partners, STD, needle sharing, injection drug use, retention in HIV care, or

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being on ART. The lack of evidence on these outcomes might imply that some behaviors are more difficult to change [9, 13, 14]. Alternatively, addressing multiple behavioral targets simultaneously may dilute the intervention effect on some of these outcomes, especially when the problem behaviors do not share common influencing factors that the interventions were intended to address. Due to few studies evaluating the outcomes that show null results, the findings need to be reassessed when additional data become available.

Aside from overall intervention effects, stratified analyses indicated several patterns that deserve attention. The effect sizes tended to be significant in interventions that were tailored to individual needs, delivered one-on-one, or delivered in settings where PLWH receive services or care. These findings corroborate previous meta-analysis findings on sexual risk behavior [8] and the recently released recommendations for HIV prevention with adults and adolescents with HIV in the United States by CDC, HRSA and NIMH [3]. Additionally, studies using standard of care or wait list control were more likely than studies using demand or attention control to show stronger intervention effects on sex without condoms and undetectable viral load. For HIV-related comparison groups, using variations of the interventions as comparison groups may greatly reduce the ability to detect intervention effects [42]. Using a standardized comparison arm that the HIV prevention field could agree upon as a prevention standard can facilitate comparing intervention effects across studies.

Our findings must be viewed within the context of the limitations of the available evidence and point to further research needs. While interventions were designed for PLWH and some specifically targeted subgroups of PLWH, there were a limited number of studies to further examine which intervention strategies work best for specific groups. Given that MSM and transgender women are disproportionately affected by HIV [1], it is important to further evaluate whether the strategies identified here work well within these groups and to determine what additional strategies may be effective in improving prevention and care outcomes for these most affected groups. Another limitation is that not all included studies clearly reported blinding, ITT, or allocation concealment. Improving reporting of RCTs by following the CONSORT statement [43] and implementing strategies to reduce the risk of bias [44] would further facilitate evaluation of HIV prevention research. Similarly, improving reporting of serostatus of partners can provide better data for assessing seroadaptive strategies practiced by PLWH and determining the level of risk that sexual behaviors pose for HIV transmission. Self-reported outcomes, such as sex without condoms and medication adherence, may be open to socially desirable responding. This might contribute to the difference in effectiveness observed on different outcomes. Acknowledging the possibility of self-reported bias, many studies attempted to ensure confidentiality of data by using computer-assisted assessments. In addition, all studies had a comparison group and randomly assigned participants which may reduce the likelihood that impression management, the driver of socially desirable responding, influenced the intervention effect.

Our meta-analysis is intended to examine a fundamental question – are integrated interventions effective in improving prevention and care outcomes? Whether integrated interventions are more “optimal” than single-target interventions is an important question, but it is beyond the scope of this systematic review. From an experimental research point of view, a single-target intervention can inform what works for changing one behavior at a

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time. However, using single-target interventions to address multiple problem behaviors may require more resources (i.e., more sessions) and time. Integrated interventions, on the other hand, can be more practical and closer to the reality of regular programmatic practices in the field. There are a few important implementation questions to consider for better informing best practices: Would the implementation of integrated interventions yield more favorable prevention and care outcomes than the use of bundled single-target interventions? What contributes to the synergistic effects of integrated interventions that are not available in single-target interventions? What are the optimal ways to combine integrated interventions with biomedical and structural interventions to reach NHAS prevention and care goals [1]?

