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A MIXED-METHODS APPROACH TO SYNTHESIZING EVIDENCE ON MEDIATORS OF INTERVENTION EFFECTS

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Abstract

Greater understanding of the mechanisms (mediators) by which behavioral change interventions work is critical to developing theory and refining interventions. Although systematic reviews have been advocated as a method for exploring mediators, this is rarely done. One challenge is that intervention researchers typically test only two paths of the mediational model: the effect of the intervention on mediators and on outcomes. We addressed this challenge by drawing information not only from intervention studies but also from observational studies, which provide data on associations between potential mediators and outcomes. We also reviewed qualitative studies of participants' perceptions of why and how interventions worked. Using data from intervention ($n=37$) and quantitative observational studies ($n=55$), we conducted a meta-analysis of the mediation effects of eight variables. Qualitative findings ($n=6$) contributed to more in-depth explanations for findings. The methods used have potential to contribute to understanding of core mechanisms of behavioral change interventions.

Keywords

systematic review; mediation analysis; meta-analysis; antiretroviral therapy; treatment adherence

Systematic reviews of complex, behavioral change interventions are key to summarizing evidence on their effectiveness. Effectiveness reviews provide little guidance, however, on the mechanisms or mediators by which interventions effect change and achieve desired outcomes, information that is central to the theory underlying the intervention (Green & Glasgow, 2006; Hawe, Shiell, & Riley, 2004). Synthesizing evidence on the mechanisms by which behavioral change interventions work could contribute to building theory and further refining interventions. To address this need, we developed a mixed-methods approach to

systematically reviewing the literature to synthesize findings on the mechanisms that are responsible for the effects of behavioral change interventions. We used as our test case interventions to improve adherence to antiretroviral therapy (ART) in adults with HIV/AIDS.

CHALLENGES IN IDENTIFYING AN INTERVENTION'S CORE MECHANISMS

Researchers who have systematically reviewed the findings of studies testing ART adherence have found considerable variation in the effects of interventions across studies (e.g., Amico, Harman, & Johnson, 2006), and yet their reviews provide only limited evidence to explain this variation. One approach reviewers have taken to identify the factors make some interventions more effective than others has been to assess the effects of the different strategies used, such as provision of didactic information, interactive discussions, and external reminders (Rueda et al., 2006; Simoni, Pearson, Pantalone, Marks, & Crepaz, 2006). However, the actual strategies delivered to participants in a study are not always clear. Behavioral change interventions are often complex, with multiple and flexible strategies (Rychetnik, Frommer, Hawe, & Shiell, 2002; van Dulmen et al., 2007). They may be tailored to the preferences and needs of subgroups, or individualized to the needs of each person. As a result, interveners deliver different components or deliver components differently across participants. Alternatively, many researchers take a “shot gun” approach, designing interventions with multiple strategies with the goal of hitting at least some of participants’ needs (Sandelowski, Voils, Chang, & Lee, 2009).

Recently, scholars have advocated identifying an intervention’s “core mechanisms” or “core elements” as an approach to identifying those components of an intervention that are responsible for its effects (Hawe, Shiell, & Riley, 2004; McKleroy et al., 2006). Core elements are those mechanisms that are central to the theory underlying the intervention, the processes or mediators by which the intervention effected change and achieved the desired outcomes (McKleroy et al., 2006). In previous reviews of ART adherence interventions, authors have broadly categorized interventions according to their overall theoretical approach, most commonly as cognitive, behavioral, and/or affective (e.g., Cote & Godin, 2005; Simoni et al., 2006). Each of these approaches posits that interventions improve adherence through their effects on a range of different mediators such as coping, knowledge, belief, and self-efficacy (cognitive interventions), barriers and facilitators to behavior change (behavioral interventions), and emotional wellbeing and social support (affective interventions; Munro, Lewin, Swart, & Volmink, 2007; van Dulmen et al., 2007). Although reviewers of ART adherence interventions have grouped interventions according to theoretical constructs, they have not focused their reviews on the evidence in support of the mediators associated with those constructs. As a result, we have only a limited understanding of the mechanisms by which different interventions affect adherence, knowledge that is central to building theory and developing more effective interventions.

Systematic reviews have long been advocated as a method for exploring mediators (Shadish, 1996), but few have done so (Finney, 2009). There are three major challenges to synthesizing evidence on mediation. Synthesis of findings on mediation ideally would involve meta-analysis of the results of within-study analyses of mediation. Yet, because researchers infrequently include mediation analysis in their study designs, within-study analyses are not available. A second challenge is that intervention researchers only rarely report the full range of data necessary to calculate mediation. The mediational model is often depicted as a triangle with relationships among interventions, mediators, and outcomes (Figure 1). Establishing mediation involves assessing associations across all three sides of the triangle: the intervention’s effect on the mediator (path a), the mediator’s effect on the outcome (path b), and the intervention’s effect on the outcome (path c; MacKinnon,

Fairchild, & Fritz, 2007). However, intervention researchers typically test only two paths of the mediational model: the effect of the intervention on the mediator (path a) and on the outcome (path c). Therefore, there is insufficient information to completely analyze a mediational model. A third challenge is the inconsistency across studies in the way researchers conceptualized and measured potential mediators. To address these challenges, we drew findings not only from intervention studies but also from observational studies, which provide data on associations between potential mediators and outcomes (path b). We also reviewed qualitative studies of participants' and interveners' perceptions of why and how interventions worked to further illuminate the ways that mediators functioned to affect outcomes (Miller, Druss, & Rohrbaugh, 2003).

PURPOSE

Our purpose in this paper is to describe a mixed-methods approach to synthesize findings on core mechanisms, using as our test case interventions to improve adherence to ART in adults with HIV/AIDS. We developed this approach in the course of a larger study the purpose of which was to develop methods for synthesizing qualitative and quantitative research. The method is novel because it integrates findings from intervention, quantitative observational, and qualitative studies. We integrated findings from across studies to identify potential mediators of ART adherence, synthesize evidence on potential mediators' relationships to interventions and adherence, and summarize findings on participants' perceptions of why and how interventions worked.

METHODS

We used a mixed-methods approach to integrate findings from reports of intervention, quantitative observational, and qualitative studies with the aim of synthesizing the evidence in support of potential mediators of the effects of interventions on adherence. For quantitative findings, we used meta-analysis techniques to synthesize findings specific to each relationship in the mediational model (Figure 1) and to test mediation effects. We identified themes in qualitative findings that related to participant and intervener perceptions of the mechanisms by which interventions affected adherence and used these findings to add further depth to the findings from the meta analysis.

Literature search

We searched for publications reporting the findings from three types of studies of ART adherence among adults in the US, including reports of: (a) intervention studies of the effects of an intervention on adherence and/or on potential mediators of adherence; (b) quantitative observational studies (i.e., cross sectional surveys) addressing correlations between potential mediators and adherence; and (c) qualitative studies of participants' perceptions of an intervention they received. We searched Academic Search Premier, CINAHL, PubMed, PsychINFO, and Sociological Abstracts for the time period 2002 to August 2009 using search terms related to HIV, antiretroviral treatment, and adherence. We included only studies conducted in the US with adult participants with none of the following characteristics that may alter the adherence experience (incarceration, serious mental illness, pregnancy). Because we are interested in developing methods for synthesizing complex behavioral change interventions, we included intervention studies that tested interventions involving repeated interactions between interveners and participants. All included intervention studies tested either teaching/counseling or directly observed therapy interventions; we excluded studies that simply tested the effects of a device (e.g., electronic reminder), journaling, or medications (e.g., antidepressant) and involved minimal interaction between intervener and participant. (Further detail on search terms and inclusion criteria are available on request to the corresponding author). Because of the volume of reports of

quantitative observational studies and because of our primary study focus on developing methods (as opposed to reporting the results of a comprehensive review of literature), we limited our search for this type of study to more recent publications and began that search at 2005.

We identified 37 relevant reports of ART intervention studies, 55 reports of quantitative observational studies, and 4 reports of qualitative studies that addressed participants' perceptions of ART adherence interventions. Qualitative data on participants' perceptions also were included from two intervention studies in which researchers asked participants or interveners open-ended questions about the intervention, bringing the number of studies with qualitative findings to six. Tables 1–3 present descriptive statistics for studies included in the review.

