Published in final edited form as:

J Adv Nurs. 2010 September ; 66(9): 1915–1930. doi:10.1111/j.1365-2648.2010.05360.x.

Implementation of Antiretroviral Therapy Adherence Interventions: A Realist Synthesis of Evidence

Jennifer Leeman, DrPH, MDiv,

Research Associate Professor, School of Nursing, University of North Carolina at Chapel Hill USA

Yun Kyung Chang, PhD, RN,

Social Research Specialist, School of Nursing, University of North Carolina at Chapel Hill USA

EunJeong Lee, MPH, RN,

Doctoral Student, School of Nursing, University of North Carolina at Chapel Hill USA

Corrine I. Voils, PhD, and

Research Health Science Specialist and Associate Professor, Health Services Research and Development Service, Durham Veterans Affairs Medical Center

Margarete Sandelowski, PhD, RN

Cary C. Boshamer Distinguished Professor, School of Nursing, University of North Carolina at Chapel Hill

Abstract

Aim—This paper is a report of a synthesis of evidence on implementation of interventions to improve adherence to antiretroviral therapy.

Background—Evidence on efficacy must be supplemented with evidence on how interventions were implemented in practice and on how that implementation varied across populations and settings.

Data Sources—Sixty-one reports were reviewed of studies conducted in the United States of America in the period 2001 to December 2008. Fifty-two reports were included in the final analysis: 37 reporting the effects of interventions and 15 reporting intervention feasibility, acceptability, or fidelity.

Review Methods—An adaptation of Pawson's realist synthesis method was used, whereby a provisional explanatory model and associated list of propositions are developed from an initial review of literature. This model is successively refined to the point at which it best explains empirical findings from the reports reviewed.

Results—The final explanatory model suggests that individuals with HIV will be more likely to enrol in interventions that protect their confidentiality, to attend when scheduling is responsive to

Conflict of interest: No conflict of interest has been declared by the authors.

Author Contributions: JL, CV & MS were responsible for the study conception and design

JL, YC & EL performed the data collection

JL, YC & EL performed the data analysis.

JL, YC, EL & CV were responsible for the drafting of the manuscript.

JL & CV made critical revisions to the paper for important intellectual content.

JC provided statistical expertise.

CV & MS obtained funding

YC & EL provided administrative, technical or material support.

MS supervised the study

their needs, and both to attend and continue with an intervention when they develop a strong, one-to-one relationship with the intervener. Participants who have limited prior experience with antiretroviral therapy will be more likely to continue with an intervention than those who are more experienced. Dropout rates are likely to be higher when interventions are integrated into existing delivery systems than when offered as stand-alone interventions.

Conclusion—The explanatory model developed in this study is intended to provide guidance to clinicians and researchers on the points in the implementation chain that require strengthening.

Keywords

literature review; implementation; Antiretroviral Therapy; Adherence; Interventions; Realist Synthesis of Evidence; Nursing; Pawson's method

INTRODUCTION

Antiretroviral therapy (ART) has dramatically improved the health and longevity of people with HIV infection, but problems with adherence have prevented many from realizing the full benefits of treatment. Researchers have tested different approaches to improving adherence to ART, and have systematically reviewed the findings of those studies. However, the findings from these reviews exemplify the limitations of reviews of behavioral change interventions. Amico et al. (2006) reported that the effects of the interventions they reviewed varied considerably across studies. Such reviews provide only limited evidence to explain variation across studies and virtually no evidence on implementation. In their review of ART adherence interventions Simoni et al. (2006, p. S34) concluded that there was “a paucity of data to guide the implementation of adherence interventions in clinical settings.”

Efforts to increase the use of evidence in practice draw heavily on findings from systematic reviews of the literature, such as those conducted for the Cochrane Collaboration. Typically, systematic reviews summarize the evidence concerning the effect of an intervention on a defined set of outcomes. Although evidence on effectiveness is critical, evidence is needed also about how interventions were implemented in practice and how implementation varied across populations and settings (Brownson et al., 2009; Rychetnik et al., 2004). This is particularly important for behavioral change interventions, which typically require multiple interactions between intervener(s) and participant(s) over an extended period of time. This interaction can be viewed as an “implementation chain” that is only as strong as its weakest link (Pawson, 2006, p. 95). With enhanced understanding of the factors that affect each link, the overall chain can be strengthened.

When reviewing research reports, reviewers synthesize findings across interventions they have rendered comparable for the purpose of the review (Sandelowski et al., 2007). In rendering interventions comparable, reviewers simplify them, systematically divorcing evidence about an intervention's effectiveness from information about the context in which it was delivered and how it was implemented in practice (Asthana & Halliday, 2006). As a result, reviewers typically conclude that the intervention works sometimes, but provide little information on how implementation may vary across different contexts and approaches (Briss et al., 2004). Indeed, it is this very information that may determine when the intervention will work.

THE REVIEW

Aim

The aim of the study was to systematically review and synthesize evidence on implementation of interventions to improve adherence to antiretroviral therapy among adults with HIV.

Design

We adapted Pawson's realist synthesis method (Pawson, 2006; Pawson et al., 2005) for this study. Pawson (2006, p. 94) advanced realist synthesis as a method to "discover the typical weak points and major stumbling blocks in the implementation of the interventions under review." Realist synthesis differs from conventional reviews in both its purpose and methods. Its goal is explanatory rather than summative. The methodology is well suited to carrying out syntheses to develop plausible explanatory models in areas where data are insufficient to identify and test relationships. The end-product of the synthesis is not a summary of the evidence in support of relationships (e.g., between an intervention and outcome), but rather a beginning theory to explain "what works for whom in what circumstances and in what respects" (Pawson, 2006, p. 74).

Methods

The steps (described below) required to carry out a realist synthesis parallel those used in conventional reviews, but are less linear and sequential. Rather than reviewing a focused literature addressing a predetermined set of research questions, the review itself—generated by a beginning set of questions—leads to more questions and, therefore, a diverse range of publications to answer them. Because its focus is explanatory, a realist synthesis explores answers to a broad range of questions about why, when, and how an intervention works. To narrow the review focus, realist synthesis begins with substantial reading and review to identify the factors with the greatest potential explanatory value. The factors identified are then integrated into a provisional model and series of propositions to guide the subsequent review.

The purpose of our review was to explain when, why, and how implementation of ART adherence interventions work well. To begin to focus the review, we read literature on the implementation of behavioral change interventions. This literature addresses theoretical and practical issues related to the components of interventions, the process of implementation, and the influence of context (e.g., Davidson et al., 2003; Hawe et al., 2004; Roen et al., 2006; Rychetnik et al., 2002). We also read literature on ART adherence and systematic reviews of ART intervention studies to identify factors specific to the context or implementation of ART adherence interventions. We identified the central steps in implementing a behavioral change intervention, and then developed a provisional model of the factors that may be important. The initial model was very basic and was intended to focus the literature search and initial data extraction, as displayed in Figure 1 and summarized here:

To change behavior, an individual must enrol in the intervention, attend intervention sessions, and continue to participate over time; an intervener must deliver the intervention with some level of fidelity. These steps may be influenced by characteristics of the participant, intervener, intervention, and setting.