In conclusion, we found evidence of benefits of integrated interventions on some HIV transmission risk behavior and medication adherence outcomes for PLWH. Insufficient evidence was found for STD, needle sharing, injection drug use, and HIV care engagement partially because of a limited number of studies. When selecting integrated interventions for PLWH, prevention providers may consider the effective intervention strategies identified in this meta-analysis. How to incorporate integrated interventions with other combination HIV prevention strategies, such as biomedical and structural interventions, to reach the optimal HIV prevention and care outcomes among PLWH requires further research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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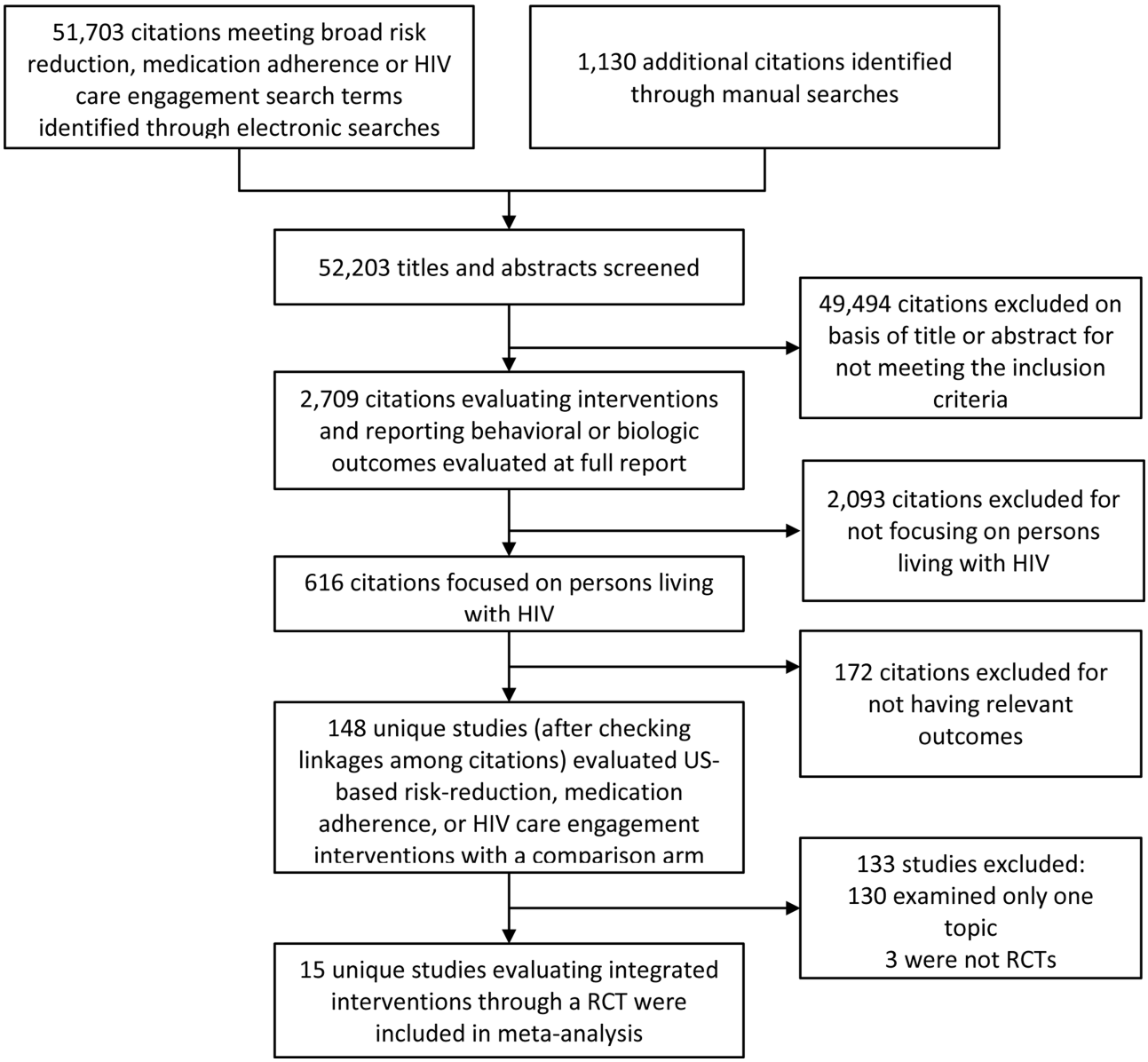

