



January 2011 – SUPPORT Summary of a systematic review

## What are the effects of interventions to improve adherence to medication?

Adherence is defined as the extent to which a patient follows the instructions given for a prescribed treatment. The term is intended to be non-judgemental and neutral. Previous terms such as ‘compliance’ that were used to describe this process, implied that blame could be apportioned to patients, prescribers or treatments if the process was not followed through. The term ‘adherence’ seeks to overcome such implicit, negative associations.

The potential benefits of effective medications may not always be achieved if patients do not take them as prescribed. Many adherence interventions are intended to assist patients with completing this task.

### Key messages

- It is very uncertain whether interventions to increase adherence to short-term treatments improve adherence or patient outcomes
- Interventions targeted to increase adherence to long-term treatments may improve the adherence, but it is very uncertain whether they improve patient outcomes



### Who is this summary for?

Clinicians and people making decisions concerning the implementation of interventions aimed to improve medication adherence.

### ! This summary includes:

- **Key findings** from research based on a systematic review
- **Considerations about the relevance of this research** for low- and middle-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:

Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD000011

### 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** – an international collaboration funded by the EU 6th Framework Programme to support the use of policy relevant reviews and trials to inform decisions about maternal and child health in low- and middle-income countries.  
[www.support-collaboration.org](http://www.support-collaboration.org)

**Glossary of terms used in this report:**  
[www.support-collaboration.org/summaries/explanations.htm](http://www.support-collaboration.org/summaries/explanations.htm)

**Background references on this topic:**  
See back page.

# Background

Poor adherence reduces treatment benefits when treatment responses depend on following a therapy dosage and schedule. This is a problem given that low adherence to prescribed treatments is very common.

Non-adherence may have numerous causes, including problems with a regimen (e.g. adverse effects), poor instructions, poor provider-patient relationships, poor patient memory, patients contesting the need to be treated, or the inability of patients to pay for treatment.

Given the multi-faceted dimension of poor adherence, a range of possible interventions can be used. Adherence is a process measure and interventions to increase adherence may themselves consume resources or have adverse effects (such as the loss of privacy and autonomy, increases in the number of the adverse effects of treatments, etc). Because interventions to improve adherence may have both positive and negative impacts, this review includes both adherence and patient outcomes.

## 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- and middle-income countries. The methods used to assess the quality of the review and to make judgements about its relevance are described here:

[www.support-collaboration.org/summaries/methods.htm](http://www.support-collaboration.org/summaries/methods.htm)

## Knowing what's not known is important

A good quality review might not find any studies from low- and middle-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.

## About the systematic review underlying this summary

**Review objective:** To summarise the effects of interventions to help patients follow prescriptions for medications

	What the review authors searched for	What the review authors found
<b>Interventions</b>	Randomised Clinical Trials (RCTs) evaluating interventions to improve adherence with prescribed, self-administered medications	78 randomised trials evaluating 93 diverse interventions that can be grouped in the following broad categories: providing more instructions for patients (e.g. written); counselling about the disease and the treatment, the importance of therapy and compliance with therapy, and patient empowerment; automated telephone, computer-assisted patient monitoring and counselling; manual telephone follow-ups; family interventions; ways to increase the convenience of care (e.g. at worksites or at home); simplified dosing; the involvement of patients in self-monitoring (e.g. of blood pressure); reminders; alternative methods of pill packaging; dose-dispensing units of medication and medication charts; appointment and prescription refill reminders; reinforcements or rewards; different medication formulations; crisis intervention (e.g. for attempted suicide); direct observation of treatments; lay health mentoring; augmented pharmacy services; psychological therapy; mailed communications; group meetings
<b>Participants</b>	Patients who were prescribed medication for a medical disorder (including psychiatric), but not for addictions	Several chronic conditions including hypertension (12), schizophrenia or acute psychosis (10), asthma or COPD (11), rheumatoid arthritis (2), hyperlipidemia (3), depression (4) and HIV (12); chronic therapies such as oral anticoagulant therapy (1) and contraception (2); multiple interventions in specific populations such as elderly patients (2); and short-term conditions such as acute infections (9)
<b>Settings</b>	Any setting	Many different settings and venues. The United States of America (USA) (30), United Kingdom (UK) (14), Spain (5), Canada (8), Australia (3), the Netherlands (3), China (3), France (2), Mexico (1), Norway (1), Italy (1), Sweden (1), Ghana (1), Denmark (1), Republic of Ireland (1), United Arab Emirates (1), Switzerland (1) and Malaysia (1)
<b>Outcomes</b>	Medication adherence and patient outcomes	9 studies on short-term and 71 on long-term treatments measuring adherence and patient outcomes
<b>Date of most recent search:</b> February 2007		
<b>Limitations:</b> This is a systematic review with moderate limitations related to the way of combining and synthesising results.		

Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. Cochrane Database of Systematic Reviews 2008,

# Summary of findings

This review found 78 studies conducted in many different settings, most of which were in high-income countries. Nine studies addressed interventions to improve adherence to short-term treatments, and 71 to long-term treatments. The studies evaluated very different interventions for each type.

## 1) Interventions to improve adherence to short-term treatments

Nine studies evaluated 10 different interventions to increase adherence in very diverse conditions. The interventions evaluated were: the provision of more detailed instructions to patients (4), the use of dose-dispensing units of medication (1), counselling about the target disease of the patients (3), the use of different medication formulations (1) and augmented pharmacy services (1)

➔ **It is very uncertain whether interventions to increase adherence to short-term treatments improve adherence or patient outcomes**

### About the quality of evidence (GRADE)

⊕⊕⊕⊕

**High:** Further research is very unlikely to change our confidence in the estimate of effect.

⊕⊕⊕○

**Moderate:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

⊕⊕○○

**Low:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

⊕○○○

**Very low:** We are very uncertain about the estimate.

For more information, see last page

Interventions to improve adherence to short-term treatments			
<p><b>Patients or population:</b> Several conditions  <b>Settings:</b> Many different settings  <b>Intervention:</b> Interventions to improve adherence to short-term treatments  <b>Comparison:</b> Any</p>			
Outcomes	Impact	Number of participants (studies)	Quality of the evidence (GRADE)
<b>Adherence</b>	Several quite simple interventions increased adherence, but the effects were inconsistent across the studies. Fewer than half of the interventions showed benefits	1,511 (9 studies)	⊕○○○ Very low
<b>Patient outcomes</b>	Several quite simple interventions increased patient outcomes, but effects were inconsistent across the studies. Fewer than half of the interventions showed benefits	1,511 (9 studies)	⊕○○○ Very low

p: p-value GRADE: GRADE Working Group grades of evidence (see above and last page)

## 2) Interventions to improve adherence to long-term treatments (more than 6 months)

71 studies evaluated 81 different interventions to increase adherence in very diverse conditions, including: asthma and chronic obstructive pulmonary disease (12), hypertension (12), diabetes (6), HIV (12), rheumatoid arthritis (2), dyslipidemia (5), mental health conditions (14), epilepsy (1), heart failure (1) and ischemic heart disease (1). Some studies focused in specific medications, such as oral anticoagulant therapy (1) and contraception (1). Two studies evaluated interventions to increase adherence to complex regimens in the elderly.

→ Interventions targeted to increase adherence to long-term treatments may improve the adherence to medications slightly

→ It is very uncertain whether interventions to increase adherence to long-term treatments improve patient outcomes

Interventions to improve adherence to long-term treatments			
<p><b>Patients or population:</b> Several conditions  <b>Settings:</b> Many different settings  <b>Intervention:</b> Interventions to improve adherence to long-term treatments  <b>Comparison:</b> Any</p>			
Outcomes	Impact	Number of participants (studies)	Quality of the evidence (GRADE)
<b>Adherence</b>	Only 34 of 81 interventions were associated with improvements in adherence. Almost all of the interventions that were effective were complex and included combinations of: more convenient care, information, reminders, changing dosing schedules, self-monitoring, reinforcement, counselling, family therapy, psychological therapy, crisis intervention, manual telephone follow-ups, and supportive care. Even the most effective interventions did not lead to large improvements in adherence	11,927 (71 studies)	⊕⊕○○ Low
<b>Patient outcomes</b>	Only 26 of 81 interventions led to improvement in at least one patient outcome. Almost all of the interventions that were effective were complex and included combinations of: more convenient care, information, reminders, changing dosing schedule, self-monitoring, reinforcement, counselling, family therapy, psychological therapy, crisis intervention, manual telephone follow-ups, and supportive care. Even the most effective interventions did not lead to large improvements in patient outcomes	11,927 (71 studies)	⊕○○○ Very low
p: p-value GRADE: GRADE Working Group grades of evidence (see above and last page)			

# Relevance of the review for low- and middle-income countries

## → Findings

## ▷ Interpretation\*

### APPLICABILITY

- The review identified 78 studies evaluating interventions to improve adherence to medications. The studies differed according to the type of setting, the conditions targeted, the type of medication, the duration of treatment, etc.
- It is very uncertain whether the majority of the effects of the interventions improved medication adherence
  - The effects on short-term treatments are very uncertain
- For long-term treatments, changing dosing schedules may lead to improved adherence and other interventions may slightly improve this. However, effects in patient outcomes are very uncertain
- The review does not indicate the countries in which the studies were conducted