Search Methods

We searched for two types of publications related to HIV adherence interventions with adults: primary reports of intervention studies and of studies of the feasibility, acceptability,

or fidelity of an intervention or programme. We searched PubMed, CINAHL, PsychINFO, Academic Search Premier, and Sociological Abstracts for the time period 2001 to December 2008 using the search terms HIV, antiretroviral treatment, and adherence. Because we were interested specifically in complex behavioral change 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. Because implementation is specific to context, and national context plays a major role in how HIV/AIDS is understood and managed, our review was focused on findings from studies conducted only in the USA. (Further details of the search strategies are available from the last author on request.)

Search Outcomes

Forty-six primary reports of intervention studies were included in the initial review. Nine of these studies were excluded from the final analysis because they included no useable data on enrolment, attendance, or retention. Table 1 gives an overview of the 37 primary reports of intervention studies included in the final analysis. Fifteen reports of feasibility, acceptability, or fidelity studies also were included in the review (Table 2).

Quality Appraisal

In realist synthesis, rather than appraising and excluding publications prior to review, the reviewer mines each publication for evidence that may contribute to fuller development of the explanatory model (Pawson, 2006). Instead of entire reports being evaluated against a priori standards for quality appraisal, each piece of evidence is appraised for its utility and relevance (Pawson, 2008). The value of evidence depends on whether it contributes to better understanding of the questions addressed in the review.

Data Abstraction and Synthesis

Drawing on our review of literature on behavioral change interventions and systematic reviews of ART adherence studies, we created a tool to cover a broad range of information and to allow the consolidation of data from across studies. Although Pawson (2006) has argued against such tools as too limiting for extracting information from diverse types of publications, our tool was flexible enough to account for this diversity. Moreover, using it did not preclude us from returning to the original papers whenever new questions requiring further exploration arose. Table 3 gives an overview of the information extracted on contextual factors that may affect implementation and the implementation process. This template was applied to the body of each report (i.e., introduction, methods, results, and discussion sections) by two members of the research team. Differences in coding were resolved by consensus with other team members.

Focusing the review—To begin refining the explanatory model, we conducted an initial review of data from all 61 studies to identify contextual factors repeatedly mentioned as facilitators or barriers at each step in the implementation process. We focused on: (a) authors' speculations about barriers and facilitators to successful implementation; (b) authors' speculations about the effects that characteristics of the intervention, participants, interveners, or setting had on implementation; (c) analysis of moderators, mediators, or other factors that influenced implementation or intervention outcomes; and (d) participant reports of satisfaction with or acceptability of the intervention.

Based on this review, we identified broad themes and created a list of propositions further to refine the explanatory model. We identified neither themes nor propositions related to interveners' delivery of the intervention because of the limited amount of information in the literature reviewed. These are displayed in Table 4 and summarized here:

Patients targeted by ART interventions tend to be those at greatest risk of not adhering, and these patients tend to have high levels of distrust, economic distress, and social instability. They have concerns about confidentiality and may resist interventions that risk disclosure of their HIV status or other personal information (i.e., in the case of interventions delivered to groups or where a healthcare worker goes to an individual's neighborhood or worksite to deliver ART and observe them take it). Adherence may have lower priority than other pressing concerns in their lives. Thus, their participation in an intervention may be more likely if they are offered instrumental support with other life concerns and/or financial incentives. Due to the instability in their lives, patients targeted by ART interventions may have trouble keeping scheduled appointments and continuing with an intervention over time. Flexible scheduling approaches may further facilitate interveners' and participants' ability to maintain contact with each other. Interventions may be implemented more successfully when they involve fewer intervention contacts and shorter durations. Developing strong relationships between the intervener and participant can lead to greater retention over time.

Synthesizing evidence—In realist synthesis, reviewers synthesize the extracted evidence by applying it to the explanatory model and then iteratively refining the model to best explain the existing data. In cases where evidence does not fit the model, the reviewer looks for other factors that may have more explanatory value. The synthesis ends with a summary of how the explanatory model has been revised.

We created a data matrix that summarized findings from each primary report of an intervention relating to each proposition (Table 5). Each step in the implementation process was coded as the rate of participation/completion of that step in a study. The approach used to code findings within each category is described in greater detail below. We then created scatter plots to represent visually the proposed relationships (e.g., enrolment rate by delivery mode) and looked for evidence of associations. If the patterns depicted by the scatter plot appeared not to fit with the proposition, we looked for an alternative proposition. If the association generally fitted the proposition, we examined the few outliers to explore why they did not fit and developed alternative propositions as needed.

We categorized interventions into four types, primarily based on delivery mode. Nineteen publications (51.4%) were reports of in-person, individual counseling/education interventions. Eight (21.6%) were reports of group counseling/education interventions, five of which also involved individual in-person or telephone-delivered contacts. Eight publications (21.6%) were reports of directly observed therapy [DOT] that involved giving participants their medications and observing them take it. Two (5.4%) were reports of telephone-delivered reminder/problem-solving interventions. In two cases, authors reported a comparison between two interventions and combined relevant data for the two interventions. In both cases, we used our judgment to determine which was the primary intervention and assigned it to that category.

RESULTS

Consistent with realist synthesis methodology, we looked at each step in the explanatory model independently, analyzing data from all publications that included data pertinent to that step.

Step 1. Patient Enrols

The first step in intervening involves getting people to enrol. We operationalized enrolment as the percentage of those approached who agreed to participate in the study. We included

only studies in which investigators identified a target population and then attempted to enrol all eligible members. Typically, the target population was all patients enrolled in clinics who met initial target criteria. We identified the proportion of patients who were eligible based on an initial screening who then declined to participate or failed to attend any of the intervention visits (i.e., viewed as passive declination). Because we were particularly interested in the number who declined to participate based on characteristics of the intervention, we also included the proportion of patients who declined following randomization where this information was available. We excluded studies in which participants were recruited through voluntary strategies (e.g., posting fliers) because those being screened to enrol were not representative of the total eligible population. Sixteen studies (43.2%) met the criteria for data on enrolment.