Figure 1.
PRISMA flow diagram of study selection process, 1996 to 2014

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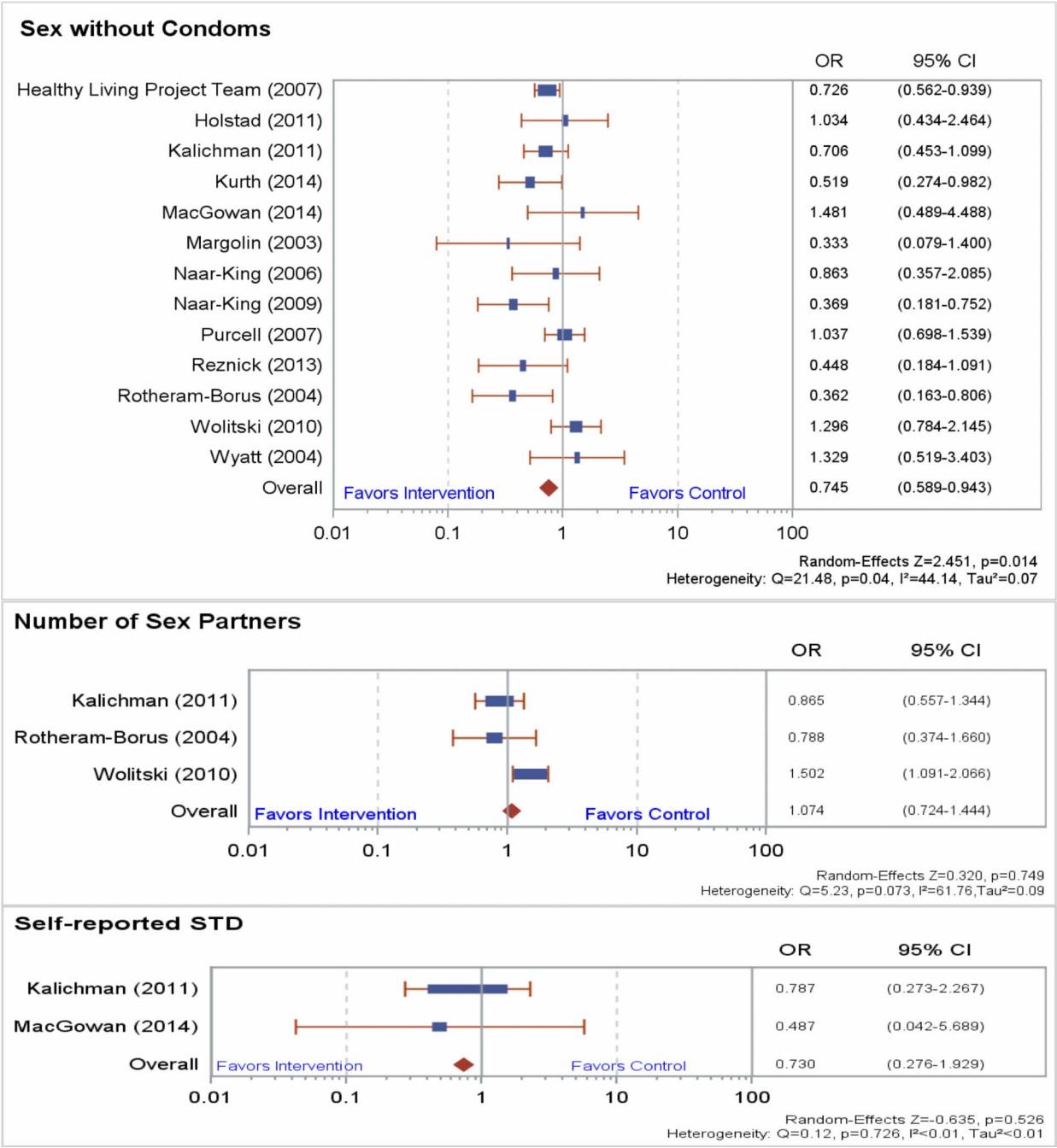

