Treatment Adherence Literature Review

Resource Inventory: **Treatment Adherence**

This is an optional resource for program development. The library is not exhaustive, and the programs and interventions described are not necessarily endorsed by HPS. The articles are offered only as a resource; applicants do not have to limit themselves to the models and approaches described in these articles.

All articles are available by request as a zip file from Betty Chan Lew. If you only wish one article, please reference the first author and title when making your request.

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Treatment Adherence Literature Review

Part 3: Treatment Adherence and Substance Use		
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Treatment Adherence Literature Review

Part 1: Factors Related to Adherence and Non-adherence

AIDS Patient Care STDS. 2009 Nov;23(11):903-14.

An evidence-based review of treatment-related determinants of patients' nonadherence to HIV medications.

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Abstract

Patients' adherence to antiretroviral medications is a primary determinant of both the effectiveness of treatment and the clinical course of HIV/AIDS. This empirical review is intended to compare the relative importance of patient and treatment characteristics on nonadherence behavior and the impact of nonadherence on treatment failure. Articles cited in PubMed and published between 2006 and June 2008 (n = 200) were reviewed to select those that address patient or treatment characteristics associated with nonadherence. Twenty-two articles were selected that provided odds ratio or hazard ratio statistics that quantified predictors of patients' level of nonadherence (e.g., <80%, 80%-95% and >95%). Results were summarized using random effects meta-analytic models. Predictors of nonadherence were divided into four predictive clusters (clinical predictors, comorbid predictors, treatment competence predictors, and dosing predictors). The summary odds ratios (ORs) of nonadherence for each cluster (in order of strength) were treatment competence 2.0 (95% confidence interval [CI]: 1.6-2.6), clinical predictors 1.6 (95% CI: 1.4-1.8), comorbid predictors 1.6 (95% CI: 1.4-1.8), and dosing predictors 1.5 (95% CI: 1.3-1.7). The effect of nonadherence on treatment failure supported the findings of two prior empirical reviews (OR 2.0, 95% CI: 1.6-2.5). Within dosing predictors, a pill burden of more versus less than 10 pills per day was associated with a much higher odds of nonadherence than twice versus once daily dosing or small differences in the number of types of antiretroviral treatments in a regimen. These results provide insight into the relative importance of various determinants of patient nonadherence that may inform the design of patient educational initiatives and initiatives to simplify treatment regimens.

J Behav Med. 2008 Oct;31(5):445-51. Epub 2008 Aug 23.

Relationship of race-, sexual orientation-, and HIV-related discrimination with adherence to HIV treatment: a pilot study.

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Adherence to highly active antiretroviral therapy (HAART) must be close to perfect in order to maintain suppression of HIV viral load, and to prevent the development of drug resistant strains of HIV. People living with HIV (PLWH) often report low levels of adherence. One variable that has been linked to poor adherence is perceived discrimination; however, research has generally not considered the possible unique effects of different types of discrimination on adherence. The present pilot study aimed to examine the association of three types of discrimination (due to HIV+ status, race, or sexual orientation) with adherence among 57 PLWH. Logistic regression analyses were conducted to demonstrate the relationships between each type of discrimination and self-reported adherence. Racial discrimination significantly predicted lower adherence levels, whereas sexual orientation- and HIV-related discrimination did not. Results underscore the importance of addressing discrimination issues, specifically racial, when designing interventions to improve adherence to HAART.

J Acquir Immune Defic Syndr. 2010 Apr;53(5):648-55.

Conspiracy beliefs about HIV are related to antiretroviral treatment nonadherence among african american men with HIV.

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BACKGROUND: Medical mistrust is prevalent among African Americans and may influence health care behaviors such as treatment adherence. We examined whether a specific form of medical mistrust-HIV conspiracy beliefs (eg, HIV is genocide against African Americans)-was associated with antiretroviral treatment nonadherence among African American men with HIV. METHODS: On baseline surveys, 214 African American men with HIV reported their agreement with 9 conspiracy beliefs, sociodemographic characteristics, depression symptoms, substance use, disease characteristics, medical mistrust, and health care barriers. Antiretroviral medication adherence was monitored electronically for one month postbaseline among 177 men in the baseline sample. RESULTS: Confirmatory factor analysis revealed 2 distinct conspiracy belief subscales: genocidal beliefs (eg, HIV is manmade) and treatment-related beliefs (eg, people who take antiretroviral treatments are human guinea pigs for the government). Both subscales were related to nonadherence in bivariate tests. In a multivariate logistic regression, only treatment-related conspiracies were associated with a lower likelihood of optimal adherence at one-month follow-up (odds ratio = 0.60, 95% confidence interval = 0.37 to 0.96, $P < 0.05$). CONCLUSIONS: HIV conspiracy beliefs, especially those related to treatment mistrust, can contribute to health disparities by discouraging appropriate treatment behavior. Adherence-promoting interventions targeting African Americans should openly address such beliefs.