Support for proposition that patients are more likely to enrol in interventions that protect confidentiality than in those that do not—We grouped interventions according to whether their mode of delivery presented a greater or lesser risk to participants' confidentiality. Those risking confidentiality included directly observed therapy (DOT) and group interventions. Individual counseling/teaching and telephone interventions posed less risk to confidentiality. Of the 16 intervention studies with data on enrolment, 10 were individual counseling/teaching interventions, 3 were DOT interventions, and 3 were group counseling/teaching interventions. Patterns of participation rates in the reports of intervention studies offer support for the proposition that more patients will decline to participate in interventions that risk confidentiality than in those that protect confidentiality (Figure 2). The four interventions with the highest refusal rates included two DOT interventions (both with 40% refusal rates) and two group interventions (53% and 40% refusal rates, respectively). Of the 10 interventions involving individual, in-person counseling/teaching, six had relatively low refusal rates (9–15%) and the remaining four had moderate rates (23%–33%). One group intervention (Koenig et al., 2008) had a low refusal rate (18%) and did not fit the pattern. We looked for an explanation and found that it targeted individuals starting their first ART regimen. We found no consistent pattern, however, when we tested the proposition that prior experience using ART would affect enrolment using data from the nine studies that had data on both enrolment and ART experience.

Additional data supported the proposition that participants may resist participation in interventions that risk confidentiality (i.e., DOT and group interventions). In reports of intervention studies, authors reported that participants declined to participate because they were uncomfortable in groups (Simoni et al., 2007), and did not want visits at home or work if assigned to the DOT arm of the study (Garland et al., 2007). One of the acceptability/feasibility studies was specifically focused on the acceptability of DOT. Santos et al. (2006) asked HIV-positive patients if they would participate in a DOT programme in which a trained healthcare provider met with patients in the location of their choosing. Only 17% of 47 respondents preferred DOT to administering their own medications; 13% saw it as a nuisance and 18% as a burden. Commonly-cited concerns were loss of privacy and interference with family, work, and home life. Of those who preferred self-administration, 33% thought that DOT would expose them to scrutiny.

Support for proposition that patients are more likely to enrol in interventions that offer financial incentives or help with instrumental needs—Nine of the 16 intervention study reports included information on the financial incentives for participants. The total amount a participant could earn through study participation ranged from US\$40 to \$1,172. Instrumental support was a component of only one of the 16 studies. There was no pattern indicating a potential relationship between enrolment rates and financial incentives or instrumental support.

Step 2. Patient Attends

We operationalized attendance as the ratio of actual contacts to planned contacts between participants and interveners. Nineteen of the reports of intervention studies (51.4%) included useable information about attendance: 10 testing individual counseling/teaching interventions, three testing DOT, 4 testing group interventions, and two testing telephone interventions.

Support for proposition that attendance rates are greater when planned contacts are fewer—No patterns were identified to support the proposition that attendance would be better when there were fewer planned contacts.

Support for proposition that participants' attendance rates are greater if scheduling is responsive to participant than if it is not—We categorized interventions as having flexible scheduling based on how readily participants could adjust the timing and/or location of the contact. DOT and telephone interventions were classified as more flexible, whereas group and individual teaching/counseling interventions with set times for sessions were classified as less flexible. Overall, patterns in the data supported the proposition that flexible scheduling explains greater rates of attendance (Figure 3). Most DOT interventions offer flexibility in the time of contacts and many offer flexibility in location; DOT interventions had the highest rates of attendance. The lowest attendance rate among DOT interventions was for the one that was not flexible and linked DOT to participants' methadone appointments (Lucas et al., 2007). Groups are particularly difficult to schedule in a fashion that is responsive to all participants, and they also had low attendance rates. Contrary to the proposition, however, in-person, individual teaching/counseling interventions had consistently good attendance rates, even though participants had to attend at a set time for their appointments.

Evaluating the new proposition that attendance rates are greater when the intervener and patient develop a strong relationship than when they do not—Because the data did not fully fit the proposition, we looked to additional data from the reports to explore possible alternative propositions for the high attendance rates at teaching/counseling interventions. We found evidence that the strength of the relationship between the intervener and participant may also affect attendance. In several studies where researchers interviewed or surveyed participants and interveners about their perceptions of ART adherence interventions, the most dominant theme was the importance of participants' of relationships with interveners. In an acceptability study, Bontempi et al. (2004) conducted focus groups with participants in two HIV programmes, and found that all participants spoke about the importance of the adherence programme nurses who gave them social support, instilled trust, and provided positive reinforcement. Participants in DOT interventions also noted the relationship with the intervener as one of the most valuable aspects of the intervention (Garland et al., 2007; Ma et al., 2008; Visnegarwala et al., 2006; Wohl et al., 2004). In the two studies in which providers of adherence support were interviewed, they described the importance of spending time and serving as liaisons between clients and other healthcare providers (Bontempi et al., 2004; Shelton et al., 2006).

Based on these findings, we decided to test the proposition that attendance rates are greater when the intervener and participant develop a strong relationship. A strong relationship was operationalized as individual, in-person contacts with an intervener (i.e., individual teaching/counseling and DOT interventions). Group and telephone interventions were classified as developing less strong relationships between participants and interveners. Although telephone interventions can develop strong relationships between participants and interveners, both telephone interventions included in the review involved brief, scripted calls

rather than more in-depth counseling. Testing the relationship between attendance and strength of relationship resulted in the same breakdown as depicted in Figure 3, which shows support for an association between strength of the relationship and attendance. Further support for this proposition is provided by one study in which investigators compared a group to an individual, in-person intervention and found that attendance was higher for the individual intervention (Purcell et al., 2007).

Step 3. Intervener Delivers

The reports of ART adherence interventions gave little information on how interventions were delivered, and therefore we were unable to develop any propositions. Although a few reports offered descriptions of the process used to monitor fidelity, only five gave information on fidelity, and the authors four of these reports discussed fidelity only in general terms (Dilorio et al., 2008; Golin et al., 2006; Johnson et al., 2007; & Purcell et al., 2007). For example, Dilorio et al. stated that, “overall,” nurses were adherent to scripts and used appropriate motivational interviewing skills. Thrasher et al. (2006) provided additional data on the integrity of delivery for a subset of 47 patients in the Golin et al. intervention study. Using a well-established coding system, they found that, despite extensive training and supervision, interveners met only two of five quality benchmarks in less than half the sessions (18.7% and 43.7%, respectively), and the other three benchmarks in 62.5%, 85.4%, and 100% of sessions, respectively. Detail also was provided on the areas where interveners needed to improve, such as using more reflective statements and open-ended questions.

Step 4. Participant Continues

We operationalized whether participants continue with an intervention as the proportion not dropping out prior to the end of the intervention. We also included data on dropouts prior to completion of study data collection if they were the only data available. Twenty-seven publications (73%) had useable data on dropout rates.

Support for proposition that participants are less likely to drop out of interventions with shorter durations—No overall patterns were found between the duration of an intervention and participant dropout rates (Figure 4.).