Data extraction

Data extraction was conducted by two members of the research team with differences in coding resolved by consensus. (The data extraction tool is available from the first author on request). The data extracted from the study reports included sample size, sample demographics, potential mediators, quantitative data on the relationships between potential mediators and adherence, intervention effects on ART adherence and on potential mediators of adherence, qualitative data on participants' and interveners' perceptions of why and how interventions improved adherence.

A potential mediator was conceptualized as any measured variable (or qualitative finding) that plausibly could be affected by an intervention and also have an effect on adherence. Ideally, we would have grouped studies according to their underlying theories and explored mediators within each of those groupings. However, only a minority of intervention researchers report data on potential mediators and even fewer identify theories. Therefore, to make the most of the data available, we combined all interventions into a single group.

Identifying potential mediators

For each of the three types of reports, the potential mediators extracted were reviewed by one of three investigators who independently grouped factors that were conceptually similar to identify and define a parsimonious list of potential mediators. A fourth investigator reviewed and integrated the three lists in consultation with the study team to create the list of eight potential mediators shown in Table 4 with their definitions. This list includes all mediators for which data were available in at least two reports of observation or intervention studies. As detailed in table 1, only 13 of the intervention studies included data on potential mediators.

Analysis of quantitative data

We used meta-analysis techniques to synthesize findings specific to each relationship in the mediational model (Figure 1) and to test mediation effects.

Synthesizing evidence on mediation—We used meta-analysis techniques to estimate effect sizes and test mediation effects. All calculations were performed using the Comprehensive Meta-Analysis (CMA) version 2 software (Borenstein, Hedges, Higgins, & Rothstein, 2005).

Calculating effect sizes—Effect sizes for the relationships between potential mediators and adherence (path b) were computed from the observational studies. The size of the effect of the interventions on potential mediators (path a) and on adherence (path c) were computed from the intervention studies (see Figure 1). Both sets of studies were required, as

none of the reports of intervention studies contain analyses of the relationship between potential mediators and adherence (path b). When a report included more than one measure of a construct (e.g., adherence measured by self report and pill counts), we first calculated an effect size for each measure and then obtained the average, which was used as the effect size for that particular construct (Durlak & Lipsey, 1991). For intervention studies with a control group, the effect size was the standardized difference between group means (Robinson, Berman, & Neimeyer, 1990), as this was easily calculable from the reported means and standard deviations. For within-subject studies, where no control group was employed, the effect size was the standardized difference between pre- and post-treatment means. If studies measured intervention effects at multiple time points, we used the earliest post-intervention measure to reflect the effect of the intervention. When available, we used the results from an intent-to-treat approach over a per-protocol approach.

From the observational studies, we calculated effect sizes for bivariate and multivariable relationships separately. Although many meta-analyses have included bivariate results only, effect sizes derived from bivariate relationships tend to be artificially large in non-controlled study settings (Voils, Crandell, Chang, Leeman, & Sandelowski, in press). Therefore, we conducted analyses separately for bivariate and multivariable results and compared them, whenever possible.

We used CMA to pool the effect size as a weighted mean, with the weight equal to the inverse variance of each effect size. The variance of the effect size is smaller in larger sample studies, allowing them to contribute more to the pooled effect size (Hedges & Olkin, 1985).

Analyzing mediation effects—Mediation was tested using the Sobel test (Preacher & Hayes, 2004; Sobel, 1982), which (like many other tests of mediation) requires regression coefficients and their standard errors. Specifically, we needed the coefficient and standard error for the simple regression describing the effect of the intervention on the mediator (path a), and for the multiple regression describing the effect of the mediator on adherence, controlling for the intervention. To compute the regression coefficients and standard errors, we first used CMA to obtain all pooled effect sizes as correlation coefficients (r). This yielded a 3×3 correlation matrix for the relationship among intervention, each mediator, and adherence.

The correlation coefficients and the sample size are sufficient information to compute the desired standardized regression coefficients and their standard errors (Premack & Hunter; Shadish, 1996). The correlation coefficients among all three variables were readily available, but the sample size appropriate to compute the standard errors was not as clear. In meta-analytic mediational modeling, it is not uncommon for the sample size in each path to vary because it is obtained from a separate meta-analysis; the number of studies that contribute to each meta-analysis also varies. Yet, the use of a single sample size to estimate the standard errors of the regression coefficients for all three paths is important to retain the validity of the Sobel test. To obtain a single sample size for the three relationships, we followed the recommendation of Viswesvaran and Ones (1995) and used the harmonic mean of the sample sizes across the three different relationships. A harmonic mean is always equal to or less than an arithmetic mean and thus provides relatively conservative estimates, yet not as conservative as using the lowest N in a pairwise deletion matrix (e.g., Albarracín et al., 2005).

The regression estimates and standard errors are then entered into the Sobel equation, which yields a z -score that can be compared to a normal distribution to test (using a 2-tailed test)

$$z = \frac{\hat{\beta}_a \times \hat{\beta}_b}{\sqrt{\hat{\beta}_b^2 \times s_a^2 + \hat{\beta}_a^2 \times s_b^2}}$$

for significance of the mediation effect: $\sqrt{\hat{\beta}_b^2 \times s_a^2 + \hat{\beta}_a^2 \times s_b^2}$, where $\hat{\beta}_a$ is the regression coefficient for path a, and $\hat{\beta}_b$ is the regression coefficient for path b, controlling for the intervention. The quantities s_a and s_b are the corresponding standard errors.

Homogeneity analysis and regression model testing—We used random effects meta-regression (Hunter & Schmidt, 2004) to examine potential sources of heterogeneity across the different types of studies used in each path of the model (i.e., intervention studies for the paths a and c, and observational studies for path b). In the 37 intervention studies, none of the intervention characteristic covariates examined (design, setting, delivery mode, dose, duration, and percentage of dropouts) explained a significant proportion of variance in effect sizes across studies ($Q=94.209, p<.001$). Therefore, we concluded that variability in effect sizes derived from random differences between studies and employed random effects models for all meta-analyses.

Analysis of qualitative data—From the reports of qualitative studies, we extracted participants' descriptions of what they valued most about the ART adherence intervention and participants' and interveners' perceptions of why and how the intervention improved adherence. Two reviewers independently extracted key findings from each of the six reports and then created thematic statements representing the findings across these reports (Sandelowski & Barroso, 2007). Discrepancies were resolved by consensus. The identified themes were then compared and contrasted to findings from the meta-synthesis to provide greater depth and nuance to findings from the meta-analysis, and to identify areas of congruence and discrepancy across the qualitative and quantitative findings.

RESULTS OF ANALYSIS

Evidence of mediation

Table 5 presents the results of estimates of mean correlations from the random effects model for all available relationships extracted from the intervention and observational studies.

Interventions' effects on potential mediators

Authors of 13 of the 37 reports of intervention studies examined the effect of the intervention on intermediate factors that could potentially mediate the intervention's effects. Overall the interventions had small effects on the potential mediators (ranging from $r = -.22$ to $.24$), with significant effects on three of the eight potential mediators: self efficacy, knowledge, and positive coping.

Mediators' effects on adherence—In the bivariate analyses from the observational studies, all potential mediators except knowledge showed significant relationships with adherence. In the multivariable analyses, all potential mediators showed significant relationships with adherence with the exception of positive coping and knowledge (Table 5).

Interventions' effects on outcomes—Overall, the 37 interventions we reviewed had a small effect ($r=.18$) on adherence, with individual effect size estimates ranging from $.12$ to $.23$.

Analysis of mediation effects—Using methods recommended by MacKinnon et al. (2002), we performed the Sobel test for the eight potential mediators to examine whether they mediated the relationship between interventions and adherence. Table 6 presents the results of the Sobel test for both bivariate and multivariable results. Using bivariate results,

five of the potential mediators were significant: emotional wellbeing, drug/alcohol use, self-efficacy, knowledge, and healthcare provider. Only drug/alcohol use and self-efficacy remained significant in the multivariable results.