AIDS Care. 2009 Apr;21(4):520-8.

The influence of symptom experiences and attributions on adherence to highly active anti-retroviral therapy (HAART): a six-month prospective, follow-up study.

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OBJECTIVE: To examine changes in individuals' experiences of symptoms over the first six months of taking highly active anti-retroviral therapy (HAART) and to assess the impact of symptom experiences and attributions on adherence to HAART. METHODS: A prospective study where consecutive HIV positive individuals initiating HAART completed validated questionnaires assessing their experiences of symptoms, depression, beliefs about HAART and adherence, before starting treatment and after one, three and six months of treatment. RESULTS: Rates of low (<95%) adherence to HAART increased over time ($p<0.001$). Overall, the number of HIV or HAART-related symptoms reported did not change significantly over follow-up. However, symptom experiences differed between those reporting high (> or =95%) adherence and those reporting low adherence. Individuals reporting high adherence experienced a decrease in symptoms they attributed to HIV ($p<0.05$), and a decrease in the symptoms they attributed to HAART-side effects ($p<0.05$) over time. This decrease in symptoms over time was not seen among individuals reporting low adherence. A lack of symptomatic improvement was associated with increasing doubts about the continued necessity for HAART ($p<0.05$). CONCLUSIONS: The findings suggest that adherence to HAART is influenced by individuals' experiences of both HIV and HAART-related symptoms. Patients who experience persistent symptoms while on HAART may begin to doubt their continued need for treatment and respond by missing doses. These findings have implications for the development of evidence-based interventions to increase adherence.

Psychosom Med. 2009 Nov;71(9):920-6. Epub 2009 Oct 29.

Overload: impact of incident stressful events on antiretroviral medication adherence and virologic failure in a longitudinal, multisite human immunodeficiency virus cohort study.

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OBJECTIVE: To examine the influence of incident stressful experiences on antiretroviral medication adherence and treatment outcomes. Past trauma history predicts poorer medication adherence and health outcomes. Human immunodeficiency virus (HIV)-infected individuals experience frequently traumatic and stressful events, such as sexual and physical assault, housing instability, and major financial, employment, and legal difficulties. METHODS: We measured prospectively incident stressful and traumatic events, medication adherence, and viral load over 27 months in an eight-site, five-state study. Using multivariable logistic and generalized estimating equation modeling, we assessed the impact of incident stressful events on 27-month changes in self-reported medication adherence and virologic failure (viral load = >or=400 c/mL). RESULTS: Of 474 participants on antiretroviral therapy at baseline, 289 persons were interviewed and still received treatment at 27 months. Participants experiencing the median number of incident stressful events (n = 9) had over twice the predicted odds (odds ratio = 2.32) of antiretroviral medication nonadherence at follow-up compared with those with no events. Stressful events also predicted increased odds of virologic failure during follow-up (odds ratio = 1.09 per event). CONCLUSIONS: Incident stressful events are exceedingly common in the lives of HIV-infected individuals and negatively affect antiretroviral medication adherence and treatment outcomes. Interventions to address stress and trauma are needed to improve HIV outcomes.

J Antimicrob Chemother. 2009 Apr;63(4):636-40. Epub 2009 Jan 18.

The impact of mental health and traumatic life experiences on antiretroviral treatment outcomes for people living with HIV/AIDS.

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Potent antiretroviral therapy (ART) has transformed HIV from a death sentence to a chronic illness. Accordingly, the goal of HIV care has shifted from delaying death to achieving optimal health outcomes through ART treatment. ART treatment success hinges on medication adherence. Extensive research has demonstrated that the primary barriers to ART adherence include mental illness, especially depression and substance abuse, as well as histories of traumatic experiences such as childhood sexual and physical abuse. These psychosocial factors are highly prevalent in people living with HIV/AIDS (PLWHA) and predict poor ART adherence, increased sexual risk behaviours, ART treatment failure, HIV disease progression and higher mortality rates. The efficacy of standard mental health interventions, such as antidepressant treatment and psychotherapy, has been well-defined, and a small but growing body of research demonstrates the potential for such interventions to improve ART adherence and reduce sexual risk behaviours. Despite this evidence, mental disorders in PLWHA frequently go undiagnosed and untreated. Challenges to the provision of mental healthcare for PLWHA in HIV clinical settings include time and resource constraints, lack of expertise in psychiatric diagnosis and treatment, and lack of available mental health referral services. Future research should prioritize the evaluation of mental health interventions that are cost-effective and feasible for widespread integration into HIV clinical care; the impact of such interventions on ART adherence and clinical outcomes; and interventions to identify individuals with histories of traumatic experiences and to elucidate the mechanisms through which such histories pose barriers to effective HIV treatment.

J Antimicrob Chemother. 2009 Sep;64(3):599-606. Epub 2009 Jul 14.