Support for proposition that retention rates are greater when the intervener and participant develop a strong relationship than when they do not—We operationalized strength of relationship as described above; relationships are stronger with in-person, individual contacts. The pattern of dropout rates in the primary reports of intervention studies provides support for the proposition that strong relationships are associated with greater retention over time (Figure 5). The group interventions all had moderately high dropout rates. The majority of DOT and individual teaching/counseling interventions had relatively low dropout rates, although two individual teaching/counseling (Harwell et al., 2003; Levin et al., 2006; Smith et al., 2003) and three DOT interventions had dropout rates greater than 40% (Harwell et al., 2003; Lucas et al., 2007; Lucas et al., 2006). We examined the data from each of these publications for alternative explanations for the high dropout rates. Three of the interventions integrated adherence into an existing care delivery process rather than designing it as a stand-alone intervention. Lucas et al. (2007;2006) integrated DOT into care delivery at a methadone maintenance clinic. Levin et al. (2007) integrated an individual teaching/counseling intervention into care delivery at an HIV/AIDS clinic. The Harwell et al. (2003) study enrolled only 11 participants and, therefore, its findings may not be representative. The authors of the report of the study with the highest dropout rate (64%) (Smith et al., 2003) speculated that the intervention delivery site may have been a barrier; this was a large medical center, and many participants lived in surrounding rural communities several miles away.

Evaluation of new proposition that retention rates are lower when ART interventions are integrated into existing delivery systems rather than delivered as stand-alone interventions—Based on the findings on an association between strong relationships and retention, we evaluated a new proposition that integrating interventions into existing delivery systems would be associated with lower retention rates than would stand-alone interventions (Figure 6). Stand-alone interventions were those that created an intervention involving separately-scheduled appointments whose primary purpose was to increase ART adherence. For DOT interventions, these typically involved a community worker meeting with the participant to deliver ART and observe its use. For individual, telephone, and group teaching/counseling interventions, stand-alone interventions typically involved a series of protocol-driven sessions whose primary purpose was to increase ART adherence. All four of the interventions that integrated delivery into existing care systems had high rates of dropout. As noted above, two integrated DOT into care delivery at a methadone maintenance clinic and the third integrated an individual teaching/counseling intervention into care delivery at an HIV/AIDS clinic (Levin et al., 2006; Lucas et al., 2007; Lucas et al., 2006). In the fourth study, researchers trained primary care providers to deliver a brief teaching/counseling intervention as part of participants' regular clinic appointments. Overall, the findings suggest that interventions integrated into an existing delivery system may be associated with higher dropout rates than stand-alone interventions.

Evaluation of new proposition that retention rates are higher when participants are less ART-experienced—An expectation of the fact that retention rates are higher when participants are less ART-experienced might be that individuals who had not had previous failures with ART would be more likely to continue with an intervention over time. We evaluated the data in support of this proposition and found that dropout rates tended to be lower when a high proportion of participants (>60%) were ART-naïve or had just one prior regimen, as compared to a high proportion who had experienced prior failures with ART (Figure 7). The nine studies that had a high proportion of experienced ART participants (>60%) had dropout rates ranging from 10 to 57%, with four having dropout rates greater than 40%. The eight studies that had a high proportion of naïve or inexperienced ART participants had dropout rates ranging from 13 to 38%, with only one having a dropout rate higher than 28%.

Revised Explanatory Model

Based on our review of evidence, we revised our initial explanatory model to that shown in Figure 8 and summarized as follows:

Participants will be more likely to enrol in interventions that protect their confidentiality, to attend when scheduling is responsive to their needs, and to both attend and continue with an intervention when they develop a strong, one-to-one relationship with the intervener. Participants who have limited prior experience with ART will be more likely to continue with an intervention than those who are more experienced. Dropout rates are likely to be higher when interventions are integrated into existing delivery systems than when offered as stand-alone interventions.

DISCUSSION

Prior reviews of ART adherence interventions have reported that interventions, on the whole, had a positive effect on levels of adherence (Amico et al., 2006; Rueda, et al 2006; Simoni et al., 2006). Data on effectiveness does not tell the whole story, however, as interventions are only effective for the people who participate in them. To improve

outcomes across affected populations, evidence also is needed on how to increase enrolment and participation in interventions over time. In response to this need, a growing number of scholars have advocated greater attention to evidence on the process of implementing interventions in practice (Green & Glasgow, 2006; Glasgow & Emmons, 2007). In this review, we systematically reviewed ART adherence interventions for the purpose of synthesizing evidence on implementation. Our final model is intended to identify factors that may help to explain strong and weak links in the process of implementing ART adherence interventions. For example, DOT interventions are weak at the point of enrolment. However, when they are scheduled to be responsive to participants' needs and are delivered by an individual committed to adherence, they have high rates of attendance and good rates of retention. Therefore, people implementing a DOT intervention should be aware that, although it has strengths, they may need to offer an alternative as a large proportion of their patients may decline to participate.

The final model also points to areas in need of further research. We found that integrating an intervention into an existing delivery system may be associated with higher dropout rates. Stand-alone interventions typically have dedicated staff and resources. Dropout rates may be higher when interventions are integrated into existing systems because staff must balance time and resources across multiple other priorities. This presents a challenge to the broadly-recognized need to embed interventions within existing systems to ensure their adoption and maintenance over time (Allotey et al., 2008). Further research might be conducted to explore the relative strengths of stand-alone versus integrated interventions, taking into account the potential differential effects on organizational versus patient maintenance of the intervention over time. Further research could also be conducted to explore ways to improve retention of patients in intervention programs when they are integrated into existing delivery systems.

We found the realist synthesis approach useful, but noted several limitations to its use in synthesizing evidence on the implementation of ART adherence interventions. Realist synthesis is suited for reviews of literature where evidence is limited, but gaps in the evidence on implementation were at times too great to allow us to develop explanatory propositions. Many of the reports of intervention studies did not contain data on enrolment, attendance, and dropout rates. Only five publications included data on the fidelity of intervention delivery. These findings are consistent with those from other reviewers who have noted the limited amount of information on implementation included in reports on behavioral change interventions (Egan et al., 2009; Leeman et al., 2006). Inconsistency in whether intervention reports include implementation-relevant data, in what data are reported, and the manner of presentation all increase the potential for bias in our findings. Moreover, as the data reported were collected as part of a research study, the findings may not be generalizable to implementing an intervention in a practice setting. For example, we do not know whether participants declined to enrol because they did not want to be part of a research study rather than because they objected to the particular intervention.

CONCLUSION

Evidence on implementation is critical to policymakers, managers, and clinicians responsible for effecting change in practice. Synthesizing evidence to inform implementation of behavioral change interventions is possible only to the extent that researchers collect and report data on enrolment, attendance, fidelity, and retention. Intervention researchers can conduct their research in ways that yield more data on implementation, such as doing more process evaluations and designing studies to include diverse patient populations across multiple delivery settings and then collecting data on how implementation varied across contexts. Researchers also can revise their research reports to include more data and guidance on implementation. An intervention is only as strong as the

weakest link in its implementation chain. The explanatory model developed in this study is intended to begin to provide the evidence needed to strengthen each link in this implementation chain.

SUMMARY STATEMENT

What is already known about this topic

- Antiretroviral therapy has dramatically improved the health and extended the lives of people with HIV, but problems with adherence have prevented many from realizing the full benefits of treatment.
- Findings from systematic reviews of antiretroviral therapy adherence intervention studies provide little information on the implementation of interventions or on how implementation may vary across different contexts and approaches.
- Clinicians need this kind of evidence to guide the implementation of interventions in practice.