Participants' perceptions of why interventions worked

In all six reports of studies with findings on participants' perceptions of interventions, participants cited social support from the intervener as an important component of the intervention; in two studies, it was the most dominant theme (Bontempi, Burleson, & Lopez, 2004; Weiss et al., 2006). Participants particularly valued interveners' attention and concern. They also appreciated when interveners provided instrumental assistance such as communicating with healthcare providers (Bontempi et al., 2004; Weiss et al., 2006) and obtaining their medications (Garland et al., 2007). Participants noted the importance of social support from peers and others in their social networks (Berg, Raminanai, Greer, Harwood, & Safren, 2008; Bontempi et al., 2004; Weiss et al., 2006).

Participants valued the knowledge they gained (Adamian, Golin, Shain, & DeVellis, 2004; Bontempi et al., 2004; Parry et al., 2005; Weiss et al., 2006) and skills learned (Adamian et al., 2004; Berg et al., 2008; Weiss et al., 2006) through their participation in interventions. They also observed that the intervention changed their perceptions of their lives and the effects of HIV and ART medications on their health (Berg et al., 2008; Weiss et al., 2006), improved their emotional wellbeing (Parry et al., 2005), and provided them with cues to remind them to take their pills (e.g., pillboxes; Weiss et al., 2006).

DISCUSSION

The findings from the meta-analysis support the role of reducing drug/alcohol use and increasing self efficacy as mediators of the effects of interventions on ART adherence in HIV-positive adults. They also provide some support for a mediating role for emotional wellbeing and knowledge. The thematic synthesis of participants' experiences with HIV interventions further confirmed these findings. Although participants did not refer to intervention effects on drug/ alcohol use as something they valued, they did refer to the value of aspects of the other potential mediators supported by the meta-analysis, namely, intervention effects on skills learned (self-efficacy), emotional wellbeing, and knowledge.

Advantages to the proposed mixed-method approach

Because we extracted data from both intervention and quantitative observational studies, we were able to do a full meta-analysis of mediation. Intervention studies contributed the data needed to calculate the average size of the interventions' effects on the targeted outcome (adherence). They also provided data on the effects of interventions on a range of potential mediators. The quantitative observational studies contributed data on the association between potential mediators and the targeted outcome. We were able to synthesize this data to do a full analysis of mediation effects for eight potential mediators.

Each of the three types of studies added distinct contributions to our understanding of potential mediators. The observational studies included assessments of some potential mediators that were largely absent from the intervention studies (e.g., beliefs). The qualitative findings provided more in-depth explanations for discrepancies in findings across study types. Findings from both qualitative and quantitative observational studies indicated a strong relationship between social support and adherence. Yet, neither intervention studies nor the meta-analysis supported social support's role as a mediator. Findings from the qualitative data suggest a possible explanation for this discrepancy. When interviewed, participants in adherence programs were very specific about the source of social support the

programs offered: support from the individuals delivering the interventions. Yet when researchers measured their interventions' effects, they typically assessed changes in global social support.

Findings from the quantitative observational and qualitative studies identified avenues for future research that would not have been identified in a synthesis of only intervention studies. The findings from the observational studies indicate a strong correlation between adherence and three variables that the interventions reviewed did not significantly affect overall (beliefs, social support, healthcare provider). Few of the intervention studies included measures of effects of interventions on these mediators, which may account, in part, for the lack of significance; beliefs and healthcare provider were each measured in only two studies. These findings suggest the potential value of including these variables as mediators in future intervention studies. Findings from all three types of studies added greater depth to understanding the mechanisms by which ART adherence interventions have their effect.

Challenges to the proposed mixed-method approach

We encountered several challenges in our use of the mixed-methods approach described in this review. Researchers reported on a diversity of potential mediators, and the review required that we merge these variables into broad categories. Findings from the meta-analysis may underestimate the overall effects of potential mediators due to the broad operationalization of the variables in studies and the merging of more tightly operationalized variables into broad categories for the purposes of the review. Social support offers a good example. In most studies, it was operationalized broadly as general social support. Yet, in one observational study, researchers addressed the effects of social support from family members and social support from partners and found that support from partners was associated with better adherence while support from other family members was associated with worse adherence (Hamilton, Razzano, & Nicole, 2007). Because our review included only the broad category of social support, we combined the findings from this study into a single measure, thereby losing important differences in the effects of social support from different sources. The need to group variables is a shortcoming of any systematic review. Yet, given the variation in studies in common domains of research, it is a shortcoming without which no review could be accomplished.

A central goal in assessing mediation is to contribute to theory development. This goal was challenged by the largely atheoretical nature of the research reviewed. Only a minority of authors identified the underlying theory guiding the variables they chose to measure. To address this challenge, we inferred theoretical constructs and categorized mediators accordingly. This workaround allowed us to synthesize existing data and begin to identify potential mediators that were supported by data from multiple studies.

We also were limited by the small sample sizes for several of the mediators reviewed. Limits resulting from small sample sizes were further exacerbated by our decision to only review quantitative observational studies that have been published since 2005. The review's finding that some variables were not supported by the evidence was likely a result of these small sample sizes. As a result, we cannot make claim about the absence of mediating effects for the variables for which we identified no significant relationships. This limitation is common to all reviews of the literature.

The review was further limited by the small number of studies of participant perspectives on how and why interventions work. Asking participants and interveners open-ended questions can tap into information not available through closed-ended measures. Through these open queries, researchers can assess the extent to which their interventions worked as posited or

through mechanisms they did not even anticipate. They also can begin to distinguish the intervention's essential from non-essential ingredients (Miller et al., 2003).

Conclusions

The mixed methods used in this review have potential to advance understanding of the mechanisms by which complex, behavioral interventions have their effects. We developed this approach in response to the lack of complete analyses of mediation in reports of research testing behavioral change interventions. The combination of meta-analysis of intervention and quantitative observational findings, and thematic synthesis of qualitative findings, offered a way more fully to mine methodologically diverse reports for this information.

To advance understanding of the theories underlying behavior change interventions, it is essential that researchers build mediator analysis into their study designs. Yet, few reports of intervention studies include such analyses. Accordingly, we developed an innovative approach to extract and synthesize findings from a broad base of prior research that included both qualitative and quantitative observational and intervention studies. The methods used could be applied to a broad range of behavior change interventions. Identifying the core mechanisms of interventions provides evidence in support of underlying intervention theories, a critical step in further refining and strengthening interventions to improve adherence.

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References

- Adamian MS, Golin CE, Shain LS, DeVellis B. Brief motivational interviewing to improve adherence to antiretroviral therapy: development and qualitative pilot assessment of an intervention. *AIDS Patient Care STDS*. 2004; 18(4):229–238. [PubMed: 15142353]
- Albarracin D, Gillette JC, Earl AN, Glasman LR, Durantini MR, Ho MH. A test of major assumptions about behavior change: a comprehensive look at the effects of passive and active HIV-prevention interventions since the beginning of the epidemic. *Psychological Bulletin*. 2005; 131(6):856–897. [PubMed: 16351327]
- Amico KR, Barta W, Konkole-Parker DJ, Fisher JD, Cornman DH, Shuper PA, et al. The Information-Motivation-Behavioral Skills Model of ART Adherence in a Deep South HIV+ Clinic Sample. *AIDS and Behavior*. 2009; 13(1):66–75. [PubMed: 17876697]
- Amico KR, Harman JJ, Johnson BT. Efficacy of antiretroviral therapy adherence interventions: a research synthesis of trials, 1996 to 2004. *Journal of Acquired Immune Deficiency Syndrome*. 2006; 41(3):285–297.
- Amico KR, Konkole-Parker DJ, Cornman DH, Barta WD, Ferrer R, Norton WE, et al. Reasons for ART non-adherence in the Deep South: Adherence needs of a sample of HIV-positive patients in Mississippi. *AIDS Care*. 2007; 19:1210–1218. [PubMed: 18071964]
- Arnsten JH, Li X, Mizuno Y, Knowlton AR, Gourevitch MN, Handley K, et al. Factors associated with antiretroviral therapy adherence and medication errors among HIV-infected injection drug users. *Journal of Acquired Immune Deficiency Syndromes*. 2007; 46(Suppl 2):S64–71. [PubMed: 18089986]