Factors associated with non-adherence to long-term highly active antiretroviral therapy: a 10 year follow-up analysis with correction for the bias induced by missing data.

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OBJECTIVES: The aim of this study was to identify factors associated with non-adherence over a 10 year follow-up of the APROCO-COPILOTE cohort during the maintenance phase of highly active antiretroviral therapy (HAART). METHODS: Overall, 1010 patients participated in this analysis, each having had at least 12 months of follow-up after HAART initiation and at least one self-reported adherence measure available during the follow-up period (month 12-month 120). Data collection was based on clinical records and self-administered questionnaires that gathered patients' psychosocial characteristics and experience with HIV disease and treatment. First, a generalized estimating equations (GEE) model was used to identify non-adherence predictors. Secondly, a Heckman two-stage approach was used in order to account for missing data bias and to measure the extent to which this could affect the results of the first model. RESULTS: Non-adherent behaviour was reported by 747 patients (2070 visits). After correcting for the bias due to missing data, non-adherence was independently associated with side effects, having a three times or more daily dosing regimen, experience of being at clinical stage B/C and being diagnosed as HIV-positive for <6 months. Non-adherence was more likely among patients who were younger, had children, were born in the European Union, had depressive symptoms, consumed alcohol daily and declared a lack of support from their main partner. Adjusting for missing outcome data changed the pattern of predictors. CONCLUSIONS: Reasons for non-adherence depended on both psychosocial conditions and treatment-related characteristics. To improve long-term patient outcomes for those at risk of adherence failure, tailor-made patient-specific psychosocial interventions and regimen-based strategies with improved tolerance need to be implemented.

Treatment Adherence Literature Review

Part 2: Intervention Research

Arch Intern Med. 2010 Feb 8;170(3):240-50.

Standard care impact on effects of highly active antiretroviral therapy adherence interventions: A meta-analysis of randomized controlled trials.

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BACKGROUND: Poor adherence to medication limits the effectiveness of treatment for human immunodeficiency virus. Systematic reviews can identify practical and effective interventions. Meta-analyses that control for variability in standard care provided to control groups may produce more accurate estimates of intervention effects. METHODS: To examine whether viral load and adherence success rates could be accurately explained by the active content of highly active antiretroviral therapy (HAART) adherence interventions when controlling for variability in care delivered to controls, databases were searched for randomized controlled trials of HAART adherence interventions published from 1996 to January 2009. A total of 1342 records were retrieved, and 52 articles were examined in detail. Directly observed therapy and interventions targeting specific patient groups (ie, psychiatric or addicted patients, patients <18 years) were excluded, yielding a final sample of 31 trials. Two coders independently retrieved study details. Authors were contacted to complete missing data. RESULTS: Twenty studies were included in the analyses. The content of adherence care provided to control and intervention groups predicted viral load and adherence success rates in both conditions ($P < .001$ for all comparisons), with an estimated impact of optimal adherence care of 55 percentage points. After controlling for variability in care provided to controls, the capacity of the interventions accurately predicted viral load and adherence effect sizes ($R(2) = 0.78$, $P = .02$; $R(2) = 0.28$, $P < .01$). Although interventions were generally beneficial, their effectiveness reduced noticeably with increasing levels of standard care. CONCLUSIONS: Intervention and control patients were exposed to effective adherence care. Future meta-analyses of (behavior change) interventions should control for variability in care delivered to active controls. Clinical practice may be best served by implementing current best practice.

Curr HIV/AIDS Rep. 2008 Nov;5(4):193-203.

The information-motivation-behavioral skills model of antiretroviral adherence and its applications.

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Suboptimal adherence to highly active antiretroviral therapy (HAART) may have serious consequences for HIV patients, and for public health overall. The Information-Motivation-Behavioral Skills (IMB) model of HAART adherence can be used to understand the dynamics of HAART adherence and to intervene with patients to promote more optimal levels of adherence. This article reviews the core hypotheses of the IMB model of HAART adherence and describes available correlational and experimental evaluations of the model, outcomes of adherence intervention trials that applied the model, and IMB model-based interventions that are currently under evaluation. It then explores one potential promising application of the model that uses a protocol originally developed and demonstrated as a structured patient-centered, provider-delivered risk reduction intervention to deliver information, motivation, and behavioral skills-based adherence-promotion strategies. This protocol could be incorporated into clinical practice as a valuable tool in working with patients individually.

Treatment Adherence Literature Review

Lancet. 2009 Dec 19;374(9707):2064-71. Epub 2009 Nov 30.

Directly observed antiretroviral therapy: a systematic review and meta-analysis of randomised clinical trials.

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Comment in: Lancet. 2009 Dec 19;374(9707):2030-2.

Abstract

BACKGROUND: Directly observed therapy has been recommended to improve adherence for patients with HIV infection who are on highly active antiretroviral therapy, but the benefit and cost-effectiveness of this approach has not been established conclusively. We did a systematic review and meta-analysis of randomised trials of directly observed versus self-administered antiretroviral treatment.