What this paper adds

- An explanatory model showing the strong and weak links in the chain of implementation of antiretroviral therapy adherence interventions.
- A step-by-step view of how realist synthesis can be used to synthesize evidence on behavioral change interventions.

Implications for practice

- The explanatory model developed in this study provides guidance on how to strengthen implementation of antiretroviral therapy adherence interventions.
- Efforts to synthesize evidence to inform implementation are possible only to the extent that researchers collect and report data on enrolment, attendance, fidelity, and retention.

Acknowledgments

The method study referred to here, 'Integrating qualitative and quantitative research findings', is funded by the National Institute of Nursing Research, National Institutes of Health (5R01NR004907, 3 June 2005–31 March 2010). This material is the result of work also supported with resources and the use of facilities at the Durham Veterans Affairs Medical Center. The views expressed in this paper are those of the authors and do not necessarily represent those of the Department of Veterans Affairs.

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 and STDs*. 2004; 18(4):229–238. [PubMed: 15142353]
- Allotey P, Reidpath DD, Ghalib H, Pagnoni F, Skelly WC. Efficacious, effective, and embedded interventions: Implementation research in infectious disease control. *BMC Public Health*. 2008; 8:343. [PubMed: 18826655]
- Altice FL, Maru DS, Bruce RD, Springer SA, Friedland GH. Superiority of directly administered antiretroviral therapy over self-administered therapy among HIV-infected drug users: A prospective, randomized, controlled trial. *Clinical Infectious Diseases*. 2007; 45(6):770–778. [PubMed: 17712763]

- 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.
- Asthana S, Halliday J. Developing an evidence base for policies and interventions to address health inequalities: the analysis of “public health regimes”. *The Milbank Quarterly*. 2006; 84(3):577–603. [PubMed: 16953811]
- Bakken S, Holzemer WL, Portillo CJ, Grimes R, Welch J, Wantland D. Utility of a standardized nursing terminology to evaluate dosage and tailoring of an HIV/AIDS adherence intervention. *Journal of Nursing Scholarship*. 2005; 37(3):251–257. [PubMed: 16235866]
- Bontempi JM, Bursleson L, Lopez MH. HIV medication adherence programs: the importance of social support. *Journal of Community Health Nursing*. 2004; 21(2):111–122. [PubMed: 15123440]
- Briss PA, Brownson RC, Fielding JE, Zaza S. Developing and using the Guide to Community Preventive Services: Lessons learned about evidence-based public health. *Annual Review of Public Health*. 2004; 25:281–302.
- Broadhead RS, Heckathorn DD, Altice FL, van Hulst Y, Carbone M, Friedland GH, et al. Increasing drug users’ adherence to HIV treatment: Results of a peer-driven intervention feasibility study. *Social Science & Medicine*. 2002; 55(2):235–246. [PubMed: 12144138]
- Brownson RC, Fielding JE, Maylahn CM. Evidence-Based Public Health: A Fundamental Concept for Public Health Practice. *Annual Review of Public Health*. 2009; 30:175–201.
- Collier AC, Ribaudo H, Mukherjee AL, Feinberg J, Fischl MA, Chesney M. A randomized study of serial teletelephone 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]
- Conn VS, Cooper PS, Ruppert TM, Russell CL. Searching for the intervention in intervention research reports. *Journal of Nursing Scholarship*. 2008; 40(1):52–59. [PubMed: 18302592]
- Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. *British Medical Journal*. 2008; 337:a1655. [PubMed: 18824488]
- Davidson KW, Goldstein M, Kaplan RM, Kaufmann PG, Knatterud GL, Orleans CT, Spring B, Trudeau KJ, Whitlock EP. Evidence-based behavioral medicine: What is it and how do we achieve it? *Annals of Behavioral Medicine*. 2003; 26(3):161–171. [PubMed: 14644692]
- Davies G, Koenig LJ, Stratford D, Palmore M, Bush T, Golde M, Malatino E, Todd-Turner M, Ellerbrock TV. Overview and implementation of an intervention to prevent adherence failure among HIV-infected adults initiating antiretroviral therapy: Lessons learned from Project HEART. *AIDS Care*. 2006; 18(8):895–903. [PubMed: 17012078]
- Dilorio C, McCarty F, Resnicow K, McDonnell Holstad M, Soet J, Yeager K, Sharma SM, Morisky DE, Ludberg B. Using motivational interviewing to promote adherence to antiretroviral medications: a randomized controlled study. *AIDS Care*. 2008; 20(3):273–283. [PubMed: 18351473]
- Dilorio 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.
- Egan M, Bamba C, Petticrew M, Whitehead M. Reviewing evidence on complex social interventions: Appraising implementation in systematic reviews of the health effects of organisational-level workplace interventions. *Journal of Epidemiology and Community Health*. 2009; 63(1):4–11. [PubMed: 18718981]
- Fielding JE, Briss PA. Promoting evidence-based public health policy: can we have better evidence and more action? *Health Affairs (Project Hope)*. 2006; 25(4):969–978. [PubMed: 16835176]
- 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]
- Glasgow RE. What types of evidence are most needed to advance behavioral medicine? *Annals of Behavioral Medicine*. 2008; 35:19–25. [PubMed: 18347901]