- Atkinson JS, Schonnesson LN, Williams ML, Timpson SC. Associations among correlates of schedule adherence to antiretroviral therapy (ART): a path analysis of a sample of crack cocaine using sexually active African-Americans with HIV infection. *AIDS Care*. 2008; 20(2):253–262. [PubMed: 18293137]
- Barclay TR, Hinkin CH, Castellon SA, Mason KI, Reinhard MJ, Marion SD, et al. Age-associated predictors of medication adherence in HIV-positive adults: health beliefs, self-efficacy, and neurocognitive status. *Health Psychology*. 2007; 26(1):40–49. [PubMed: 17209696]
- Barnett PG, Sorensen JL, Wong W, Haug NA, Hall SM. Effect of incentives for medication adherence on health care use and costs in methadone patients with HIV. *Drug & Alcohol Dependence*. 2009; 100(1–2):115–121. [PubMed: 19054631]
- Beach MC, Keruly J, Moore RD. Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV? *Journal of General Internal Medicine*. 2006; 21:661–665. [PubMed: 16808754]
- Berg C, Raminanai S, Greer J, Harwood M, Safren S. Participants' perspectives on cognitive-behavioral therapy for adherence and depression in HIV. *Psychotherapy Research*. 2008; 18:271–280. [PubMed: 18815979]
- Boarts JM, Sledjeski EM, Bogart LM, Delahanty DL. The differential impact of PTSD and depression on HIV disease markers and adherence to HAART in people living with HIV. *AIDS and Behavior*. 2006; 10(3):253–261. [PubMed: 16482405]
- Bontempi JM, Bureson L, Lopez MH. HIV medication adherence programs: the importance of social support. *Journal of Community Health Nursing*. 2004; 21(2):111–122. [PubMed: 15123440]
- Borenstein, M.; Hedges, L.; Higgins, J.; Rothstein, H. *Comprehensive Meta-analysis Version 2*. Englewood, NJ: Biostat; 2005.
- Bottonari KA, Roberts JE, Ciesla JA, Hewitt RG. Life stress and adherence to antiretroviral therapy among HIV-positive individuals: A preliminary investigation. *AIDS Patient Care and STDs*. 2005; 19:719–727. [PubMed: 16283832]
- Braithwaite RS, McGinnis KA, Conigliaro J, Maisto SA, Crystal S, Day N, et al. A temporal and dose-response association between alcohol consumption and medication adherence among veterans in care. *Alcoholism, Clinical and Experimental Research*. 2005; 29(7):1190–1197.
- Cardarelli R, Weis S, Adams E, Radaford D, Vecino I, Munguia G, et al. General health status and adherence to antiretroviral therapy. *Journal of the International Association of Physicians in AIDS Care (Chicago, Ill: 2002)*. 2008; 7(3):123–129.
- Cha E, Erlen JA, Kim KH, Sereika SM, Caruthers D. Mediating roles of medication-taking self-efficacy and depressive symptoms on self-reported medication adherence in persons with HIV: a questionnaire survey. *International Journal of Nursing Studies*. 2008; 45(8):1175–1184. [PubMed: 17949723]
- Chander G, Lau B, Moore RD. Hazardous alcohol use: A risk factor for non-adherence and lack of suppression in HIV infection. *Journal of Acquired Immune Deficiency Syndromes*. 2006; 43(4):411–417. [PubMed: 17099312]
- Collier AC, Ribaud H, Mukherjee AL, Feinberg J, Fischl MA, Chesney M. A randomized study of serial telephone call support to increase adherence and thereby improve virologic outcome in persons initiating antiretroviral therapy. *The Journal of Infectious Diseases*. 2005; 192(8):1398–1406. [PubMed: 16170757]
- Cook PF, McCabe MM, Emiliozzi S, Pointer L. Telephone nurse counseling improves HIV medication adherence: An effectiveness study. *The Journal of the Association of Nurses in AIDS Care*. 2009; 20(4):316–325. [PubMed: 19576548]
- Cote JK, Godin G. Efficacy of interventions in improving adherence to antiretroviral therapy. *International Journal of STD and AIDS*. 2005; 16(5):335–343. [PubMed: 15949060]
- Cruess DG, Minor S, Antoni MH, Millon T. Utility of the Millon Behavioral Medicine Diagnostic (MBMD) to predict adherence to highly active antiretroviral therapy (HAART) medication regimens among HIV-positive men and women. *Journal of Personality Assessment*. 2007; 89(3):277–290. [PubMed: 18001228]
- de Jong BC, Prentiss D, McFarland W, Machekano R, Israelski DM. Marijuana use and its association with adherence to antiretroviral therapy among HIV-infected persons with moderate to severe

- nausea. *Journal of Acquired Immune Deficiency Syndromes*. 2005; 38(1):43–46. [PubMed: 15608523]
- Dieckhaus KD, Odesina V. Outcomes of a multifaceted medication adherence intervention for HIV-positive patients. *AIDS Patient Care and STDs*. 2007; 21(2):81–91. [PubMed: 17328657]
- DiIorio C, McCarty F, DePadilla L, Resnicow K, Holstad MM, Yeager K, et al. Adherence to antiretroviral medication regimens: A test of a psychosocial model. *AIDS & Behavior*. 2009; 13(1):10–22. [PubMed: 17978868]
- DiIorio C, McCarty F, Resnicow K, McDonnell Holstad M, Soet J, Yeager K, et al. Using motivational interviewing to promote adherence to antiretroviral medications: a randomized controlled study. *AIDS Care*. 2008; 20(3):273–283. [PubMed: 18351473]
- DiIorio C, Resnicow K, McDonnell M, Soet J, McCarty F, Yeager K. Using motivational interviewing to promote adherence to antiretroviral medications: a pilot study. *The Journal of the Association of Nurses in AIDS Care*. 2003; 14(2):52–62. [PubMed: 12698766]
- Durlak JA, Lipsey MW. A practitioner's guide to meta-analysis. *American Journal of Community Psychology*. 1991; 19:291–332.
- Finney JW. Meta-analyses and the search for specific and common mediators of substance misuse intervention effects. *Addiction*. 2009; 104:716–718. [PubMed: 19413786]
- French T, Weiss L, Waters M, Tesoriero J, Finkelstein R, Agins B. Correlation of a brief perceived stress measure with nonadherence to antiretroviral therapy over time. *Journal of Acquired Immune Deficiency Syndromes*. 2005; 38(5):590–597. [PubMed: 15793371]
- Friedman MS, Marshal MP, Stall R, Kidder DP, Henny KD, Courtenay-Quirk C, et al. Associations between substance use, sexual risk taking and HIV treatment adherence among homeless people living with HIV. *AIDS Care*. 2009; 21(6):692–700. [PubMed: 19806485]
- Garland WH, Wohl AR, Valencia R, Witt MD, Squires K, Kovacs A, et al. The acceptability of a directly-administered antiretroviral therapy (DAART) intervention among patients in public HIV clinics in Los Angeles, California. *AIDS Care*. 2007; 19(2):159–167. [PubMed: 17364394]
- Golin CE, Earp J, Tien HC, Stewart P, Porter C, Howie L. A 2-arm, randomized, controlled trial of a motivational interviewing-based intervention to improve adherence to antiretroviral therapy (ART) among patients failing or initiating ART. *Journal of Acquired Immune Deficiency Syndrome*. 2006; 42(1):42–51.
- Gonzalez JS, Penedo FJ, Llabre MM, Duran RE, Antoni MH, Schneiderman N, et al. Physical symptoms, beliefs about medications, negative mood, and long-term HIV medication adherence. *Annals of Behavioral Medicine*. 2007; 34:46–55. [PubMed: 17688396]
- Graham J, Bennett IM, Holmes WC, Gross R. Medication beliefs as mediators of the health literacy-antiretroviral adherence relationship in HIV-infected individuals. *AIDS & Behavior*. 2007; 11(3):385–392. [PubMed: 17053858]
- Green LW, Glasgow RE. Evaluating the relevance, generalization, and applicability of research: issues in external validation and translation methodology. *Evaluation and the Health Professions*. 2006; 29(1):126–153.
- Gross R, Tierney C, Andrade A, Lalama C, Rosenkranz S, Eshleman SH, et al. Modified directly observed antiretroviral therapy compared with self-administered therapy in treatment-naïve HIV-1-infected patients: a randomized trial. *Archives of Internal Medicine*. 2009; 169(13):1224–1232. [PubMed: 19597072]
- Halkitis PN, Palamar J. A mediation model to explain HIV antiretroviral adherence among gay and bisexual men. *Journal of Gay & Lesbian Social Services*. 2006; 19:35–55.
- Halkitis PN, Kutnick AH, Slater S. The social realities of adherence to protease inhibitor regimens: substance use, health care and psychological states. *Journal of Health Psychology*. 2005; 10(4):545–558. [PubMed: 16014391]
- Hamilton MM, Razzano LA, Martin NB. The relationship between type and quality of social support and HIV medication adherence. *Journal of HIV/AIDS & Social Services*. 2007; 6:39–63.
- Hawe P, Shiell A, Riley T. Complex interventions: how “out of control” can a randomised controlled trial be? *British Medical Journal*. 2004; 328:1561–1563. [PubMed: 15217878]
- Hedges, LV.; Olkin, I. *Statistical methods for meta-analysis*. San Diego, CA: Academic Press; 1985.