METHODS: We did duplicate searches of databases (from inception to July 27, 2009), searchable websites of major HIV conferences (up to July, 2009), and lay publications and websites (March-July, 2009) to identify randomised trials assessing directly observed therapy to promote adherence to antiretroviral therapy in adults. Our primary outcome was virological suppression at study completion. We calculated relative risks (95% CIs), and pooled estimates using a random-effects method.

FINDINGS: 12 studies met our inclusion criteria; four of these were done in groups that were judged to be at high risk of poor adherence (drug users and homeless people). Ten studies reported on the primary outcome (n=1862 participants); we calculated a pooled relative risk of 1.04 (95% CI 0.91-1.20, p=0.55), and noted moderate heterogeneity between the studies (I(2)= 53.8%, 95% CI 0-75.7, p=0.0247) for directly observed versus self-administered treatment.

INTERPRETATION: Directly observed antiretroviral therapy seems to offer no benefit over self-administered treatment, which calls into question the use of such an approach to support adherence in the general patient population.

FUNDING: None.

J Acquir Immune Defic Syndr. 2010 Jun;54(2):167-79.

Effect of directly observed therapy for highly active antiretroviral therapy on virologic, immunologic, and adherence outcomes: a meta-analysis and systematic review.

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Abstract

INTRODUCTION: Directly observed therapy of highly active antiretroviral therapy (DOT-HAART) is a feasible adherence intervention. Prospective DOT-HAART studies have shown mixed results, and optimal target groups have yet to be defined. We performed a meta-analysis and systematic review to assess the effect of DOT-HAART on adherence and virologic and immunologic response.

METHODS: We performed a comprehensive search through August 2009 to identify peer-reviewed controlled studies that involved outpatient DOT-HAART among adults and reported at least 1 outcome assessed in this meta-analysis. Random-effects meta-analyses were performed; differences in effect on virologic suppression were examined using stratified meta-analyses and meta-regression on several study characteristics.

RESULTS: Seventeen studies met inclusion criteria. Compared with control groups, DOT-HAART recipients were more likely to achieve an undetectable viral load (random effects risk ratio 1.24, 95% confidence interval (CI): 1.08 to 1.41), a greater increase in CD4 cell count (random effects weighted mean difference 43 cells/microL, 95% CI: 12 to 74 cells/microL), and HAART adherence of > or =95% (random effects risk ratio 1.17, 95% CI: 1.03 to 1.32). Results varied with respect to virologic response. DOT-HAART did not have a significant effect on virologic suppression when restricted to randomized controlled studies. Post-treatment effect was not observed in a limited number of studies.

CONCLUSIONS: DOT-HAART had a significant effect on virologic, immunologic, and adherence outcomes, although its efficacy was not supported when restricting analysis to randomized controlled trials. DOT-HAART shows greatest treatment effect when targeting individuals with greater risk of nonadherence and when delivering the intervention that maximizes participant convenience and provides enhanced adherence support. Further investigation is needed to assess the postintervention effect and cost-effectiveness of DOT-HAART.

Ann Behav Med. 2010 Oct 5. [Epub ahead of print]

Improving Coping Skills for Self-management of Treatment Side Effects Can Reduce Antiretroviral Medication Nonadherence among People Living with HIV.

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BACKGROUND: Human immunodeficiency virus (HIV) treatment side effects have a deleterious impact on treatment adherence, which is necessary to optimize treatment outcomes including morbidity and mortality. PURPOSE: To examine the effect of the Balance Project intervention, a five-session, individually delivered HIV treatment side effects coping skills intervention on antiretroviral medication adherence. METHODS: HIV+ men and women (N = 249) on antiretroviral therapy (ART) with self-reported high levels of ART side effect distress were randomized to intervention or treatment as usual. The primary outcome was self-reported ART adherence as measured by a combined 3-day and 30-day adherence assessment. RESULTS: Intent-to-treat analyses revealed a significant difference in rates of nonadherence between intervention and control participants across the follow-up time points such that those in the intervention condition were less likely to report nonadherence. Secondary analyses revealed that intervention participants were more likely to seek information about side effects and social support in efforts to cope with side effects. CONCLUSIONS: Interventions focusing on skills related to ART side-effects management show promise for improving ART adherence among persons experiencing high levels of perceived ART side effects.

Psychosom Med. 2008 Jun;70(5):593-7. Epub 2008 Jun 2.

Co-occurrence of treatment nonadherence and continued HIV transmission risk behaviors: implications for positive prevention interventions.