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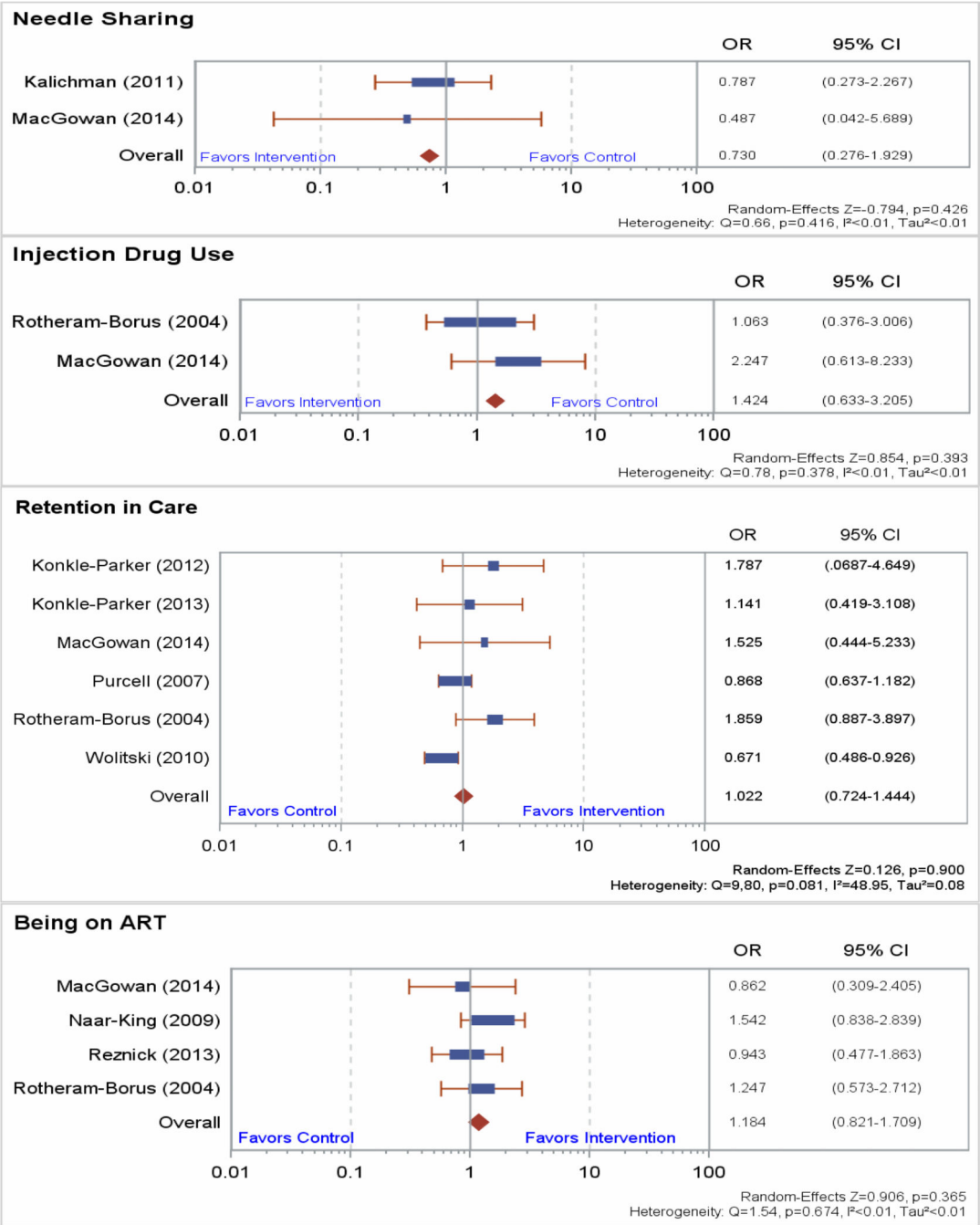

