



February 2017 – SUPPORT Summary of a systematic review

What are the effects of behavioral interventions to improve adherence to antiretroviral therapy?

Adherence can be defined as the extent to which patients follow the instructions they are given for prescribed treatments. Highly active antiretroviral therapy (HAART) has demonstrated remarkable success in reducing morbidity, mortality, and healthcare costs for HIV-positive people. The lifesaving benefits of HAART are not achieved if patients do not take them as prescribed. Behavioral interventions are intended to assist patients with this task.

Key messages

- Behavioral interventions probably lead to slightly better adherence to HAART.
- Behavioral interventions may slightly improve the number of patients with undetectable viral load (a laboratory measure of successful HAART).
- No studies measuring patient outcomes such as morbidity and mortality were identified.
- Only one included study was conducted in a low-income country.



Who is this summary for?

Clinicians and people making decisions concerning the implementation of interventions aimed at improving adherence to HAART.

! This summary includes:

- Key findings from research based on a systematic review
- Considerations about the relevance of this research for low-income countries

X Not included:

- Recommendations
- Additional evidence not included in the systematic review
- Detailed descriptions of interventions or their implementation

This summary is based on the following systematic review:

Simoni JM, Pearson CR, Pantalone DW, et al. Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials. *J Acquir Immune Defic Syndr* 2006; 43(Suppl 1):S23-35.

Simoni JM. Antiretroviral adherence interventions: translating research findings to the real world clinic. *Curr HIV/AIDS Rep* 2010; 7:44-51.

What is a systematic review?

A summary of studies addressing a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise the relevant research, and to collect and analyse data from the included studies

SUPPORT was an international project to support the use of policy relevant reviews and trials to inform decisions about maternal and child health in low- and middle-income countries, funded by the European Commission (FP6) and the Canadian Institutes of Health Research.

Glossary of terms used in this report:
www.supportsummaries.org/glossary-of-terms

Background references on this topic:
See back page

Background

Highly active antiretroviral therapy (HAART) has demonstrated remarkable success in inhibiting HIV viral replication and reducing morbidity, mortality, and overall healthcare costs for HIV-positive people. Without strict attention to dosing schedules and dietary restrictions, the effectiveness of HAART is severely compromised. Non-adherence to HAART is very common. Potential causes include problems with the regimen (e.g. adverse effects), poor instructions, poor provider-patient relationships, poor memory, and patients' disagreement with the need for treatment or inability to pay for it. Given the multifaceted dimensions of this phenomenon, there is a wide array of possible interventions. Behavioral interventions represent a key strategy for addressing non-adherence to HAART.

How this summary was prepared

After searching widely for systematic reviews that can help inform decisions about health systems, we have selected ones that provide information that is relevant to low-income countries. The methods used to assess the reliability of the review and to make judgements about its relevance are described here: www.supportsummaries.org/how-support-summaries-are-prepared/

Knowing what's not known is important

A reliable review might not find any studies from low-income countries or might not find any well-designed studies. Although that is disappointing, it is important to know what is not known as well as what is known.

A lack of evidence does not mean a lack of effects. It means the effects are uncertain. When there is a lack of evidence, consideration should be given to monitoring and evaluating the effects of the intervention, if it is used.

About the systematic review underlying this summary

Review objective: To summarise literature on the effects of patient support strategies and education for improving adherence to highly active antiretroviral therapy (HAART) in people living with HIV/AIDS.

Types of	What the review authors searched for	What the review authors found
Study designs & Interventions	Randomised trials evaluating behavioral interventions to improve adherence to HAART	19 randomised trials of diverse behavioral interventions: 1-on-1 counselling (10 trials), and group format (3). Components of the intervention were: didactic information on HAART (15 studies); interactive discussions addressing cognitions, motivations, and expectations (15); Behavioral strategies (16), such as cue dosing or cognitive-behavior therapy; external reminders such as pagers (5). Many interventions included more than one of these components.
Participants	Adults infected with HIV and receiving HAART	7 studies restricted inclusion to patients exhibiting some marker of risk for non-adherence, such as poor baseline adherence or detectable viral load. Participants in the US studies were mostly racial/ethnic minorities.
Settings	Any setting	Most studies (16) studies took place in outpatient HIV primary care clinics in high-income countries: United States (14), Spain (2), France (2) and Switzerland (1).
Outcomes	Any measure of adherence or HIV-1 RNA viral load (a measure of successful HAART)	Adherence was measured in 18 studies. Data on undetectable viral load were available from 14 studies.