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Effective treatment regimens for HIV infection demand very high levels of adherence and people infected with HIV are expected to adhere to safer sex and drug use practices throughout their lives. Treatment nonadherence overlaps with continued unsafe sexual practices for some people living with HIV/AIDS. The co-occurrence of nonadherence and HIV transmission risk behavior poses particular risk for the spread of drug-resistant variants of HIV. There are common correlates of both nonadherence and risk behavior, particularly substance use and depression. Interventions designed to address treatment nonadherence and those designed to reduce risk behavior also share common elements, particularly self-efficacy enhancement and behavioral skills training. The common correlates and shared intervention elements suggest that integrated intervention approaches that simultaneously address adherence and risk reduction may be feasible. Research is currently testing interventions that simultaneously increase HIV treatment adherence and reduce behaviors that risk HIV transmission.

J Adv Nurs. 2010 Sep;66(9):1915-30.

Implementation of antiretroviral therapy adherence interventions: a realist synthesis of evidence.

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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 enroll in interventions that protect their confidentiality, to attend when scheduling is responsive to 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.

The Lancet 10 November 2010(Article in Press DOI: 10.1016/S0140-6736(10)61997-6)

Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial

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Mobile (cell) phone communication has been suggested as a method to improve delivery of health services. However, data on the effects of mobile health technology on patient outcomes in resource-limited settings are limited. We aimed to assess whether mobile phone communication between health-care workers and patients starting antiretroviral therapy in Kenya improved drug adherence and suppression of plasma HIV-1 RNA load. WelTel Kenya1 was a multisite randomised clinical trial of HIV-infected adults initiating antiretroviral therapy (ART) in three clinics in Kenya. Patients were randomised (1:1) by simple randomisation with a random number generating program to a mobile phone short message service (SMS) intervention or standard care. Patients in the intervention group received weekly SMS messages from a clinic nurse and were required to respond within 48 h. Randomisation, laboratory assays, and analyses were done by investigators masked to treatment allocation; however, study participants and clinic staff were not masked to treatment. Primary outcomes were self-reported ART adherence (>95% of prescribed doses in the past 30 days at both 6 and 12 month follow-up visits) and plasma HIV-1 viral RNA load suppression (<400 copies per mL) at 12 months. The primary analysis was by intention to treat. This trial is registered withClinicalTrials.gov,NCT00830622. Between May, 2007, and October, 2008, we randomly assigned 538 participants to the SMS intervention (n=273) or to standard care (n=265). Adherence to ART was reported in 168 of 273 patients receiving the SMS intervention compared with 132 of 265 in the control group (relative risk [RR] for non-adherence 0·81, 95% CI 0·69–0·94; p=0·006). Suppressed viral loads were reported in 156 of 273 patients in the SMS group and 128 of 265 in the control group, (RR for virologic failure 0·84, 95% CI 0·71–0·99; p=0·04). The number needed to treat (NNT) to achieve greater than 95% adherence was nine (95% CI 5·0–29·5) and the NNT to achieve viral load suppression was 11 (5·8–227·3). Patients who received SMS support had significantly improved ART adherence and rates of viral suppression compared with the control individuals. Mobile phones might be effective tools to improve patient outcome in resource-limited settings. US President's Emergency Plan for AIDS Relief.

Ann Behav Med. 2010 Oct;40(2):176-83.

Self-reevaluation as a critical component in sustained viral load change for HIV+ adults with alcohol problems.

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Self-reevaluation is one of the ten processes of change in the transtheoretical model and involves cognitive reappraisal of how behavior change is part of one's identity. Although self-reevaluation is a critical motivator for individuals in the contemplation stage of change, few studies have examined its impact on disease progression associated with sustained behavior change. This study investigated the contribution of self-reevaluation on sustained viral load improvement among 143 participants in a randomized controlled trial testing an eight-session intervention (Project Positive Living through Understanding and Support) designed to improve treatment adherence among HIV+ adults with alcohol problems. Participants' self-reevaluation scores at 3 months emerged as significant and independent predictors of sustained improvement in viral load at 6 months, over and above self-reported HAART dose adherence ($p < 0.05$). Results underscore the role of self-reevaluation as a critical factor in behavioral interventions and highlight its role in sustained change necessary to slow disease progression.

Curr HIV/AIDS Rep. 2010 Feb;7(1):44-51.

Antiretroviral adherence interventions: translating research findings to the real world clinic.

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The success of potent combination antiretroviral therapy (ART) for HIV infection is compromised primarily by failure to maintain optimal levels of adherence over the long term. Recent reviews suggest behavioral interventions to promote ART adherence can have significant effects, but these tend to be small and to diminish over time; sustained improvements in biomarkers are particularly elusive. In this article, we update current reviews, focusing specifically on the 13 studies evaluating behavioral interventions to promote ART adherence published since September 2007. We describe the range of intervention strategies employed and qualitatively summarize findings of their efficacy. In conclusion, we consider implications and offer strategies for enhancing adherence in clinic-based HIV care prior to ART initiation, at initiation, and over the course of treatment.

Curr Infect Dis Rep. 2008 Nov;10(6):515-21.

Strategies for promoting adherence to antiretroviral therapy: a review of the literature.