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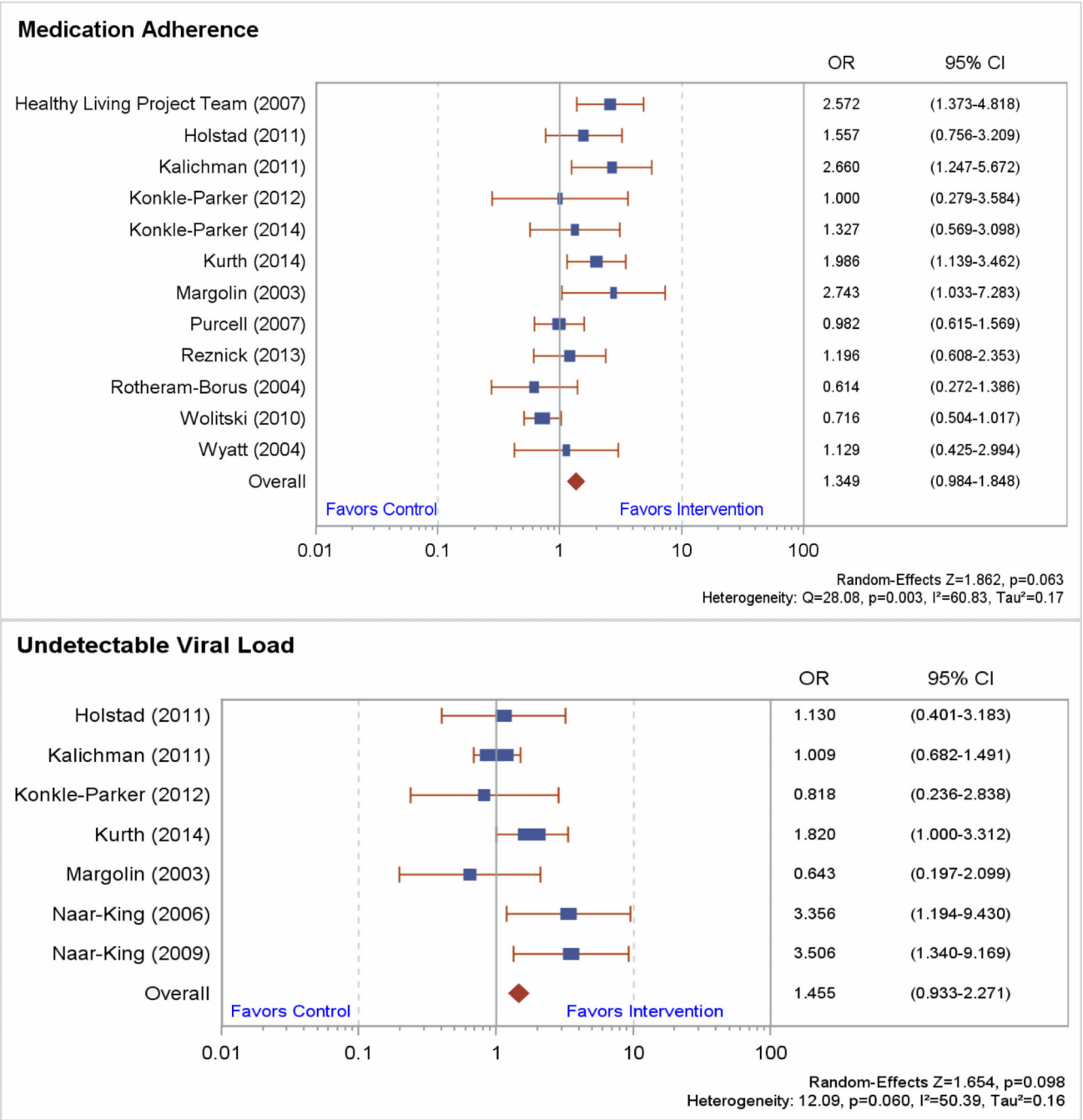

Figure 2.

Effects of Integrated Interventions on 9 outcomes: sex without condoms, number of sex partners, self-reported STD, needle sharing, injection drug use, retention in HIV care, being on ART, medication adherence and undetectable viral load. Abbreviation: OR, odds ratio; CI, confidence interval; ART, antiretroviral therapy.

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Table 1

Descriptive Characteristics of 15 Randomized Controlled Trials Evaluated Integrated Interventions for Persons Living with HIV (PLWH)