- Hicks PL, Mulvey KP, Chander G, Fleishman JA, Josephs JS, Korthuis PT, et al. The impact of illicit drug use and substance abuse treatment on adherence to HAART. *AIDS Care*. 2007; 19(9):1134–1140. [PubMed: 18058397]
- Hinkin CH, Barclay TR, Castellon SA, Levine AJ, Durvasula RS, Marion SD, et al. Drug use and medication adherence among HIV-1 infected individuals. *AIDS & Behavior*. 2007; 11(2):185–194. [PubMed: 16897351]
- Holmes WC, Bilker WB, Wang H, Chapman J, Gross R. HIV/AIDS-specific quality of life and adherence to antiretroviral therapy over time. *Journal of Acquired Immune Deficiency Syndromes*. 2007; 46(3):323–327. [PubMed: 17846560]
- Holstad MK, Pace JC, De AK, Ura DR. Factors associated with adherence to antiretroviral therapy. *The Journal of the Association of Nurses in AIDS Care*. 2006; 17(2):4–15. [PubMed: 16800163]
- Holzemer WL, Bakken S, Portillo CJ, Grimes R, Welch J, Wantland D, et al. Testing a nurse-tailored HIV medication adherence intervention. *Nursing Research*. 2006; 55(3):189–197. [PubMed: 16708043]
- Horberg MA, Silverberg MJ, Hurley LB, Towner WJ, Klein DB, Bersoff-Matcha S, et al. Effects of depression and selective serotonin reuptake inhibitor use on adherence to highly active antiretroviral therapy and on clinical outcomes in HIV-infected patients. *Journal of Acquired Immune Deficiency Syndromes*. 2008; 47(3):384–390. [PubMed: 18091609]
- Hunter, JE.; Schmidt, FL. *Methods of meta-analysis: Correcting error and bias in research findings*. 2. Thousand Oaks, CA: Sage Publications; 2004.
- Ingersoll KS, Heckman CJ. Patient-clinician relationships and treatment system effects on HIV medication adherence. *AIDS and Behavior*. 2005; 9(1):89–101. [PubMed: 15812616]
- Johnson CJ, Heckman TG, Hansen NB, Kochman A, Sikkema KJ. Adherence to antiretroviral medication in older adults living with HIV/AIDS: a comparison of alternative models. *AIDS Care*. 2009; 21:541–551. [PubMed: 19444661]
- Johnson MO, Charlebois E, Morin SF, Remien RH, Chesney MA. Effects of a behavioral intervention on antiretroviral medication adherence among people living with HIV: the healthy living project randomized controlled study. *Journal of Acquired Immune Deficiency Syndrome*. 2007; 46(5):574–580.
- Johnson MO, Chesney MA, Goldstein RB, Remien RH, Catz S, Gore-Felton C, et al. Positive provider interactions, adherence self-efficacy, and adherence to antiretroviral medications among HIV-infected adults: A mediation model. *AIDS Patient Care and STDs*. 2006; 20:258–268. [PubMed: 16623624]
- Johnson MO, Elliott TR, Neilands TB, Morin SF, Chesney MA. A Social Problem-Solving Model of Adherence to HIV Medications. *Health Psychology*. 2006; 25(3):355–363. [PubMed: 16719607]
- Jones DL, McPherson-Baker S, Lydston D, Camille J, Brondolo E, Tobin JN, et al. Efficacy of a group medication adherence intervention among HIV positive women: The SMART/EST Women's Project. *AIDS and Behavior*. 2007; 11(1):79–86. [PubMed: 17028992]
- Kalichman SC, Cherry J, Cain D. Nurse-delivered antiretroviral treatment adherence intervention for people with low literacy skills and living with HIV/AIDS. *The Journal of the Association of Nurses in AIDS Care*. 2005; 16(5):3–15. [PubMed: 16433105]
- Kalichman SC, Pope H, White D, Cherry C, Amaral CM, Swetzes C, et al. Association between health literacy and HIV treatment adherence: further evidence from objectively measured medication adherence. *Journal of the International Association of Physicians in AIDS Care (Chicago, Ill: 2002)*. 2008; 7(6):317–323.
- Kapadia F, Vlahov D, Yingfeng W, Cohen MH, Greenblatt RM, Howard AA, et al. Impact of drug abuse treatment modalities on adherence to ART/HAART among a cohort of HIV seropositive women. *American Journal of Drug & Alcohol Abuse*. 2008; 34:161–170. [PubMed: 18293232]
- Koenig LJ, Pals SL, Bush T, Pratt Palmore M, Stratford D, Ellerbrock TV. Randomized controlled trial of an intervention to prevent adherence failure among HIV-infected patients initiating antiretroviral therapy. *Health Psychology*. 2008; 27(2):159–169. [PubMed: 18377134]
- Kremer H, Ironson G, Porr M. Spiritual and mind-body beliefs as barriers and motivators to HIV-treatment decision-making and medication adherence? A qualitative study. *AIDS Patient Care and STDs*. 2009; 23(2):127–134. [PubMed: 19133751]

- Lazo M, Gange SJ, Wilson TE, Anastos K, Ostrow DG, Witt MD, et al. Patterns and predictors of changes in adherence to highly active antiretroviral therapy: longitudinal study of men and women. *Clinical Infectious Diseases*. 2007; 45(10):1377–1385. [PubMed: 17968839]
- Leserman J, Ironson G, O’Cleirigh C, Fordiani JM, Balbin E. Stressful life events and adherence in HIV. *AIDS Patient Care and STDs*. 2008; 22(5):403–411. [PubMed: 18373416]
- Levin TR, Klibanov OM, Axelrod P, Finley GL, Gray A, Holdsworth C, et al. A randomized trial of educational materials, pillboxes, and mailings to improve adherence with antiretroviral therapy in an inner city HIV clinic. *Journal of Clinical Outcomes Management*. 2006; 13(4):217–221.
- Liu H, Longshore D, Williams JK, Rivkin I, Loeb T, Warda US, et al. Substance abuse and medication adherence among HIV-positive women with histories of child sexual abuse. *AIDS & Behavior*. 2006; 10(3):279–286. [PubMed: 16501869]
- Liu H, Miller LG, Hays RD, Golin CE, Zhao H, Wenger NS, et al. A comprehensive evaluation of survey questions for adherence to antiretroviral medications and exploratory analyses for identifying optimal sets of survey questions. *AIDS Patient Care and STDs*. 2006; 20(11):760–772. [PubMed: 17134350]
- Lynam I, Catley D, Goggin K, Rabinowitz JL, Gerkovich MM, Williams K, et al. Autonomous regulation and locus of control as predictors of antiretroviral medication adherence. *Journal of Health Psychology*. 2009; 14(4):578–586. [PubMed: 19383658]
- Ma M, Brown BR, Coleman M, Kibler JL, Loewenthal H, Mitty JA. The feasibility of modified directly observed therapy for HIV-seropositive African American substance users. *AIDS Patient Care and STDs*. 2008; 22(2):139–146. [PubMed: 18260805]
- MacKinnon DP, Fairchild AJ, Fritz MS. Mediation analysis. *Annual Review of Psychology*. 2007; 58:593–614.
- Margolin A, Avants SK, Warburton LA, Hawkins KA, Shi J. A randomized clinical trial of a manual-guided risk reduction intervention for HIV-positive injection drug users. *Health Psychology*. 2003; 22(2):223–228. [PubMed: 12683743]
- McKleroy VS, Galbraith JS, Cummings B, Jones P, Harshbarger C, Collins C, GElauide D, Carey JW. Adapting evidence-based behavioral interventions to new settings and target populations. *AIDS Education & Prevention*. 2006; 18:59–73. [PubMed: 16987089]
- Meade CS, Hansen NB, Kochman A, Sikkema KJ. Utilization of medical treatments and adherence to antiretroviral therapy among HIV-positive adults with histories of childhood sexual abuse. *AIDS Patient Care and STDs*. 2009; 23(4):259–266. [PubMed: 19260772]
- Miguez-Burbano MJ, Espinoza L, Lewis JE. HIV treatment adherence and sexual functioning. *AIDS & Behavior*. 2008; 12(1):78–85. [PubMed: 17295075]
- Milam J, Richardson JL, McCutchan A, Stoyanoff S, Weiss J, Kemper C, et al. Effect of a brief antiretroviral adherence intervention delivered by HIV care providers. *Journal of Acquired Immune Deficiency Syndrome*. 2005; 40(3):356–363.
- Miller CL, Druss BG, Rohrbaugh RM. Using qualitative methods to distill the active ingredients of a multifaceted intervention. *Psychiatric Services*. 2003; 54(4):568–571. [PubMed: 12663848]
- Munro S, Lewin S, Swart T, Volmink J. A review of health behaviour theories: how useful are these for developing interventions to promote long-term medication adherence for TB and HIV/AIDS? *BMC Public Health*. 2007; 7:104. [PubMed: 17561997]
- Murphy DA, Lu MC, Martin D, Hoffman D, Marelich WD. Results of a pilot intervention trial to improve antiretroviral adherence among HIV-positive patients. *The Journal of the Association of Nurses in AIDS Care*. 2002; 13(6):57–69. [PubMed: 12469544]
- Murphy DA, Marelich WD, Rappaport NB, Hoffman D, Farthing C. Results of an Antiretroviral Adherence Intervention: STAR (Staying Healthy: Taking Antiretrovirals Regularly). *Journal of the International Association of Physicians in AIDS Care (Chicago, Ill: 2002)*. 2007; 6(2):113–124.
- Parry MF, Wright P, Stewart J, McLeod GX, Tucker J, Weinberg AR. Impact of an Adherence Program on the Health and Outlook of HIV-Infected Patients Failing Antiretroviral Therapy. *Journal of the International Association of Physicians in AIDS Care (Chicago, Ill: 2002)*. 2005; 4(3):59–65.