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The success of antiretroviral therapy (ART) for HIV infection, though widespread and resounding, has been limited by inadequate adherence to its unforgiving regimens, especially over the long term. This article summarizes the literature on behavioral interventions to promote ART adherence and highlights some of the most recent and innovative research on patient education and case management, modified directly observed therapy, contingency management, interventions emphasizing social support, and novel technologies to promote awareness. Research in the area of adherence in pediatric HIV infection and in resource-constrained international settings also is considered. Although adherence interventions have been successful in experimental trials, they may not be feasible or adaptable given the constraints of real-world clinics and community-based settings. Implementation and dissemination of adherence interventions needs increased attention as ART adherence research moves beyond its first decade. We conclude with suggestions for incorporating research findings into clinical practice.

Curr Opin Psychiatry. 2010 Mar;23(2):139-44.

Innovation in sexually transmitted disease and HIV prevention: internet and mobile phone delivery vehicles for global diffusion.

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Abstract

PURPOSE OF REVIEW: Efficacious behavioral interventions and practices have not been universally accepted, adopted, or diffused by policy makers, administrators, providers, advocates, or consumers. Biomedical innovations for sexually transmitted disease (STD) and HIV prevention have been embraced but their effectiveness is hindered by behavioral factors. Behavioral interventions are required to support providers and consumers for adoption and diffusion of biomedical innovations, protocol adherence, and sustained prevention for other STDs. Information and communication technology such as the Internet and mobile phones can deliver behavioral components for STD/HIV prevention and care to more people at less cost.

RECENT FINDINGS: Recent innovations in STD/HIV prevention with information and communication technology-mediated behavioral supports include STD/HIV testing and partner interventions, behavioral interventions, self-management, and provider care. Computer-based and Internet-based behavioral STD/HIV interventions have demonstrated efficacy comparable to face-to-face interventions. Mobile phone STD/HIV interventions using text-messaging are being broadly utilized but more work is needed to demonstrate efficacy. Electronic health records and care management systems can improve care, but interventions are needed to support adoption.

SUMMARY: Information and communication technology is rapidly diffusing globally. Over the next 5-10 years smart-phones will be broadly disseminated, connecting billions of people to the Internet and enabling lower cost, highly engaging, and ubiquitous STD/HIV prevention and treatment support interventions.

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AIDS Care. 2009 Oct;21(10):1321-34.

Common elements in self-management of HIV and other chronic illnesses: an integrative framework.

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HIV/AIDS is widely recognized as a chronic illness within HIV care, but is often excluded from chronic disease lists outside the field. Similar to other chronic diseases, HIV requires lifetime changes in physical health, psychological functioning, social relations, and adoption of disease-specific regimens. The shift from acute to chronic illness requires a self-management model in which patients assume an active and informed role in healthcare decision making to change behaviors and social relations to optimize health and proactively address predictable challenges of chronic diseases generally and HIV specifically. This article reviews literature on chronic disease self-management to identify factors common across chronic diseases, highlight HIV-specific challenges, and review recent developments in self-management interventions for people living with HIV (PLH) and other chronic diseases. An integrated framework of common elements or tasks in chronic disease self-management is presented that outlines 14 elements in three broad categories: physical health; psychological functioning; and social relationships. Common elements for physical health include: a framework for understanding illness and wellness; health promoting behaviors; treatment adherence; self-monitoring of physical status; accessing appropriate treatment and services; and preventing transmission. Elements related to psychological functioning include: self-efficacy and empowerment; cognitive skills; reducing negative emotional states; and managing identity shifts. Social relationship elements include: collaborative relationships with healthcare providers; social support; disclosure and stigma management; and positive social and family relationships. There is a global need to scale up chronic disease self-management services, including for HIV, but there are significant challenges related to healthcare system and provider capacities, and stigma is a significant barrier to HIV-identified service utilization. Recognizing that self-management of HIV has more in common with all chronic diseases than differences suggests that the design and delivery of HIV support services can be incorporated into combined or integrated prevention and wellness services.

Treatment Adherence Literature Review

Curr Opin HIV AIDS. 2009 Nov;4(6):488-92.

Adherence to antiretroviral therapy: the more you look, the more you see.

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PURPOSE OF REVIEW: There is evolving understanding of adherence to antiretroviral therapy (ART) and the consequences of nonadherence. The present review aims to discuss recent research findings that illuminate lingering clinical questions or contribute to the contextual framework for future research.
RECENT FINDINGS: Although some patients can achieve undetectable viral load at moderate adherence levels, studies confirmed that achieving very high adherence optimizes virological and clinical outcomes. In computer modeling, earlier initiation of ART despite suboptimal adherence was associated with improved survival and quality-adjusted life years. Better adherence and virological outcomes occurred when ART was initiated during hospitalization versus outpatient setting, and when depressed patients were treated with selective serotonin reuptake inhibitors. Differential adherence to individual drugs in an antiretroviral regimen appears to be common. Preliminary data from randomized studies designed to evaluate patient-selected treatment partners showed no clear benefit on long-term viral suppression.
SUMMARY: Earlier initiation of ART may be desirable even in some patients with suboptimal adherence. Adherence should be reinforced during periods of viral suppression, maximum adherence should be targeted, and attention paid to differential adherence and treatment of depression.