- Glasgow RE, Emmons KM. How can we increase translation of research into practice? Types of evidence needed. *Annual Review of Public Health*. 2007; 28:413–433.
- 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.
- Green LW, Glasgow RE. Evaluating the relevance, generalization, and applicability of research: Issues in external validation and translation methodology. *Evaluation & Health Professions*. 2006; 29:126–153.
- Greenhalgh T, Kristjansson E, Robinson V. Realist review to understand the efficacy of school feeding programmes. *BMJ (Clinical research edition)*. 2007; 335(7625):858–861.
- Harwell JI, Flanagan TP, Mitty JA, Macalino GE, Caliendo AM, Ingersoll J, Stenzel MS, Carpenter CC, Cu-Uvin S. Directly observed antiretroviral therapy to reduce genital tract and plasma HIV-1 RNA in women with poor adherence. *AIDS*. 2003; 17(13):1990–1993. [PubMed: 12960835]
- Hawe P, Shiell A, Riley T, Gold L. Methods for exploring implementation variation and local context within a cluster randomised community intervention trial. *Journal of Epidemiology and Community Health*. 2004; 58(9):788–793. [PubMed: 15310806]
- Holzemer WL, Bakken S, Portillo CJ, Grimes R, Welch J, Wantland D, Mullan JT. Testing a nurse-tailored HIV medication adherence intervention. *Nursing Research*. 2006; 55(3):189–197. [PubMed: 16708043]
- Javanbakht M, Prosser P, Grimes T, Weinstein M, Farthing C. Efficacy of an individualized adherence support program with contingent reinforcement among nonadherent HIV-positive patients: Results from a randomized trial. *Journal of the International Association of Physicians in AIDS Care (Chicago, Ill:2002)*. 2006; 5(4):143–150.
- 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, Gamarel KE, Dawson Rose C. Changing HIV treatment expectancies: A pilot study. *AIDS Care*. 2006; 18(6):550–553. [PubMed: 16831781]
- Jones DL, McPherson-Baker S, Lydston D, Camille J, Brondolo E, Tobin JN, Weiss SM. 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]
- 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]
- Leeman J, Jackson B, Sandelowski M. An evaluation of how well research reports facilitate the use of findings in practice. *Journal of Nursing Scholarship*. 2006; 38(2):171–177. [PubMed: 16773922]
- Levin TR, Klibanov OM, Axelrod P, Finley GL, Gray A, Holdsworth C, Moyer DV, Tedaldi EM, Samuel R. 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.
- Lucas GM, Mullen BA, McCaul ME, Weidle PJ, Hader S, Moore RD. Adherence, drug use, and treatment failure in a methadone-clinic-based program of directly administered antiretroviral therapy. *AIDS Patient Care and STDs*. 2007; 21(8):564–574. [PubMed: 17711381]
- Lucas GM, Mullen BA, Weidle PJ, Hader S, McCaul ME, Moore RD. Directly administered antiretroviral therapy in methadone clinics is associated with improved HIV treatment outcomes, compared with outcomes among concurrent comparison groups. *Clinical Infectious Diseases*. 2006; 42(11):1628–1635. [PubMed: 16652321]
- 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]

- Macalino GE, Mitty JA, Bazerman LB, Singh K, McKenzie M, Flanigan T. Modified directly observed therapy for the treatment of HIV-seropositive substance users: Lessons learned from a pilot study. *Clinical Infectious Diseases*. 2004; 5(Suppl. 2004):S393–397.
- Mannheimer SB, Morse E, Matts JP, Andrews L, Child C, Schmetter B, Friedland GH. Sustained benefit from a long-term antiretroviral adherence intervention: Results of a large randomized clinical trial. *Journal of Acquired Immune Deficiency Syndrome*. 2006; 43(Suppl 1):S41–47.
- 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]
- Marino P, Simoni JM, Silverstein LB. Peer support to promote medication adherence among people living with HIV/AIDS: The benefits to peers. *Social Work in Health Care*. 2007; 45(1):67–80. [PubMed: 17804348]
- Milam J, Richardson JL, McCutchan A, Stoyanoff S, Weiss J, Kemper C, Larsen RA, Hollander H, Weismuller P, Bolan R. Effect of a brief antiretroviral adherence intervention delivered by HIV care providers. *Journal of Acquired Immune Deficiency Syndrome*. 2005; 40(3):356–363.
- Mitchell CG, Freels S, Creticos CM, Oltean A, Douglas R. Preliminary findings of an intervention integrating modified directly observed therapy and risk reduction counseling. *AIDS Care*. 2007; 19(4):561–564. [PubMed: 17453598]
- 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]
- 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, 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]
- Pawson, R. Evidence-based policy: A realist perspective. London: SAGE; 2006.
- Pawson, R. Method mix, technical hex, and theory fix. In: Bergman, MM., editor. *Advances in mixed methods research: Theories and applications*. Los Angeles, CA: Sage; 2008. p. 120-137.
- Pawson R, Greenhalgh T, Harvey G, Walshe K. Realist review--a new method of systematic review designed for complex policy interventions. *Journal of Health Services Research & Policy*. 2005; 10(Suppl 1):21–34. [PubMed: 16053581]
- Pope C, Mays N, Popay J. How can we synthesize qualitative and quantitative evidence for healthcare policy-makers and managers? *Healthcare Management Forum*. 2006; 19(1):27–31. [PubMed: 17330642]
- Purcell DW, Latka MH, Metsch LR, Latkin CA, Gomez CA, Mizuno Y, Arnsten JH, Wilkinson JD, Knight KR, Knowlton AR, Santibanez S, Tobin KE, Rose CD, Valverde EE, Gourevitch MN, Eldred L, Borkowf CB. 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.
- 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, Crawford KH, Goodwin SD, Tolson JM, Williams VC, Shaefer MS. 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, Stirratt MJ, Dolezal C, Dognin JS, Wagner GJ, Carballo-Diequez A, El-Bassel N, Yung TM. 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, Smith S, Ickovics J, Robbins GK. Telephone support to improve antiretroviral medication adherence: A multisite, randomized controlled trial. *Journal of Acquired Immune Deficiency Syndrome*. 2008; 47(1):62–68.
- Roen K, Arai L, Roberts H, Popay J. Extending systematic reviews to include evidence on implementation: Methodological work on a review of community-based initiatives to prevent injuries. *Social Science & Medicine*. 2006; 63(4):1060–1071. [PubMed: 16574289]
- Rosen MI, Dieckhaus K, McMahon TJ, Valdes B, Petry NM, Cramer J, Rounsaville B. Improved adherence with contingency management. *AIDS Patient Care and STDs*. 2007; 21(1):30–40. [PubMed: 17263651]
- Rueda S, Park-Wyllie LY, Bayoumi AM, Tynan AM, Antoniou TA, Rourke SB, Glazier RH. Patient support and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS. *Cochrane Database of Systematic Reviews*. 2006; 3:CD001442.
- Rychetnik L, Frommer M, Hawe P, Shiell A. Criteria for evaluating evidence on public health interventions. *Journal of Epidemiology and Community Health*. 2002; 56(2):119–127. [PubMed: 11812811]
- Rychetnik L, Hawe P, Waters E, Barratt A, Frommer M. A glossary for evidence based public health. *Journal of Epidemiology and Community Health*. 2004; 58(7):538–545. [PubMed: 15194712]
- Samet JH, Horton NJ, Meli S, Dukes K, Tripps T, Sullivan L, Freedberg KA. 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, Voils CI, Barroso J. Comparability work and the management of difference in research synthesis studies. *Social Science & Medicine*. 2007; 64(1):236–247. [PubMed: 17029691]
- Santos CQ, Adeyemi O, Tenorio AR. Attitudes toward directly administered antiretroviral therapy (DAART) among HIV-positive inpatients in an inner city public hospital. *AIDS Care*. 2006; 18(7):808–811. [PubMed: 16971292]
- Shelton RC, Golin CE, Smith SR, Eng E, Kaplan A. Role of the HIV/AIDS case manager: analysis of a case management adherence training and coordination program in North Carolina. *AIDS Patient Care and STDs*. 2006; 20(3):193–204. [PubMed: 16548716]
- 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]
- Sorensen JL, Haug NA, Delucchi KL, Gruber V, Kletter E, Batki SL, Tulskey JP, Barnett P, Hall S. Voucher reinforcement improves medication adherence in HIV-positive methadone patients: a randomized trial. *Drug and Alcohol Dependence*. 2007; 88(1):54–63. [PubMed: 17056206]
- Thrasher AD, Golin CE, Earp JA, Tien H, Porter C, Howie L. Motivational interviewing to support antiretroviral therapy adherence: the role of quality counseling. *Patient Education and Counseling*. 2006; 62(1):64–71. [PubMed: 16023824]
- Tunis SR, Stryer DB, Clancy CM. Practical clinical trials: Increasing the value of clinical research for decision making in clinical and health policy. *JAMA*. 2003; 290:1624–1632. [PubMed: 14506122]
- van Servellen G, Carpio F, Lopez M, Garcia-Teague L, Herrera G, Monterrosa F, Gomez R, Lombardi E. Program to enhance health literacy and treatment adherence in low-income HIV-infected Latino men and women. *AIDS Patient Care and STDs*. 2003; 17(11):581–594. [PubMed: 14746666]