First Author, Year [Citation Number], Study Years	Targeted Behaviors	HIV-positive Subpopulation (Baseline Sample Size)	Comparison Group, Power Analysis to Estimate Sample Size (Yes/No)	Intervention Name (# of sessions; total hours), Intervention Level, Tailored/not Tailored to Individual, Deliverer, Service/Care Setting (vs. Other)
Holstad et al., 2011 [35], 2005-2008	• Risk reduction • Medication adherence	Women who were prescribed antiretroviral medicine (203)	Attention control, Power analysis: No	Group Motivational Interviewing (8;16) Group format, Tailored, delivered by health care provider or counselor, in service/care setting
Kalichman et al., 2011 [41], 2005-2009	• Risk reduction • Medication adherence	None (436)	Attention control, Power analysis: Yes	In the Mix (7;12) One-on-one & group format, Not Tailored, delivered by trained Facilitator, in service/care setting
Konkle-Parker et al., 2012 [27], 2005-2006	• HIV care engagement • Medication adherence	Clinic patients starting or restarting antiretroviral medicine (56)	Standard of care, Power analysis: No	Pilot study of an HIV medication adherence intervention (8;3) One-on-one delivery, Tailored, delivered by trained facilitator, in service/care setting
Konkle-Parker et al., 2014 [28], 2009-2011	• HIV care engagement • Medication adherence	Clinic patients with medication or visit adherence problems (100)	Standard of care, Power analysis: No	CLIMB: Cornerstones of Life: Information, Motivation, Behavioral Skills (8;4) One-on-one delivery, Tailored, delivered by trained facilitator, in service/care setting
Kurth et al., 2014 [29], 2006-2007	• Risk reduction • Medication adherence	Clinic patients who were prescribed antiretroviral medicine (240)	Standard of care, Power analysis: Yes	CARE+: Computer Assessment & Rx Education for HIV-positive people (4;2) One-on-one delivery, Tailored, delivered by computer, in service/care Setting
MacGowan et al., 2014 [37], 2008-2009	• Risk reduction • HIV care engagement • Medication adherence	Inmates reentering the community (73)	HIV demand control, Power analysis: No	POST: Positive Transitions (6;9) One-on-one delivery, Not Tailored, Delivered by trained facilitator, in other setting (e.g., prison, community)
Margolin et al., 2003 [30], 1997-2001	• Risk reduction • Medication adherence	Clinic patients who were Injection drug users in methadone maintenance treatment (90)	HIV demand control, Power analysis: No	HHRP+: HIV+ Harm Reduction Program (48;minimum of 96) One-on-one and & group format, Not Tailored, delivered by health care provider or counselor, in service/care setting
Naar-King et al., 2006 [32], NR	• Risk reduction • Medication adherence	Clinic patients who were adolescents aged 16-25 years (65)	Standard of care, Power analysis: No	Healthy Choices pilot Study (4;4) One-on-one delivery, Tailored, delivered by health care provider or counselor, in service/care setting
Naar-King et al., 2009 [31], 2005-2007	• Risk reduction • Medication adherence	Clinic patients who were adolescents aged 16-24 years with medication adherence, substance abuse or sexual risk problems (205)	Standard of care, Power analysis: No	Healthy Choices (4;6) One-on-one delivery, Tailored, delivered by health care provider or counselor, in service/care setting
Healthy Living Project Team, 2007 [40], 2000-2004	• Risk reduction • Medication adherence	Unprotected sex with HIV-negative or status unknown partners (936)	Waitlist, Power analysis: Yes	Healthy Living Project (15;22.5) One-on-one delivery, Not Tailored, delivered by trained facilitator, in service/care setting
Purcell et al., 2007 [34], 2001-2004	• Risk reduction • HIV care engagement • Medication adherence	Injection drug users (966)	HIV demand control, Power analysis: Yes	INSPIRE: Interventions for Seropositive Injectors – Research and Evaluation (10;20) Group format, Not Tailored, delivered by trained facilitator, in other setting (e.g., research facility)

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First Author, Year [Citation Number], Study Years	Targeted Behaviors	HIV-positive Subpopulation (Baseline Sample Size)	Comparison Group, Power Analysis to Estimate Sample Size (Yes/No)	Intervention Name (# of sessions; total hours), Intervention Level, Tailored/not Tailored to Individual, Deliverer, Service/Care Setting (vs. Other)
Reznick et al., 2013 [38] NR	• Risk reduction • Medication adherence	Inmates reentering the community (151)	HIV demand control, Power analysis: No	Ecosystems-based intervention (2-18;NR) One-on-one & group format, Tailored, delivered by health care provider or counselor, in other setting (e.g., prison, community)
Rotheram-Borus et al., 2004 [33], 1999-2003	• Risk reduction • HIV care engagement • Medication adherence	Young substance abusers aged 16 to 29 years (175)	Waitlist, Power analysis: No	CLEAR: Choosing Life: Empowerment, Actions, Results (18;27) One-on-one delivery, Not Tailored, Delivered by health care provider or counselor, in other setting (e.g., coffee shops, community, parks, residences)
Wolitski et al., 2010 [39], 2004-2007	• Risk reduction • HIV care engagement • Medication adherence	Homeless or at severe risk of homelessness (644)	HIV demand control, Power analysis: Yes	Housing Assistance & HIV Prevention (case management + 2 HIV sessions;1.25) One-on-one delivery, Not Tailored, Delivered by trained facilitator, in other setting (e.g., housing project)
Wyatt et al., 2004 [36], NR	• Risk reduction • Medication adherence	Women with histories of childhood sexual abuse (147)	HIV demand control, Power analysis: No	Enhance Sexual Health Intervention (11;22) Group format, Not Tailored, delivered by trained facilitator, in other setting (e.g., research facility)

