



August 2016 – SUPPORT Summary of a systematic review

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

The potential benefits of effective medications may not always be achieved if patients do not take them as prescribed. Adherence is defined as the extent to which a patient follows the instructions given for a prescribed treatment. Many adherence interventions are intended to assist patients with completing this task.

Key messages

- **It is uncertain whether interventions to increase adherence to short-term treatments improve adherence or patient outcomes.**
- **Interventions aimed at increasing adherence to long-term treatments may improve adherence, but it is uncertain whether they improve patient outcomes.**
- **Most of the included studies assessed complex interventions with multiple components in high-income countries.**
 - Adherence interventions may be difficult to implement in low-income countries where health systems face greater challenges.



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-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, et al. 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 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

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, such as providing more instructions for patients, counselling and patient empowerment, automated telephone or computer-assisted patient monitoring, manual telephone follow-ups, family interventions, ways to increase the convenience of care, simplified dosing, involvement of patients in self-monitoring, reminders, alternative methods of pill packaging, dose-dispensing units of medication and medication charts, 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 and group meetings.

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 the effects of interventions to help patients follow prescriptions for medications

Types of	What the review authors searched for	What the review authors found
Study designs & Interventions	Randomised trials evaluating interventions to improve adherence with prescribed, self-administered medications	78 trials evaluating 93 diverse interventions
Participants	Patients who were prescribed medication for a medical disorder (including psychiatric), but not for addictions	Patients with several different chronic conditions including hypertension (12 studies), schizophrenia or acute psychosis (10), asthma or chronic obstructive pulmonary disease (COPD) (11), rheumatoid arthritis (2), hyperlipidaemia (3), depression (4) and HIV (12)
Settings	Any setting	Many different settings and venues were included. Trials were conducted in the USA (30 studies), 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).
Outcomes	Medication adherence and patient outcomes	9 studies on short-term and 71 on long-term treatments measuring adherence and patient outcomes
Date of most recent search: February 2007		
Limitations: This is a systematic review with moderate limitations related to how the results were synthesized.		

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

Summary of findings

An update of this review, published in 2014, included 109 new randomized trials, bringing the total number of included studies to 182. The interventions differed widely and the authors did not classify studies according to the type of intervention. Instead, a narrative focused on the results of 17 studies with low-risk of bias and a database of the 182 studies (without any synthesis of the findings) was provided. We therefore have not prepared a SUPPORT Summary of the updated review. Only five of the studies in the updated review found an improvement in both medicine adherence and clinical outcomes, and no common characteristics for their success could be identified. Overall, even the most effective interventions did not lead to large improvements in adherence or clinical outcomes.

This previous 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 types of interventions.

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 studies), 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 uncertain whether interventions to increase adherence to short-term treatments improve adherence or patient outcomes. The certainty of this evidence is very low.**

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.

Interventions to improve adherence to short-term treatments		
People	Patients with several different medical conditions	
Settings	Many different settings	
Intervention	Interventions to improve adherence to short-term treatments	
Comparison	Any	
Outcomes	Impact	Certainty of the evidence (GRADE)
Adherence	Several quite simple interventions increased adherence, but the effects were inconsistent across the studies. Fewer than half of the interventions showed benefits.	⊕○○○ Very low
Patient outcomes	Several quite simple interventions improved patient outcomes, but effects were inconsistent across the studies. Fewer than half of the interventions showed benefits.	⊕○○○ Very low
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 studies), 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 on 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 aimed at increasing adherence to long-term treatments may slightly improve the adherence to medications. The certainty of this evidence is low.

→ It is uncertain whether interventions to increase adherence to long-term treatments improve patient outcomes. The certainty of this evidence is very low.

Interventions to improve adherence to long-term treatments		
People	Patients with several different conditions	
Settings	Many different settings	
Intervention	Interventions to improve adherence to long-term treatments	
Comparison	Any	
Outcomes	Impact	Certainty of the evidence (GRADE)
Adherence	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.	⊕⊕○○ Low
Patient outcomes	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.	⊕○○○ Very low
GRADE: GRADE Working Group grades of evidence (see above and last page)		

Relevance of the review for low-income countries

→ Findings	▷ Interpretation*
APPLICABILITY	
<ul style="list-style-type: none">→ 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 and the duration of treatment.→ Most studies were conducted in high-income countries.→ It is uncertain whether the majority of the effects of the interventions improved medication adherence.	<ul style="list-style-type: none">▷ Almost all the interventions that were found to be effective were complex, and included combinations of interventions, and the size of their effects on patient outcomes is uncertain.▷ Complex adherence interventions may be difficult to implement in low-income countries.
EQUITY	
<ul style="list-style-type: none">→ The studies did not directly address the issue of equity.	<ul style="list-style-type: none">▷ Factors causing poor adherence often impact upon disadvantaged populations more (e.g. poor memory, inability to pay for the treatment). Therefore, effective interventions to increase adherence might selectively help such populations achieve the benefits of effective medication.▷ There might be differential effects of interventions to improve adherence according to gender, education, religion, socioeconomic status, and racial/ethnic factors. However, the review did not find evidence to support or refute such differential effects.
ECONOMIC CONSIDERATIONS	
<ul style="list-style-type: none">→ The included studies provide no data about the cost of the interventions.	<ul style="list-style-type: none">▷ The cost-effectiveness of these interventions cannot be determined based on the information available.
MONITORING & EVALUATION	
<ul style="list-style-type: none">→ In the majority of studies, adherence was measured using self-reporting or other methods that were not reliable.→ 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 the included studies.	<ul style="list-style-type: none">▷ Measuring adherence is a complex task and frequently used methods (e.g. self-reporting) may not be accurate. 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.▷ Interventions to increase adherence consume resources and attempts to increase adherence can have adverse effects (such as the loss of privacy and autonomy and increased adverse effects of treatment). It is important not only to monitor effects, but also to monitor adverse effects and costs.▷ Randomised trials addressing the above issues in low-income countries are needed.

*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

- Nieuwlaat R, Wilczynski N, Navarro T, et al. Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews* 2014, Issue 11. Art. No.: CD000011.
- Horne R, Weinman J, Barber N, et al. Concordance, adherence and compliance in medicine taking: a scoping exercise. London: NCCSDO; 2005.
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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.

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Conflict of interest

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

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This review should be cited as

Haynes RB, Ackloo E, Sahota N, et al. Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews* 2008, Issue 2. Art. No.: CD000011.

The summary should be cited as

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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 (EVIPONet) 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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