AIDS Care. 2009 Oct;21(10):1321-34.
Med Decis Making. 2008 May-Jun;28(3):359-76. Epub 2008 Mar 18.

The cost-effectiveness of counseling strategies to improve adherence to highly active antiretroviral therapy among men who have sex with men.

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OBJECTIVE: Inadequate adherence to highly active antiretroviral therapy (HAART) may lead to poor health outcomes and the development of HIV strains that are resistant to HAART. The authors developed a model to evaluate the cost-effectiveness of counseling interventions to improve adherence to HAART among men who have sex with men (MSM). METHODS: The authors developed a dynamic
compartmental model that incorporates HIV treatment, adherence to treatment, and infection transmission and progression. All data estimates were obtained from secondary sources. The authors evaluated a counseling intervention given prior to initiation of HAART and before all changes in drug regimens, combined with phone-in support while on HAART. They considered a moderate-prevalence and a high-prevalence population of MSM. RESULTS: If the impact of HIV transmission is ignored, the counseling intervention has a cost-effectiveness ratio of $25,500 per quality-adjusted life year (QALY) gained. When HIV transmission is included, the cost-effectiveness ratio is much lower: $7400 and $8700 per QALY gained in the moderate- and high-prevalence populations, respectively. When the intervention is twice as costly per counseling session and half as effective as estimated in the base case (in terms of the number of individuals who become highly adherent, and who remain highly adherent), then the intervention costs $17,100 and $19,600 per QALY gained in the 2 populations, respectively. CONCLUSIONS: Counseling to improve adherence to HAART increased length of life, modestly reduced HIV transmission, and cost substantially less than $50,000 per QALY gained over a wide range of assumptions but did not reduce the proportion of drug-resistant strains. Such counseling provides only modest benefit as a tool for HIV prevention but can provide significant benefit for individual patients at an affordable cost.

Treatment Adherence Literature Review

Part 3: Treatment Adherence and Substance Use

Lancet. 2010 Jul 31;376(9738):367-87.

Treatment of medical, psychiatric, and substance-use comorbidities in people infected with HIV who use drugs.

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HIV-infected drug users have increased age-matched morbidity and mortality compared with HIV-infected people who do not use drugs. Substance-use disorders negatively affect the health of HIV-infected drug users, who also have frequent medical and psychiatric comorbidities that complicate HIV treatment and prevention. Evidence-based treatments are available for the management of substance-use disorders, mental illness, HIV and other infectious complications such as viral hepatitis and tuberculosis, and many non-HIV-associated comorbidities. Tuberculosis co-infection in HIV-infected drug users, including disease caused by drug-resistant strains, is acquired and transmitted as a consequence of inadequate prescription of antiretroviral therapy, poor adherence, and repeated interfaces with congregate settings such as prisons. Medication-assisted therapies provide the strongest evidence for HIV treatment and prevention efforts, yet are often not available where they are needed most. Antiretroviral therapy, when prescribed and adherence is at an optimum, improves health-related outcomes for HIV infection and many of its comorbidities, including tuberculosis, viral hepatitis, and renal and cardiovascular disease. Simultaneous clinical management of multiple comorbidities in HIV-infected drug users might result in complex pharmacokinetic drug interactions that must be adequately addressed. Moreover, interventions to improve adherence to treatment, including integration of health services delivery, are needed. Multifaceted, interdisciplinary approaches are urgently needed to achieve parity in health outcomes in HIV-infected drug users.

Treatment Adherence Literature Review

AIDS. 2010 Jan 28;24(3):331-40.

Medication-assisted treatment and HIV/AIDS: aspects in treating HIV-infected drug users.

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Drug use and HIV/AIDS remain serious public health issues in the US. The intersection of the twin epidemics of HIV and drug/alcohol use, results in difficult medical management issues for the healthcare providers who work in the HIV prevention and treatment fields. Access to care and treatment, medication adherence to multiple therapeutic regimens and concomitant drug-drug interactions of prescribed treatments are difficult barriers for drug users to overcome without directed interventions. Injection drug users are frequently disenfranchised from medical care and suffer stigma and discrimination creating additional barriers to care and treatment for their substance use disorders as well as HIV infection. Controlling the transmission of HIV will require access to care and treatment of individuals who abuse illicit drugs and alcohol. Improving health outcomes (e.g. access to and adherence to antiretroviral therapy) among HIV-infected substance users will also require access to evidenced-based pharmacological therapies for the treatment of drug abuse and dependence. The current review presents an overview of issues regarding the use of medication-assisted treatments for substance abuse and dependence among HIV-infected individuals, providing medical management paradigms for their care and treatment.