- ▷ *Almost all the interventions that were effective were complex, and included combinations of interventions. Even the most effective interventions did not lead to large improvements in treatment outcomes*
- ▷ *These findings indicate that interventions to improve medication adherence should be used with caution given that there is a high degree of uncertainty about both their effects and costs*

### EQUITY

- The studies did not directly address the issue of equity

- ▷ *Factors causing poor adherence often impact upon disadvantaged populations more (e.g. poor memory, inability to pay for the treatment). Therefore interventions to increase adherence might selectively help such populations achieve the theoretical benefits of effective medication*
- ▷ *It is important to consider there might be a differential effect of interventions to improve adherence according to gender, education, religion, socioeconomic status, and racial/ethnic factors.*
- ▷ *Unfortunately, these theoretical effects remain unproven*

### ECONOMIC CONSIDERATIONS

- The included studies provide no data about the cost of the interventions

- ▷ *The cost-benefit advantages of these interventions are difficult to calculate based on the information available. However, the effects shown in this review suggest that it is highly unlikely that more complex or expensive interventions will provide better cost-benefit outcomes*

### MONITORING & EVALUATION

- The way of measuring adherence in the majority of studies was self-reporting, or other methods that were not sufficiently sensitive
- This review found evidence that some interventions may lead to better patient outcomes
- Studies measuring adherence but not measuring patient outcomes were not included in this review
- There is little information about adverse effects or costs in existing studies

- ▷ *Measuring adherence is a complex task and frequently used methods (e.g. self reporting) may lack both sensitivity and specificity. Objective measures provide a more accurate measure of true adherence but they are more expensive*
- ▷ *Future research should focus on those interventions that are most promising*
- ▷ *It cannot be assumed that measures to increase adherence do more good than harm even if they increase adherence*
- ▷ *Interventions to increase adherence consume resources and attempts to increase adherence can have adverse effects (such as the loss of privacy and autonomy, increased adverse effects of treatments, etc.). It is important not only to monitor effects, but also to monitor adverse effects and costs*

\*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- and middle-income countries. For additional details about how these judgements were made see: <http://www.support-collaboration.org/summaries/methods.htm>

# Additional information

## Related literature

Horne R, Weinman J, Barber N, Elliot R, Morgan M. Concordance, adherence and compliance in medicine taking: a scoping exercise. London: NCCSDO; 2005.

Schroeder K, Fahey T, Ebrahim S. Interventions for improving adherence to treatment in patients with high blood pressure in ambulatory settings. Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD004804. DOI: 10.1002/14651858.CD004804

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Al-aqeel S, Al-sabhan J. Strategies for improving adherence to antiepileptic drug treatment in patients with epilepsy. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD008312. DOI: 10.1002/14651858.CD008312.pub2

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## Conflict of interest

None declared. For details, see: [www.support-collaboration.org/summaries/coi.htm](http://www.support-collaboration.org/summaries/coi.htm)

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## Keywords

*All Summaries:* evidence-informed health policy, evidence-based, systematic review, health systems research, health care, low- and middle-income countries, developing countries, primary health care, medication adherence, medication compliance, medication non-compliance, medication non-adherence, patient compliance, treatment refusal

## About quality of evidence (GRADE)

The quality of the evidence is a judgement about the extent to which we can be confident that the estimates of effect are correct. These judgements are made using the GRADE system, and are provided for each outcome. The judgements are based on the type of study design (randomised trials versus observational studies), the risk of bias, the consistency of the results across studies, and the precision of the overall estimate across studies. For each outcome, the quality of the evidence is rated as high, moderate, low or very low using the definitions on page 3.

### For more information about GRADE:

[www.support-collaboration.org/summaries/grade.htm](http://www.support-collaboration.org/summaries/grade.htm)

## SUPPORT collaborators:

**The Alliance for Health Policy and Systems Research (HPSR)** is an international collaboration aiming to promote the generation and use of health policy and systems research as a means to improve the health systems of developing countries. [www.who.int/alliance-hpsr](http://www.who.int/alliance-hpsr)

**The Cochrane Effective Practice and Organisation of Care Group (EPOC)** is a Collaborative Review Group of the Cochrane Collaboration: an international organisation that aims to help people make well informed decisions about health care by preparing, maintaining and ensuring the accessibility of systematic reviews of the effects of health care interventions.

[www.epocoslo.cochrane.org](http://www.epocoslo.cochrane.org)

**The Evidence-Informed Policy Network (EVIPNet)** is an initiative to promote the use of health research in policymaking. Focusing on low- and middle-income countries, EVIPNet promotes partnerships at the country level between policy-makers, researchers and civil society in order to facilitate both policy development and policy implementation through the use of the best scientific evidence available. [www.evipnet.org](http://www.evipnet.org)

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