- Parsons JT, Golub SA, Rosof E, Holder C. Motivational interviewing and cognitive-behavioral intervention to improve HIV medication adherence among hazardous drinkers: a randomized controlled trial. *Journal of Acquired Immune Deficiency Syndrome*. 2007; 46(4):443–450.
- Parsons JT, Rosof E, Mustanski B. Patient-related factors predicting HIV medication adherence among men and women with alcohol problems. *Journal of Health Psychology*. 2007; 12(2):357–370. [PubMed: 17284499]
- Parsons JT, Rosof E, Mustanski B. Medication adherence mediates the relationship between adherence self-efficacy and biological assessments of HIV health among those with alcohol use disorders. *AIDS & Behavior*. 2008; 12(1):95–103. [PubMed: 17503172]
- Parsons JT, Rosof E, Punzalan JC, Di Maria L. Integration of motivational interviewing and cognitive behavioral therapy to improve HIV medication adherence and reduce substance use among HIV-positive men and women: results of a pilot project. *AIDS Patient Care and STDs*. 2005; 19(1):31–39. [PubMed: 15665633]
- Phillips KD, Moneyham L, Murdaugh C, Boyd MR, Tavakoli A, Jackson K, et al. Sleep disturbance and depression as barriers to adherence. *Clinical Nursing Research*. 2005; 14(3):273–293. [PubMed: 15995155]
- Pomeroy EC, Thompson S, Gober K, Noel L. Predictors of medication adherence among HIV/AIDS clients. *Journal of HIV/AIDS & Social Services*. 2007; 6:65–81.
- Purcell DW, Latka MH, Metsch LR, Latkin CA, Gomez CA, Mizuno Y, et al. Results from a randomized controlled trial of a peer-mentoring intervention to reduce HIV transmission and increase access to care and adherence to HIV medications among HIV-seropositive injection drug users. *Journal of Acquired Immune Deficiency Syndrome*. 2007; 46(Suppl 2):S35–47.
- Preacher KJ, Hayes AF. SPSS and SAS procedures for estimating indirect effects in simple mediation model. *Behavior Research Methods, Instruments, & Computers*. 2004; 36:717–731.
- Premack SL, Hunter JE. Individual unionization decisions. *Psychological Bulletin*. 1988; 103:223–234.
- Rathbun RC, Farmer KC, Stephens JR, Lockhart SM. Impact of an adherence clinic on behavioral outcomes and virologic response in treatment of HIV infection: a prospective, randomized, controlled pilot study. *Clinical Therapeutics*. 2005; 27(2):199–209. [PubMed: 15811483]
- Rawlings MK, Thompson MA, Farthing CF, Brown LS, Racine J, Scott RC, et al. Impact of an educational program on efficacy and adherence with a twice-daily lamivudine/zidovudine/abacavir regimen in underrepresented HIV-infected patients. *Journal of Acquired Immune Deficiency Syndrome*. 2003; 34(2):174–183.
- Remien RH, Exner TM, Morin SF, Ehrhardt AA, Johnson MO, Correale J, et al. Medication adherence and sexual risk behavior among HIV-infected adults: implications for transmission of resistant virus. *AIDS & Behavior*. 2007; 11(5):663–675. [PubMed: 17243012]
- Remien RH, Stirratt MJ, Dolezal C, Dognin JS, Wagner GJ, Carballo-Diequez A, et al. Couple-focused support to improve HIV medication adherence: a randomized controlled trial. *AIDS*. 2005; 19(8):807–814. [PubMed: 15867495]
- Reynolds NR, Testa MA, Su M, Chesney MA, Neidig JL, Frank I, et al. Telephone support to improve antiretroviral medication adherence: a multisite, randomized controlled trial. *Journal of Acquired Immune Deficiency Syndrome*. 2008; 47(1):62–68.
- Robinson LA, Berman JS, Neimeyer RA. Psychotherapy for the treatment of depression: A comprehensive review of controlled outcome research. *Psychological Bulletin*. 1990; 108:30–49. [PubMed: 2200072]
- Rosen MI, Dieckhaus K, McMahon TJ, Valdes B, Petry NM, Cramer J, et al. Improved adherence with contingency management. *AIDS Patient Care and STDs*. 2007; 21(1):30–40. [PubMed: 17263651]
- Royal SW, Kidder DP, Patrabanish S, Wolitski RJ, Holtgrave DR, Aidala A, et al. Factors associated with adherence to highly active antiretroviral therapy in homeless or unstably housed adults living with HIV. *AIDS Care*. 2009; 21(4):448–455. [PubMed: 19401865]
- Rueda S, Park-Wyllie LY, Bayoumi AM, Tynan AM, Antoniou TA, Rourke SB, et al. Patient support and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS. *Cochrane Database Systematic Review*. 2006; 3:CD001442.