J Acquir Immune Defic Syndr. 2009 Oct 1;52(2):180-202.
Alcohol use and antiretroviral adherence: review and meta-analysis.

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BACKGROUND: Alcohol use is frequently implicated as a factor in nonadherence to highly active antiretroviral therapy (HAART). There have not been efforts to systematically evaluate findings across studies. This meta-analysis provides a quantitative evaluation of the alcohol-adherence association by aggregating findings across studies and examining potential moderators.
METHODS: Literature searches identified 40 qualifying studies totaling over 25,000 participants. Studies were coded on several methodological variables.
RESULTS: In the combined analysis, alcohol drinkers were approximately 50%-60% as likely to be classified as adherent [odds ratio (OR) = 0.548, 95% confidence interval (CI): 0.490 to 0.612] compared with abstainers (or those who drank relatively less). Effect sizes for problem drinking, defined as meeting the National Institute on Alcohol Abuse and Alcoholism criteria for at-risk drinking or criteria for an alcohol use disorder, were greater (OR = 0.474, 95% CI = 0.408 to 0.550) than those reflecting any or global drinking (OR = 0.604, 95% CI = 0.531 to 0.687). Several variables moderated the alcohol-adherence association.
CONCLUSIONS: Results support a significant and reliable association of alcohol use and medication nonadherence. Methodological variables seem to moderate this association and could contribute to inconsistent findings across studies. Future research would benefit from efforts to characterize theoretical mechanisms and mediators and moderators of the alcohol-adherence association.

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**Social and structural determinants of HAART access and adherence among injection
drug users.**

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Highly active antiretroviral therapy (HAART) has dramatically improved health outcomes among people living with HIV/AIDS. However, significant rates of HIV-related morbidity and mortality have persisted among HIV-positive injection drug users (IDU) globally. To date, research as well as programmatic and policy responses have failed to adequately address barriers to HAART access and adherence among IDU both in developing/transitional and developed countries. A review of existing literature suggests that this is due to a shortage of context-specific evidence and an overemphasis on individual-level and behavioural variables. We propose a conceptual shift away from understanding suboptimal HAART adherence as determined predominantly by individual factors modifiable through individually focused interventions, towards a greater acknowledgement of the influence of social and structural factors such as stigmatization and social exclusion, unstable housing environments, the organization of health care systems and the continued prohibitionist approach to illicit drug policy. Globally, the future of a successful HAART treatment approach for HIV-positive IDU relies largely on a more careful consideration of these social and structural barriers that IDU face and, importantly, on a serious commitment to effect social and structural changes that will foster conditions which allow IDU to enjoy the full benefits of HAART.

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Substance abuse, adherence with antiretroviral therapy, and clinical outcomes among HIV-infected individuals.

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Substance abuse and addiction are highly prevalent in HIV-infected individuals. Substance abuse is an important comorbidity that affects the delivery and outcomes of HIV medical management. In this paper I will review data examining the associations between substance abuse and HIV treatment and potential strategies to improve outcomes in this population that warrant further investigation. Current - but not past - substance abuse adversely affects engagement in care, acceptance of antiretroviral therapy, adherence with therapy, and long-term persistence in care. Substance abuse treatment appears to facilitate engagement in HIV care, and access to evidence-based treatment for substance abuse is central to addressing the HIV epidemic. Strategies that show promise for HIV-infected substance abusers include integrated treatment models, directly observed therapy, and incentive-based interventions.

AIDS Care. 2008 Nov;20(10):1202-10.

The effects of low literacy and cognitive impairment on medication adherence in HIV-positive injecting drug users.

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Low literacy and cognitive impairment have each been separately identified as risks for non-adherence in HIV infection. However, no studies to date have evaluated these skill deficits in combination. We therefore characterized the nature of literacy and cognitive skills in a sample of HIV-positive injecting drug users and assessed their combined effects on adherence. A community-recruited sample of 57 HIV-positive injecting drug users completed the study. Participants were classified into one of four groups based on their performance on a reading test and a brief neuropsychological battery: high literacy/high cognition, low literacy/high cognition, high literacy/low cognition and low literacy/low cognition. Chi-square and bivariate analyses were used to characterize the literacy and cognitive skills of the overall sample and logistic regression analysis was used to test the relation of the four groups to non-adherence (< 95%). In general, performance on measures of literacy and cognitive functioning were below average, with severe deficits noted in psychomotor functioning. Additionally, after adjusting for recent cocaine use, those classified as low literate/low cognition were over nine times more likely to be non-adherent than the referent high literate/high cognition group. Low literacy and cognitive impairment placed HIV-positive drug users at high risk for non-adherence, even after adjusting for recent cocaine use. The findings suggest that targeted interventions to improve these skill deficits in this population may help to improve adherence to HIV medications.