



October 2016 – SUPPORT Summary of a systematic review

# What is the effectiveness of interventions to improve antibiotic prescribing practices for hospital inpatients?

In-hospital infections caused by antibiotic-resistant bacteria and *Clostridium difficile* are associated with higher rates of death, illness and prolonged hospital stay which is a serious problem for patients and healthcare systems. These infections occur because antibiotics are used too often and incorrectly.

## Key messages

- Restrictive interventions may improve antibiotic prescribing at one month, but may lead to little or no difference in antibiotic prescribing at longer follow-up compared with persuasive interventions.
- Interventions intended to decrease unnecessary antibiotic prescribing probably lead to little or no difference in all-cause mortality.
- It is uncertain whether interventions intended to decrease unnecessary antibiotic prescribing affect the length of stay or readmissions.
- Interventions intended to increase effective antibiotic prescribing for pneumonia may decrease mortality.
- None of the included studies were conducted in a low-income country.



## Who is this summary for?

People deciding whether to introduce interventions to improve antibiotic prescribing for hospital inpatients

### ! 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:

Davey P, Brown E, Charani E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database of Systematic Reviews 2013; 4:CD003543.

## 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](http://www.supportsummaries.org/glossary-of-terms)

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

# Background

Antibiotic usage in hospitals is increasing and over a third of prescriptions are not compliant with evidence-based guidelines. One of the consequences, besides worse patient outcomes, is antimicrobial resistance which is considered a major public health problem in terms of health outcomes and costs. This review assessed the effects of professional interventions in antibiotic stewardship for hospital inpatients.

‘Antibiotic stewardship’ is used to capture the twin aims of ensuring effective treatment of patients with infection and minimizing collateral damage from antimicrobial use through appropriate antibiotic prescribing. The interventions were classified as: persuasive (dissemination of educational materials in printed form or via educational meetings reminders, audit and feedback, educational outreach); restrictive (financial and healthcare system changes as compulsory order form, expert approval, removing restricted antibiotics from drug cupboards, changing of prescription by reviewers); and structural (new technology for laboratory testing or computerized decision support).

## 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/](http://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 assess the effectiveness of professional interventions that, alone or in combination, are effective in antibiotic stewardship for hospital inpatients.

Types of	What the review authors searched for	What the review authors found
<b>Study designs &amp; Interventions</b>	Randomised trials, non-randomised trials, controlled before–after studies and interrupted time series studies of interventions directed to antibiotic stewardship	89 included studies (95 interventions): 25 randomised trials, 3 non-randomised trials, 5 controlled before–after studies, and 56 interrupted time series studies. 84% of the interventions targeted the antibiotic prescribed and the remaining 16% aimed to change exposure of patients to antibiotics by targeting the decision to treat or the duration of treatment.
<b>Participants</b>	Healthcare professionals who prescribe antibiotics to hospital inpatients	Interventions were delivered by multidisciplinary teams (39%), specialist physicians in infectious diseases or microbiology (33%), pharmacists (20%), and department physicians (8%).
<b>Settings</b>	Hospital settings worldwide	USA (48), UK (12), Netherlands (6), Canada (4), Switzerland (3), Australia (3), Thailand (2), Colombia (2), France (2), Germany (2), Spain (2), Israel (2), Austria (1), Belgium (1), Brazil (1), Hong Kong (1), Italy (1), Norway (1), and Sweden (1)
<b>Outcomes</b>	Antibiotic prescribing process measures (decision to treat, choice of drug, dose, route or duration of treatment); clinical outcome measures (mortality, length of hospital stay); microbial outcome measure (colonization or infection with <i>clostridium difficile</i> or antibiotic-resistant bacteria)	Appropriate prescribing of antibiotics, microbial outcomes, patient outcomes (mortality), length of stay, readmissions

**Date of most recent search:** February 2009

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

Davey P, Brown E, Charani E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database of Systematic Reviews 2013; 4:CD003543.