NR=not reported

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Table 2

Effects of Integrated Interventions on Sex without Condoms, Medication Adherence, and Viral Load–Stratified by Intervention and Study Characteristics

	Sex without Condoms		Medication Adherence		Undetectable Viral Load	
	k	**OR (95% CI)**	**k**	**OR (95% CI)**	**k**	**OR (95% CI)**
Overall	13	0.74 (0.59-0.94), p=0.01	12	1.35 (0.98-1.85), p=0.063	7	1.46 (0.93-2.27), p=0.098
Intervention characteristics						
Tailoring						
Individually-Tailored	5	0.57 (0.39-0.82), p=0.002	5	1.51 (1.09-2.10), p=0.013	5	1.91 (1.18-3.09)[a], p=0.009
Not Tailored	8	0.89 (0.58-1.36), p=0.214	7	1.32 (0.82-2.13), p=0.260	2	0.97 (0.67-1.40), p=0.850
Delivery						
One-on-one	7	0.69 (0.48-0.99), p=0.047	6	1.22 (0.72-2.07), p=0.470	4	2.12 (1.23-3.65)[a], p=0.007
Group	6	0.82 (0.60-1.12), p=0.207	6	1.46 (1.02-2.08)[b], p=0.040	3	0.98 (0.69-1.39), p=0.920
Intensity						
High (≥4 sessions)	9	0.76 (0.59-0.98), p=0.031	10	1.42 (1.04-1.94), p=0.029	4	0.97 (0.69-1.36), p=0.860
Low (<4 sessions)	4	0.69 (0.38-1.26), p=0.232	2	1.16 (0.43-3.16), p=0.770	3	2.38 (1.51-3.75)[a], p=0.000
Deliverer						
Health care provider/Counselor	6	0.52 (0.35-0.76), p=0.001	4	1.29 (0.75-2.22), p=0.365	4	1.78 (0.80-3.94), p=0.156
Trained Staff	6	0.92 (0.72-1.17), p=0.477	7	1.30 (0.84-2.02), p=0.243	2	0.99 (0.68-1.44), p=0.957
Setting						
Service or HIV Care	7	0.68 (0.56-0.82), p=0.000	7	1.99 (1.50-2.65)[a], p=0.000	7	1.46 (0.93-2.27), p=0.098
Other	6	0.89 (0.58-1.36), p=0.583	5	0.84 (0.66-1.07), p=0.157	0	---
Study Design Characteristics						
Risk of Bias						
Low Risk (score ≥5)	8	0.74 (0.57-0.96), p=0.022	6	1.44 (0.90-2.29), p=0.130	4	1.91 (1.03-3.54), p=0.040
High Risk (score <5)	5	0.78 (0.42-1.44), p=0.406	6	1.25 (0.84-1.87), p=0.270	3	0.87 (0.45-1.68), p=0.670
Power Analyses						
Conducted	5	0.82 (0.63-1.07), p=0.150	5	1.50 (1.86-2.60), p=0.150	2	1.30 (0.73-2.29), p=0.380
Not Conducted/Not Reported	8	0.65 (0.42-0.99)[a], p=0.390	7	1.24 (0.90-1.71), p=0.190	4	1.56 (0.77-3.14), p=0.210
Control Group						

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	Sex without Condoms		Medication Adherence		Undetectable Viral Load	
	k	**OR (95% CI)**	**k**	**OR (95% CI)**	**k**	**OR (95% CI)**
Standard-of-Care or Waitlist	5	0.57 (0.42-0.79)[a], p=0.001	5	1.45 (0.87-2.41), p=0.160	4	2.12 (1.23-3.66)[a], p=0.007
Other	8	0.93 (0.70-1.22), p=0.571	7	1.28 (0.87-1.90), p=0.210	3	0.98 (0.69-1.39), p=0.920

K, number of studies

[a] $p<0.05$ for between-group effect

[b] This finding is mainly driven by studies with both one-on-one and group format (OR=1.95, 95% CI=1.10, 3.43, p=0.020, k=3)