Date of most recent search: September 2005 in Simoni 2006, updated October 2009 in Simoni 2010

Limitations: This is a well-conducted systematic review with only minor limitations.

Simoni JM, Pearson CR, Pantalone DW, et al. Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials. *J Acquir Immune Defic Syndr* 2006; 43(Suppl 1):S23-35.

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Summary of findings

This review found 19 studies conducted in high-income countries, mostly in primary care HIV clinics. Studies evaluated behavioral interventions consisting of one or more of the following components: didactic information, interactive discussion, behavioral therapy, and reminders.

- Behavioral interventions probably lead to slightly better adherence to HAART. The certainty of this evidence is moderate.
- Behavioral interventions may slightly improve the number of patients with undetectable viral load. The certainty of this evidence is low.
- No studies measuring patient outcomes such as morbidity and mortality were identified.

About the certainty of the evidence (GRADE) *

⊕⊕⊕⊕

High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate.

⊕⊕○○

Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

* This is sometimes referred to as 'quality of evidence' or 'confidence in the estimate'.

† Substantially different = a large enough difference that it might affect a decision

See last page for more information.

Behavioral interventions for patients receiving HAART						
People	Adults infected with HIV and receiving highly active antiretroviral therapy (HAART)					
Settings	Any setting					
Intervention	Behavioral interventions					
Comparison	Routine care or less intense behavioral interventions					
Outcomes	Absolute effects		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Without a behavioral intervention	With a behavioral intervention Difference (Margin of error)				
Adherence to HAART (>95%)	50 per 100	60 per 100 (54 to 66)	1.5 (1.16 to 1.94)	1633 (18 studies)	⊕⊕⊕○ Moderate	An update of the review including 10 additional randomised trials, found 9/10 beneficial
Viral load (undetectable)	55 per 100	60 per 100 (55 to 66)	1.25 (0.99 to 1.59)	1247 (14 studies)	⊕⊕○○ Low	An update of the review including 8 additional randomised trials, found mixed results for viral load
Patient outcomes	No data were reported for this outcome.					
Margin of error = Confidence interval (95% CI) RR: Risk ratio GRADE: GRADE Working Group grades of evidence (see above and last page)						

Relevance of the review for low-income countries

→ Findings	▷ Interpretation*
APPLICABILITY	
<p>→ All studies were conducted in high-income countries. The update of the review includes 3 studies in Brazil, China, and Mozambique, with mixed results.</p>	<p>▷ There are several ways in which the effects of interventions to improve adherence in high-income countries and low-income countries might differ, for instance cultural differences or availability of technologies.</p> <p>▷ In some regions, especially in sub-Saharan Africa, HAART programs have started recently and attrition is a major problem.</p>
EQUITY	
<p>→ The included studies did not address equity issues.</p>	<p>▷ There might be differential effects of behavioral interventions on HAART adherence according to gender, education, religion, socioeconomic status, and racial or ethnic factors.</p>
ECONOMIC CONSIDERATIONS	
<p>→ None of the included studies assessed costs associated with behavioral interventions for improving adherence to HAART.</p>	<p>▷ Effective treatment of HIV is highly cost-effective. However, some behavioral interventions may be very expensive, especially when substantial human resources are required. This may pose a burden in low-income countries in addition to the already costly provision of HAART.</p>
MONITORING & EVALUATION	
<p>→ Adherence was measured by self-report or other unreliable methods in some studies.</p> <p>→ This review was not able to determine which components of combined interventions are the ones that increase adherence.</p> <p>→ There was little information about costs and adverse effects in the included studies.</p>	<p>▷ Measuring adherence is a complex task and frequently used methods such as self-report may lack both sensitivity and specificity. Future studies should use objective measures to provide a more accurate measure of true adherence, although these are more expensive.</p> <p>▷ Future research should investigate which components of behavioral interventions improve adherence.</p> <p>▷ Interventions to increase adherence consume resources and attempts to increase adherence can have adverse effects, such as loss of privacy and autonomy, and increased adverse effects of treatments. Adverse effects and costs should be monitored, as well as adherence.</p>