# Summary of findings

89 studies were included. Of the 95 interventions reported in these studies, 79 aimed to decrease excessive antibiotic use, 11 aimed to increase effective treatment and 5 aimed to reduce inappropriate antibiotic use but did not distinguish between excessive and ineffective use.

## 1) Restrictive versus persuasive interventions to improve antibiotic prescribing

Appropriate prescribing of antibiotics was assessed by 53 indirect comparisons from 40 studies and microbial outcomes by 20 indirect comparisons from 14 studies.

- Restrictive interventions may improve antibiotic prescribing at one month but may lead to little or no difference at longer follow-up compared with persuasive interventions. The certainty of this evidence is low.
- Restrictive interventions may improve antibiotic prescribing at six months but may lead to little or no difference at longer follow-up compared with persuasive interventions. The certainty of this evidence is 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.

Restrictive versus persuasive interventions to improve antibiotic prescribing		
<b>People</b>	Healthcare professionals	
<b>Settings</b>	Secondary care (inpatients in acute, not long term care only)	
<b>Intervention</b>	Restrictive interventions (compared to usual care in studies)†	
<b>Comparison</b>	Persuasive interventions (compared to usual care in studies)†	
Outcomes	Impact (percent change in level)	Certainty of the evidence (GRADE)
<b>Appropriate prescribing of antibiotics</b>	The change was 32% larger for restrictive interventions at one month (95% CI 2 to 61%) compared to persuasive interventions and there was little or no difference at 6, 12, and 24 months.	⊕⊕○○ Low†
<b>Microbial outcomes</b> (colonization or infection with <i>Clostridium difficile</i> or antibiotic-resistant bacteria)	The change was 53% larger for restrictive interventions at 6 months (95% CI 31 to 75%) compared to persuasive interventions and there was little or no difference at 12 and 24 months.	⊕⊕○○ Low†
GRADE: GRADE Working Group grades of evidence (see above and last page)		
† Indirect comparison between studies that provide data about effect of either persuasive or restrictive interventions		

## 2) Interventions intended to decrease unnecessary antibiotic prescribing

Mortality was assessed by 11 comparisons from 11 studies; length of stay by six comparisons from six studies and readmissions by five comparisons from five studies.

- ➔ Interventions intended to decrease unnecessary antibiotic prescribing probably lead to little or no difference in all-cause mortality. The certainty of this evidence is moderate.
- ➔ It is uncertain whether interventions intended to decrease unnecessary antibiotic prescribing affect the length of stay or readmissions. The certainty of this evidence is very low.

Interventions intended to decrease unnecessary antibiotic prescribing		
<b>People</b>	Healthcare professionals	
<b>Settings</b>	Secondary care (inpatients in acute, not long term care only)	
<b>Intervention</b>	Interventions intended to decrease unnecessary antibiotic prescribing	
<b>Comparison</b>	Usual care	
Outcomes	Impact	Certainty of the evidence (GRADE)
<b>All-cause mortality</b>	Risk ratio for intervention versus control 0.92 (95% CI 0.81 to 1.06)	⊕⊕⊕○ Moderate
<b>Length of stay</b>	Difference (in days) for intervention versus control -0.04 days (95% CI - 0.34 to 0.25)	⊕○○○ Very low
<b>Readmissions</b>	Risk ratio for intervention versus control 1.26 (95% CI 1.02 to 1.57)	⊕○○○ Very low
GRADE: GRADE Working Group grades of evidence (see above and last page)		

## 3) Interventions intended to increase effective antibiotic prescribing for pneumonia

Mortality was assessed by four comparisons from four studies.

- ➔ Interventions intended to increase effective antibiotic prescribing for pneumonia may decrease mortality. The certainty of this evidence is low.