- van Servellen G, Nyamathi A, Carpio F, Pearce D, Garcia-Teague L, Herrera G, Lombardi E. 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]
- Visnegarwala F, Rodriguez-Barradass MC, Graviss EA, Caprio M, Nykyforchyn M, Laufman L. Community outreach with weekly delivery of anti-retroviral drugs compared to cognitive-behavioural health care team-based approach to improve adherence among indigent women newly starting HAART. *AIDS Care*. 2006; 18(4):332–338. [PubMed: 16809110]
- Wagner GJ, Kanouse DE, Golinelli D, Miller LG, Daar ES, Witt MD, Diamond C, Tiles JG, Kemper CA, Larsen R, Goicoechea M, Haubrich RH. Cognitive-behavioral intervention to enhance adherence to antiretroviral therapy: A randomized controlled trial (CCTG 578). *AIDS*. 2006; 20(9):1295–1302. [PubMed: 16816559]
- 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, Squires K, Witt M, Larsen R, Kovacs A, Hader S, Weidle PJ. The feasibility of a community-based directly administered antiretroviral therapy program. *Clinical Infectious Diseases*. 2004; 38(Suppl 5):S388–392. [PubMed: 15156427]
- Wohl AR, Garland WH, Valencia R, Squires K, Witt MD, Kovacs A, Larsen R, Hader S, Anthony MN, Weidle PJ. A randomized trial of directly administered antiretroviral therapy and adherence case management intervention. *Clinical Infectious Diseases*. 2006; 42(11):1619–1627. [PubMed: 16652320]

Figure 1.
Provisional Explanatory Model of Implementation

* Each • represents a primary study

DOT = Directly observed therapy

Figure 2.
Percent Decline by Delivery Mode

Figure 3.
Attendance Rates by Intervention Type

Figure 4.
Dropout Rates by Intervention Duration

* Each dot represents a primary study
Error bars = 95% interval (CI)

Figure 5.
Dropout Rates by Delivery Mode

Figure 6.
Dropout Rates by Whether Stand Alone or Integrated

* Each • represents a primary study

Figure 7.
Dropout Rates Based on Antiretroviral Therapy (ART) Experience Level

ART = Antiretroviral therapy

Figure 8.
Revised Explanatory Model

Table 1

Profile of Intervention Studies

Report	Research design	N (% female, % AA, % Hispanic)	ART experienced (%)	History substance use (%)	Type of intervention ¹	Setting	Effect size ²
Alice et al., 2007	RCT	141 (31, 58, 22)	NA	100	DOT	Clinic	.53
Collier et al., 2005	RCT	282 (20, 29, 19)	65	15	Telephone	Multisite	-.08
Dilorio et al., 2003	RCT, pilot	17 (47, 82, NA)	NA	NA	Individual	Clinic	.79
Dilorio et al., 2008	RCT	213 (33, 89, NA)	NA	38	Individual	Clinic	.29
Garland et al., 2007	One arm of RCT	82 (27, 20, 70)	59	65	DOT	Participant choice	NA
Golin et al., 2006	RCT	155 (34, 66, NA)	NA	NA	Individual	Clinic	.28
Harwell et al., 2003	One group pre-post	6 (NA)	100	100	DOT	Participant choice	2.13 ^v
Holzemer et al., 2006	RCT	240 (35, 72, NA)	NA	NA	Individual	Clinic	-.04
Javanbakht et al., 2006	RCT	90 (10, 36, 39)	100	40	Individual, telephone	Clinic	.60 ^v
Johnson et al., 2007	RCT	204 (22, 56, 7)	NA	NA	Individual	Clinic	.30
Jones et al., 2007	RCT	177 (100, 83, 12)	NA	57	Group	Clinic	.39
Koenig et al., 2008	RCT	226 (36, 83, NA)	0	NA	Group, Individual, telephone	Clinic	.29
Levin et al., 2006	RCT	49 (41, 80, 12)	63	63	Individual	Clinic	.81
Lucas et al., 2006	4-group cohort	82 (55, 83, NA)	27	100	DOT	Methadone clinic	.57 ^v
Lucas et al., 2007	One group prospective	88 (56, 80, NA)	64	100	DOT	Methadone clinic	NA
Ma et al., 2008	One group pre-post	31 (55, 100, 0)	NA	100	DOT	Participant choice	2.66
Mannheimer et al., 2006	RCT	928 (22, 55, 17)	0	15	Individual telephone	Clinic	.30
Margolin et al., 2003	RCT	90 (30, 49, 16)	NA	100	Group	Methadone clinic	.58
Milam et al., 2005	RCT	437 (12, 15, 39)	100	NA	Individual	Clinic	.53
Murphy et al., 2002	RCT	33 (12, 46, 18)	NA	NA	Group, individual	Clinic	-.30
Parsons et al., 2005	One group pre-post	15 (7, NA, NA)	NA	100	Individual	NA	.70
Parsons et al., 2007	RCT	143 (21, 66, 18)	NA	NA	Individual	Private office	.42
Purcell et al., 2007	RCT	966 (36, 66, 15)	NA	100	Group, individual	NA	.01
Rathbun et al., 2005	RCT	33 (15, 21, 9)	78	12	Individual, telephone	Clinic	.47
Rawlings et al., 2003	RCT	195 (35, 71, 21)	9	20	Individual	Clinic	-.11
Remien et al., 2005	RCT	215 (46, 62, 24)	NA	NA	Individual	Clinic	.85
Reynolds et al., 2008	RCT	109 (15, 43, NA)	0	NA	Telephone	Centralized call center	.42

Report	Research design	N (% female, % AA, % Hispanic)	ART experienced (%)	History substance use (%)	Type of intervention ¹	Setting	Effect size ²
Rosen et al., 2007	RCT	56 (41, 59, 31)	NA	86	Individual	Clinic	.63
Samet et al., 2005	RCT	151 (19, 47, NA)	NA	63	Individual	Clinic, home	.07
Simoni et al., 2007	RCT	136 (45, 46, 44)	89	52	Group, telephone	Clinic	-.12
Smith et al., 2003	RCT	43 (19, NA, NA)	NA	NA	Individual	Clinic	1.59
Sorensen et al., 2007	RCT	66 (41, 32, 12)	NA	52	Individual	Clinic	.35
van Servellen et al., 2005	RCT	85 (9, 0, 100)	NA	2	Group, individual, telephone	Clinic	.25
Visnegarwala et al., 2006	Pilot test	54 (100, 83, NA)	54	67	DOT	Clinic	1.30
Wagner et al., 2006	RCT	230 (20, 14, 49)	100	NA	Individual	Clinic	.43
Williams et al., 2006	RCT	171 (48, 35, 19)	NA	81	Individual	Home	.26
Wohl et al., 2006	RCT	250 (23, 24, 64)	54	NA	DOT	Participant choice	.13

Note: NA = information not available.