*Judgements made by the authors of this summary, not necessarily those of the review authors, based on the findings of the review and consultation with researchers and policymakers in low-income countries. For additional details about how these judgements were made see: www.supportsummaries.org/methods

Additional information

Related literature

Mills EJ, Lester R, Thorlund K, et al. Interventions to promote adherence to antiretroviral therapy in Africa: a network meta-analysis. *Lancet HIV* 2014; 1(3):e104-11.

Haynes RB, Ackloo E, Sahota N, et al. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2008; (2):CD000011.

Manias E, Williams A. Medication adherence in people of culturally and linguistically diverse backgrounds: a meta-analysis. *Ann Pharmacother* 2010; 44:964-82.

Hart JE, Jeon CY, Ivers LC, et al. Effect of directly observed therapy for highly active antiretroviral therapy on virologic, immunologic, and adherence outcomes: a meta-analysis and systematic review. *J Acquir Immune Defic Syndr* 2010; 54:167-79.

Mills EJ, Nachega JB, Buchan I, et al. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis. *JAMA* 2006 9;296:679-90.

Reisner MSL, Mimiaga MJ, Skeer MM, et al. A review of HIV antiretroviral adherence and intervention studies among HIV-infected youth. *Top HIV Med* 2009; 17:14-25.

Malta M, Magnanini MMF, Strathdee SA, et al. Adherence to antiretroviral therapy among HIV-infected drug users: a meta-analysis. *AIDS Behav* 2010; 14:731-47.

Wise J, Operario D. Use of electronic reminder devices to improve adherence to antiretroviral therapy: a systematic review. *AIDS Patient Care STDS* 2008; 22:495-504.

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Conflict of interest

None declared. For details, see: www.supportsummaries.org/coi

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About certainty of the evidence (GRADE)

The “certainty of the evidence” is an assessment of how good an indication the research provides of the likely effect; i.e. the likelihood that the effect will be substantially different from what the research found. By “substantially different” we mean a large enough difference that it might affect a decision. These judgements are made using the GRADE system, and are provided for each outcome. The judgements are based on the study design (randomised trials versus observational studies), factors that reduce the certainty (risk of bias, inconsistency, indirectness, imprecision, and publication bias) and factors that increase the certainty (a large effect, a dose response relationship, and plausible confounding). For each outcome, the certainty of the evidence is rated as high, moderate, low or very low using the definitions on page 3.

For more information about GRADE: www.supportsummaries.org/grade

SUPPORT collaborators:

The Cochrane Effective Practice and Organisation of Care Group (EPOC) is part of the [Cochrane Collaboration](http://www.cochrane.org). The Norwegian EPOC satellite supports the production of Cochrane reviews relevant to health systems in low- and middle-income countries. www.epocoslo.cochrane.org

The Evidence-Informed Policy Network (EVIPNet) is an initiative to promote the use of health research in policymaking in low- and middle-income countries. www.evipnet.org

The Alliance for Health Policy and Systems Research (HPSR) is an international collaboration that promotes the generation and use of health policy and systems research in low- and middle-income countries. www.who.int/alliance-hpsr

Norad, the Norwegian Agency for Development Cooperation, supports the Norwegian EPOC satellite and the production of SUPPORT Summaries. www.norad.no

The Effective Health Care Research Consortium is an international partnership that prepares Cochrane reviews relevant to low-income countries. www.evidence4health.org

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