- Rychetnik L, Frommer M, Hawe P, Shiell A. Criteria for evaluating evidence on public health interventions. *Journal of Epidemiology & Community Health*. 2002; 56(2):119–127. [PubMed: 11812811]
- Safren SA, O'Cleirigh C, Reilly LC, Tan JY, Raminani SR, Otto MW, et al. A randomized controlled trial of cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected individuals. *Health Psychology*. 2009; 28(1):1–10. [PubMed: 19210012]
- Samet JH, Horton NJ, Meli S, Dukes K, Tripps T, Sullivan L, et al. A randomized controlled trial to enhance antiretroviral therapy adherence in patients with a history of alcohol problems. *Antiviral Therapy*. 2005; 10(1):83–93. [PubMed: 15751766]
- Sandelowski M.; Barroso, J. *Handbook for synthesizing qualitative research*. New York: Springer; 2007.
- Sandelowski M, Voils CI, Chang Y, Lee EJ. A systematic review comparing antiretroviral adherence descriptive and intervention studies conducted in the USA. *AIDS Care*. 2009; 21(8):953–966. [PubMed: 20024751]
- Shadish SR. Meta-analysis and the exploration of causal mediating processes: A primer of examples, methods, and issues. *Psychological Methods*. 1996; 1:47–65.
- Shuter J, Bernstein SL. Cigarette smoking is an independent predictor of nonadherence in HIV-infected individuals receiving highly active antiretroviral therapy. *Nicotine & Tobacco Research*. 2008; 10(4):731–736. [PubMed: 18418794]
- Simoni JM, Frick PA, Huang B. A longitudinal evaluation of a social support model of medication adherence among HIV-positive men and women on antiretroviral therapy. *Health Psychology*. 2006; 25(1):74–81. [PubMed: 16448300]
- Simoni JM, Pantalone DW, Plummer MD, Huang B. A randomized controlled trial of a peer support intervention targeting antiretroviral medication adherence and depressive symptomatology in HIV-positive men and women. *Health Psychology*. 2007; 26(4):488–495. [PubMed: 17605569]
- Simoni JM, Pearson CR, Pantalone DW, Marks G, Crepaz N. Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials. *Journal of Acquired Immune Deficiency Syndrome*. 2006; 43(Suppl 1):S23–35.
- Smith SR, Rublein JC, Marcus C, Brock TP, Chesney MA. A medication self-management program to improve adherence to HIV therapy regimens. *Patient Education and Counseling*. 2003; 50(2):187–199. [PubMed: 12781934]
- Sobel, ME. Asymptotic intervals for indirect effects in structural equations models. In: Leinhard, S., editor. *Sociological Methodology* 1982. San Francisco, CA: Jossey-Bass; 1982. p. 290-312.
- Sorensen JL, Haug NA, Delucchi KL, Gruber V, Kletter E, Batki SL, et al. Voucher reinforcement improves medication adherence in HIV-positive methadone patients: a randomized trial. *Drug and Alcohol Dependence*. 2007; 88(1):54–63. [PubMed: 17056206]
- van Dulmen S, Sluijs E, van Dijk L, de Ridder D, Heerdink R, Bensing J. Patient adherence to medical treatment: a review of reviews. *BMC Health Services Research*. 2007; 7:55. [PubMed: 17439645]
- van Servellen G, Lombardi E. Supportive relationships and medication adherence in HIV-infected, low-income Latinos. *Western Journal of Nursing Research*. 2005; 27(8):1023–1039. [PubMed: 16275696]
- van Servellen G, Nyamathi A, Carpio F, Pearce D, Garcia-Teague L, Herrera G, et al. Effects of a treatment adherence enhancement program on health literacy, patient-provider relationships, and adherence to HAART among low-income HIV-positive Spanish-speaking Latinos. *AIDS Patient Care and STDs*. 2005; 19(11):745–759. [PubMed: 16283835]
- Viswesvaran C, Ones DS. Theory testing: Combining psychometric meta-analysis and structural equations modeling. *Personnel Psychology*. 1995; 48:865–885.
- Voils C, Crandell JL, Chang YK, Leeman J, Sandelowski M. Combining adjusted and unadjusted findings in mixed research synthesis. *Journal of Evaluation in Clinical Practice*. In press.
- Vranceanu AM, Safren SA, Lu M, Coady WM, Skolnik PR, Rogers WH, et al. The relationship of post-traumatic stress disorder and depression to antiretroviral medication adherence in persons with HIV. *AIDS Patient Care and STDs*. 2008; 22(4):313–321. [PubMed: 18338960]

- Vyavaharkar M, Moneyham L, Tavakoli A, Phillips KD, Murdaugh C, Jackson K, et al. Social support, coping, and medication adherence among HIV-positive women with depression living in rural areas of the southeastern United States. *AIDS Patient Care and STDs*. 2007; 21(9):667–680. [PubMed: 17919094]
- Wagner GJ, Kanouse DE, Golinelli D, Miller LG, Daar ES, Witt MD, et al. Cognitive-behavioral intervention to enhance adherence to antiretroviral therapy: a randomized controlled trial (CCTG 578). *AIDS*. 2006; 20(9):1295–1302. [PubMed: 16816559]
- Waldrop-Valverde D, Valverde E. Homelessness and psychological distress as contributors to antiretroviral nonadherence in HIV-positive injecting drug users. *AIDS Patient Care and STDs*. 2005; 19(5):326–334. [PubMed: 15916495]
- Webb MS, Venable PA, Carey MP, Blair DC. Medication adherence in HIV-infected smokers: The mediating role of depressive symptoms. *AIDS Education & Prevention*. 2009:94–105. [PubMed: 19537957]
- Weiss L, French T, Waters M, Netherland J, Agins B, Finkelstein R. Adherence to HAART: perspectives from clients in treatment support programs. *Psychology, Health & Medicine*. 2006; 11(2):155–170.
- Williams AB, Fennie KP, Bova CA, Burgess JD, Danvers KA, Dieckhaus KD. Home visits to improve adherence to highly active antiretroviral therapy: a randomized controlled trial. *Journal of Acquired Immune Deficiency Syndrome*. 2006; 42(3):314–321.
- Wohl AR, Garland WH, Witt MD, Valencia R, Boger A, Squires K, et al. An adherence-focused case management intervention for HIV-positive patients in a public care setting. *Journal of HIV/AIDS & Social Services*. 2009; 8(1):80–94.
- Wyatt GE, Longshore D, Chin D, Carmona JV, Loeb TB, Myers HF, et al. The efficacy of an integrated risk reduction intervention for HIV-positive women with child sexual abuse histories. *AIDS and Behavior*. 2004; 8(4):453–462. [PubMed: 15690118]

Figure 1.
Mediation

Table 1

Profile of Intervention Studies

Report	N	Male (%)	Design	Potential Mediators
Barnett, 2009	66	59	RCT	
Collier, 2005	282	80	RCT	
Cook, 2009	98	61	Pre-post study	
Diekhaus, 2007	161	54	Cohort study	
DiIorio, 2003	17	53	RCT	
DiIorio, 2008	213	65	RCT	
Golin, 2006	155	66	RCT	Drug/alcohol use, social support, emotional wellbeing, positive coping, self efficacy, beliefs, health care provider
Gross, 2009	243	79	RCT	
Holzemer, 2006	240	65	RCT	
Jones, 2007	177	0	RCT	Positive coping
Johnson, 2007	204	78	RCT	
Kalichman, 2005	30	57	Pre-post study	Self efficacy, knowledge
Koenig, 2008	226	64	RCT	
Levin, 2006	49	59	RCT	
Ma, 2008	31	45	Pre-post study	
Margolin, 2003	90	70	RCT	
Milam, 2005	437	88	RCT	
Murphy, 2002	33	88	RCT	Social support, emotional wellbeing, positive coping, self efficacy, beliefs
Murphy, 2007	141	82	RCT	Drug/alcohol use, social support, emotional wellbeing, self efficacy
Parsons, 2005	15	93	Pre-post study	Drug/alcohol use
Parsons, 2007	143	79	RCT	Drug/alcohol use
Purcell, 2007	966	61	RCT	
Rathbun, 2005	33	85	RCT	
Rawlings, 2003	195	65	RCT	
Remien, 2005	215	54	RCT	
Reynolds, 2008	109	85	RCT	
Rosen, 2007	56	59	RCT	
Safren, 2009	45	NA	RCT	Emotional wellbeing
Samet, 2005	151	81	RCT	Drug/alcohol use
Simoni, 2007	136	55	RCT	Social support, emotional wellbeing
Smith, 2003	43	80	RCT	
Sorensen, 2007	66	53	RCT	
Van Servellen, 2005	85	91	RCT	Self efficacy, knowledge, health care provider
Wagner, 2006	230	80	RCT	
Williams, 2006	171	52	RCT	
Wohl, 2009	84	74	Pre-post study	
Wyatt, 2004	147	0	RCT	