Interventions intended to increase effective antibiotic prescribing for pneumonia		
<b>People</b>	Healthcare professionals	
<b>Settings</b>	Secondary care (inpatients in acute care only)	
<b>Intervention</b>	Interventions intended to increase effective antibiotic prescribing for pneumonia	
<b>Comparison</b>	Usual care	
Outcomes	Impact	Certainty of the evidence (GRADE)
<b>Mortality</b>	Risk ratio for intervention versus control 0.89 (95% CI 0.82 to 0.97)	⊕⊕○○ Low
GRADE: GRADE Working Group grades of evidence (see above and last page)		

# Relevance of the review for low income countries

→ Findings	▷ Interpretation*
APPLICABILITY	
→ <b>None of the included studies were conducted in a low-income country.</b>	▷ <i>When assessing the transferability of these findings to low-income countries the following factors should be considered:</i> <ul style="list-style-type: none"> <li>– <i>The availability of resources specially for persuasive and structural interventions</i></li> <li>– <i>The acceptability and costs of the interventions</i></li> <li>– <i>Locally tailored up to date antibiotic treatment guidelines</i></li> </ul>
EQUITY	
→ <b>There was no information in the included studies regarding differential effects of the interventions on resource-disadvantaged populations.</b>	▷ <i>Resources needed for interventions may be less available in disadvantaged settings.</i> ▷ <i>The interventions may increase inequity if they are not applied or adapted to these populations.</i>
ECONOMIC CONSIDERATIONS	
→ <b>Limited data showed that savings exceeded the cost of the intervention in 8 out of 10 studies.</b>	▷ <i>Scaling up many of the interventions will require resources, that should be considered.</i> ▷ <i>Local costing should be undertaken, particularly in settings differing from the original investigations.</i>
MONITORING & EVALUATION	
→ <b>There is evidence that interventions to improve antibiotic prescribing for pneumonia may decrease mortality. No clear evidence of benefit and safety was found for other outcomes.</b>	▷ <i>Future studies should provide information about the resources required for development, dissemination and implementation of guidelines and other relevant interventions.</i> ▷ <i>Larger and more rigorous studies to determine the effectiveness, safety and cost-effectiveness of interventions are needed, particularly in resource-poor settings.</i>

\*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](http://www.supportsummaries.org/methods)

# Additional information

## Related literature

Pulcini C, Gyssens IC. How to educate prescribers in antimicrobial stewardship practices. *Virulence* 2013; 4(2):192–202.

Aryee A, Price N. Antimicrobial stewardship – can we afford to do without it? *British Journal of Clinical Pharmacology* 2015; 79(2):173–81.

Chung GW, Wu JE, Yeo CL, Chan D, Hsu LY. Antimicrobial stewardship: a review of prospective audit and feedback systems and an objective evaluation of outcomes. *Virulence* 2013; 4(2):151–7.

Reed EE, Stevenson KB, West JE, et al. Impact of formulary restriction with prior authorization by an antimicrobial stewardship program. *Virulence* 2013; 4(2):158–62.

Wagner B, Filice GA, Drekonja D, et al. Antimicrobial stewardship programs in inpatient hospital settings: a systematic review. *Infection Control and Hospital Epidemiology* 2014; 35(10):1209–28.

Chandy SJ, Naik GS, Charles R, et al. The impact of policy guidelines on hospital antibiotic use over a decade: a segmented time series analysis. *PloS One* 2014; 9(3):e92206.

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## Conflict of interest

None declared. For details, see: [www.supportsummaries.org/coi](http://www.supportsummaries.org/coi)

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This summary has been peer reviewed by: Gavin Barlow, Göran Tomson, and Peter Davey.

## This review should be cited as

Davey P, Brown E, Charani E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database of Systematic Reviews* 2013; 4:CD003543.

## The summary should be cited as

Ciapponi A. Do interventions improve antibiotic prescribing to hospital inpatients? A SUPPORT Summary of a systematic review. October 2016. [www.supportsummaries.org](http://www.supportsummaries.org)

## 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](http://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](http://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](http://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](http://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](http://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](http://www.evidence4health.org)

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