¹ Individual: Individual/In-Person.

² Adherence effect size was used unless unavailable, in which case viral load was used as indicated by ³.

ART = Antiretroviral therapy

RCT = Randomised controlled trial

DOT = Directly observed therapy

Table 2

Profile of Feasibility/Acceptability/Fidelity Studies

Report	Focus/Research design	N (% female, % AA, % Hispanic)	ART- experienced (%)	History substance use (%)	Type of intervention ³	Setting	Findings
Adamian et al., 2004	Acceptability via interview post intervention	20 (30, 90, NA)	NA	NA	Individual	Clinic	Most participants found the intervention useful and helpful.
Bakken et al., 2005	Fidelity via structured instrument	117 (36, 75, 12)	NA	29	Individual	Clinic	Number of interventions received and intervention time were tailored to diagnosis of patients' problems.
Bontempi et al., 2004	Acceptability & process evaluation via interview and document review	29 (31, 21, 76)	NA	NA	Individual	Home, clinic, advocacy program	Program clients valued emotional and social support, education on medication, and communications with health providers.
Broadhead et al., 2003	Feasibility one group pre-post pilot	14 (43, 71, 0)	NA	100	Individual	Storefront	Intervention attendance and retention data and consistency in data collection suggest feasibility.
Davies et al., 2006	Feasibility evaluation component of RCT	227 (37, 83, 2)	0	91	Group, individual, telephone	Clinic	Participants could identify support partners, most support partners attended at least one session, & participants' valued support partners.
Johnson, et al., 2006	Feasibility & acceptability pilot RCT	22 (NA)	0	NA	Group	Clinic	Intervention recruitment, attendance, and retention data demonstrated feasibility; participants rated the intervention highly.
Macalino et al., 2004	Feasibility & acceptability one group pre-post pilot	25 (48, 32, 28)	100	100	DOT	Participant's choice	Attendance, retention, trends in viral load, and participant satisfaction suggest feasibility.
Marino et al., 2007	Acceptability via interview	9 (56, 67, 22)	NA	56	Group, telephone	Clinic	Participants valued social acceptance, reciprocal support, and personal growth and empowerment and identified challenges.

Report	Focus/Research design	N (% female, % AA, % Hispanic)	ART - experienced (%)	History substance use (%)	Type of intervention ³	Setting	Findings
Mitchell et al., 2007	Feasibility one group pre-post pilot	30 (17, 90 ¹)	NA	Many	DOT, individual	Clinic	Retention rates and trends in viral load suggest feasibility.
Santos et al., 2006	Acceptability via interview	47 (32, 85, 13)	79	72	DOT	Public hospital (inpatient)	Most participants preferred to self-administer ART; few preferred DOT.
Shelton et al., 2006	Acceptability & feasibility via interview and document review	16 (94, NA, NA) Case managers	NA	NA	Individual	NA	Case managers identified strategies used and barriers to adherence care
Thrasher et al., 2006	Fidelity via structured instrument	47 (21, 90 ²)	NA	NA	Individual	Clinic	On 3 of 5 criteria, most sessions achieved quality benchmarks; associations were found between ART adherence and some measures of quality.
van Servellen et al., 2003	Acceptability & effectiveness pilot RCT	81 (10, 0, 100)	NA	NA	Group, individual, telephone	Clinic	Participants rated the program highly and significantly improved HIV/AIDS knowledge but not adherence mastery or behaviors as compared to control group.
Weiss et al., 2006	Acceptability via interview	32 (28, 63, 13)	75	69	Group, individual	Clinic, AIDS Service	Participants reported perceptions of services received: reminder tools (e.g., pillboxes), education, counseling and support, and linkages to healthcare providers.
Wohl et al., 2004	Feasibility one group pre-post pilot	67 (22, 21, 69)	61	34	DOT	Organizations Clinic	Investigators present implementation lessons learned from pilot.

Note: NA = information not available;

¹ African American and Hispanic together;

² All minority;

³ Individual = Individual/In-Person.

ART = Antiretroviral therapy

RCT = Randomised controlled trial

DOT = Directly observed therapy

Table 3**Categories of Information Extracted from Primary Reports**

Contextual factors (Extract from introduction, methods, or findings sections)	
•	Characteristics of participants: sex, race/ethnicity, education, income, age, substance abuse, men having sex with men, ART-naïve, mentally ill, and inclusion and exclusion criteria
•	Characteristics of intervener: number, discipline, other
•	Characteristics of setting: number, type, other
•	Characteristics of intervention: theory, intended dose (number, length, frequency of contacts), intended duration, delivery mode, content, whether tailored to subgroups
•	Identification and/or analysis of moderators or mediators of the intervention's effect (Extract from discussion section)
•	Authors' speculations on effects characteristics of the intervention, participants, interveners, or setting had on implementation.
Implementation process (Extract from introduction, methods, or findings sections)	
•	Participants enrolled: number screened, number ineligible following screen, number declined to participate
•	Participants attending: actual dose (number, length, frequency of contacts), test of dose on intervention effects, perception of satisfaction or acceptability
•	Intervener/system delivery: findings from process evaluation or measures of fidelity/integrity, description of implementation process
•	Participant continuing: Proportion who drop out before completing intervention (Extract from discussion section)
•	Authors' speculation on barriers and facilitators to successful implementation.

ART = Antiretroviral therapy

Table 4

Propositions further refining the explanatory model

Step	Propositions
Participant enrolment is	more likely if confidentiality is protected more likely if financial incentives are offered more likely if help with instrumental needs is offered
Patient attendance is	greater if contacts are fewer (i.e., number of intended sessions)greater if scheduling is responsive to participant
Patient continuation is	more likely with stronger relationship between patient and intervener less likely with longer duration (i.e., months intervention intended to last)

Table 5

Data matrix

Publication	Intervention Category	Enrol Rate	Attendance Rate	Retention Rate	Planned Contacts	Planned Duration	Strength of Relationship	Responsive Scheduling	Incentives or Instrumental Support
-------------	-----------------------	------------	-----------------	----------------	------------------	------------------	--------------------------	-----------------------	------------------------------------