* RCT: randomized controlled trial

Table 2

Profile of Quantitative Observational Studies

Report	N	Male (%)	Potential Mediators
Amico 2007	72	54	Emotional wellbeing
Amico 2009	149	58	Self-efficacy
Arnstein 2007	636	65	Drug/alcohol use, emotional wellbeing, self- efficacy, beliefs
Atkinson 2008	130	74	Self-efficacy, beliefs
Barclay 2007	185	78	Drug/alcohol use, social support, self-efficacy, beliefs
Beach 2006	4594	61	Health care provider
Boarts 2006	57	82	Emotional wellbeing
Bottonari 2005	24	96	Emotional wellbeing
Braithwaite 2005	2774	94	Drug/alcohol use
Cardarelli 2008	101	76	Drug/alcohol use, social support, emotional wellbeing, beliefs
Cha 2008	215	67	Social support, emotional wellbeing, self- efficacy
Chander 2006	1957	64	Drug/alcohol use
Cruess 2007	117	63	Emotional wellbeing, positive coping
de Jong 2005	168	76	Drug/alcohol use
DiIorio 2009	236	66	Social support, emotional wellbeing, positive coping, self-efficacy, beliefs, health care provider
French 2005	590	NS	Emotional wellbeing
Friedman 2009	602	69	Drug/alcohol use
Gonzalez 2007	325	60	Beliefs
Graham 2007	87	75	Knowledge
Halkitis 2005	300	100	Drug/alcohol use, self-efficacy
Halkitis 2007	300	100	Drug/alcohol use
Hamilton, 2007	98	71	Social support
Hicks 2007	659	70	Drug/alcohol use
Hinkin 2007	150	83	Drug/alcohol use
Holmes 2007	116	81	Drug/alcohol use, social support, emotional wellbeing
Holstad 2006	120	60	Drug/alcohol use, social support, positive coping, self-efficacy, beliefs, health care provider
Horberg 2008	3359	83	Emotional wellbeing
Ingersoll 2005	120	62	Drug/alcohol use, emotional wellbeing, health care provider
Johnson Chesney 2006	2765	74	Self-efficacy, health care provider
Johnson Elliott 2006	552	17	Drug/alcohol use
Johnson Heckman 2009	244	71	Social support, emotional wellbeing
Kalichman 2008	145	69	Drug/alcohol use, social support, emotional wellbeing
Kapadia 2008	573	0	Drug/alcohol use, emotional wellbeing
Kremer 2009	79	65	Positive coping
Lazo 2007	1944	33	Drug/alcohol use, emotional wellbeing
Leserman 2008	105	61	Drug/alcohol use, emotional wellbeing
Liu Longshore 2006	148	0	Drug/alcohol use, emotional wellbeing, self efficacy
Liu Miller 2006	128	81	Drug/alcohol use, beliefs, health care provider
Lynam 2009	189	73	Self-efficacy, beliefs

Report	N	Male (%)	Potential Mediators
Meade 2009	268	50	Drug/alcohol use, social support, emotional wellbeing
Miguez-Burbano 2008	135	100	Emotional wellbeing, beliefs
Parsons 2007	272	78	Drug/alcohol use, beliefs
Parsons 2008	275	77	Drug/alcohol use, self-efficacy
Phillips, 2005	173	0	Emotional wellbeing
Pomeroy 2007	184	78	Social support, beliefs, knowledge, health care provider
Remien 2007	2849	74	Drug/alcohol use
Royal 2009	358	72	Drug/alcohol use, emotional wellbeing, beliefs
Shuter 2008	64	55	Drug/alcohol use, emotional wellbeing,
Simoni 2006	136	55	Social support, emotional wellbeing, positive coping, self-efficacy
van Servellen 2005	85	90	Social support, emotional wellbeing, self- efficacy, health care provider
Vranceanu 2008	156	76	Emotional wellbeing
Vyavaharkar 2007	224	0	Social support, positive coping
Waldrop-Valverde 2005	58	76	Emotional wellbeing
Webb 2009	168	54	Emotional wellbeing

Table 3

Profile of Qualitative Studies of Participant's Perceptions of Interventions

Report	N	Design	Male (%)	Participants' perception
Adamian, 2004	20	Descriptive	70	Social support, knowledge, learning new skills
Berg, 2008	14	Descriptive	93	Social support, health care provider
Bontempi, 2004	29	Descriptive	70	Social support, knowledge, instrumental assistance, social support from peers
Garland, 2007	82	Interview data from intervention study	72	Social support, instrumental assistance
Parry, 2005	46	Interview data from intervention study	NA	Social support, knowledge
Weiss, 2006	32	Descriptive	72	Social support, knowledge, instrumental assistance, social support from peers, learning new skills, useful tools

Table 4**Potential Mediators of ART Adherence**

<ul style="list-style-type: none">• Drug/alcohol use: Current use, typically amount and frequency over a specified time period• Social support: Perceived level of or satisfaction with social support either in general or specific to HIV status• Emotional wellbeing: Depression, stress, anxiety, self-esteem, general psychological wellbeing, and others• Positive coping: Use of problem and emotion-focused strategies to manage living with HIV and/or adhering to ART, includes use of spiritual strategies• Self efficacy: Confidence in ability to manage living with HIV and/or adhering to ART• Beliefs: Perceptions of and attitudes towards HIV and ART and also includes measures of locus of control and outcome expectancies specific to HIV and ART• Knowledge: Factual understanding of HIV treatment, ART, and HIV progression• Healthcare provider: Perception of or satisfaction with healthcare provider
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Table 5

Estimates of Mean Correlation from Random Effects Model

Mediating Variable	k	N	Mean r	95% CI
<u>Intervention to Mediator</u>				
Drug/alcohol use	5	592	-.21	-.45 to .05
Social support	4	465	-.03	-.16 to .10
Emotional wellbeing	5	510	-.18	-.36 to .01
Positive coping	3	365	.13*	.02 to .23
Self efficacy	5	444	.17***	.08 to .26
Beliefs	2	188	.13	-.08 to .34
Knowledge	2	115	.20*	.002 to .38
Healthcare provider	2	240	.10	-.04 to .24
<u>Mediator to Adherence</u>				
Bivariate Results				
Drug/alcohol use	21	13970	-.16***	-.19 to -.12
Social support	13	2124	.12***	.07 to .17
Emotional wellbeing	25	7784	-.14***	-.17 to -.10
Positive coping	6	912	.07**	.02 to .17
Self efficacy	9	2292	.27***	.12 to .41
Beliefs	11	2597	.08*	.00 to .17
Knowledge	2	271	.27	-.07 to .54
Healthcare provider	6	5447	.13***	.06 to .19
Multivariable Results				
Drug/alcohol use	14	8002	-.13***	-.18 to -.07
Social support	4	634	.01*	.001 to .02
Emotional/Psychological	11	2739	-.03***	-.05 to -.01
Positive coping	2	344	.05	-.06 to .17
Self efficacy	8	3778	.15***	.09 to .20
Beliefs	6	1254	.10**	.03 to .16
Knowledge	1	87	.09	-.01 to .19
Healthcare provider	4	7655	.04***	-.005 to .08
<u>Intervention to adherence</u>				
All intervention studies	37	5770	.18***	.12 to .23

k: number of studies, N: sample size

*
p<.05,**
p<.01,***
p<.001.

Table 6**Sobel Test Results**

Mediating Variable	Assumed N	Intervention to mediator coefficient (SE)	Mediator to adherence coefficient (SE)	Sobel test statistics
Bivariate Results				
Drug/alcohol use	1551	-.21 (.03)	-.12 (.03)	4.13 ***
Social support	1073	-.03 (.03)	.12 (.03)	-.96
Emotional wellbeing	1326	-.18 (.03)	-.12 (.03)	3.49 ***
Positive coping	748	.13 (.04)	.05 (.04)	1.18
Self efficacy	1048	.17 (.03)	.25 (.03)	4.51 ***
Beliefs	510	.13 (.04)	.06 (.04)	1.18
Knowledge	239	.20 (.06)	.24 (.07)	2.35 *
Healthcare provider	663	.10 (.04)	.11 (.04)	1.95
Multivariable Results				
Drug/alcohol use	1509	-.21 (.03)	-.09 (.03)	3.30 ***
Social support	769	-.03 (.03)	.02 (.04)	-.38
Emotional wellbeing	1200	-.18 (.03)	.001 (.03)	-.03
Positive coping	515	.18 (.04)	.03 (.04)	.70
Self efficacy	1115	.17 (.03)	.12 (.03)	3.23 **
Beliefs	477	.13 (.04)	.07 (.05)	1.38
Knowledge	147	.20 (.06)	.06 (.08)	.67
Healthcare provider	671	.10 (.04)	.02 (.04)	0.55

*
p<.05,**
p<.01,***
p<.001.