

Antimicrobial prescribing guidelines: managing common infections

Interim process and methods guide

May 2017

1 Introduction

This interim process and methods guide explains how antimicrobial prescribing guidelines are developed and updated. The guide is based on [Developing NICE guidelines: the manual \(2014\)](#).

These processes are designed to ensure that robust, quality-assured guidance is developed for the NHS in an open, transparent and timely way, with appropriate input from key groups.

1.1 Background

The National Institute for Health and Care Excellence (NICE) provides national guidance and advice to improve health and social care in England. Further information about NICE and its work is available on the [NICE website](#). NICE has received a referral from the Department of Health to develop a suite of prescribing guidelines for managing common infections.

Antimicrobial prescribing guidelines aim to ensure prescribing recommendations are consistent with antimicrobial resistance patterns, trends and data, and the best available published evidence.

1.2 Key principles for developing guidelines

See section 1.4 of *Developing NICE guidelines: the manual (2014)*. See also [section 8](#) of this guide.

1.3 Who is involved

See section 1.5 of *Developing NICE guidelines: the manual (2014)*. The Centre for Guidelines (CfG) develops guidelines containing recommendations on the

appropriate treatment and care of people with specific diseases and conditions within the health and social care in England. Recommendations are based on the best available published evidence. The committee developing antimicrobial prescribing guidelines is a multidisciplinary standing committee made up of topic experts and lay members. The standing committee works on a series of guidelines for managing a number of common infections.

1.4 *Main stages of guideline development*

See section 1.6 of Developing NICE guidelines: the manual (2014). The development time for each antimicrobial prescribing guideline is usually between 20 and 30 weeks.

1.5 *Publication and implementation of the guideline*

See section 1.7 of Developing NICE guidelines: the manual (2014).

2 *The scope*

See section 2 of Developing NICE guidelines: the manual (2014).

2.1 *Purpose of the scope*

Section 2.1 of Developing NICE guidelines: the manual (2014) describes the purpose of the scope for NICE guidelines. Antimicrobial prescribing guidelines differ from this in that a single scope covers all topics (listing the first 8 to be developed). See also [section 8](#) of this guide.

2.2 *Who is involved in developing the scope*

See section 2.2 of Developing NICE guidelines: the manual (2014).

2.3 *Stages of scope development*

See section 2.3 of Developing NICE guidelines: the manual (2014).

3 *Decision-making committees*

3.1 *Introduction*

See section 3.1 of Developing NICE guidelines: the manual (2014).

3.2 *Forming the committee*

See section 3.2 of Developing NICE guidelines: the manual (2014).

3.3 *Standing committees*

See section 3.3 of Developing NICE guidelines: the manual (2014). The committee is a multidisciplinary standing committee made up of topic experts and lay members. The committee works on a series of antimicrobial prescribing guidelines for managing a number of common infections.

3.4 *Other attendees at committee meetings*

See section 3.5 of Developing NICE guidelines: the manual (2014).

3.5 *Code of conduct and declaration of interests*

See section 3.6 of Developing NICE guidelines: the manual (2014).

3.6 *Identifying and meeting training needs of committee members*

See section 3.7 of Developing NICE guidelines: the manual (2014).

3.7 *Committee meetings*

See section 3.8 of Developing NICE guidelines: the manual (2014). See also [section 8](#) of this guide.

3.8 *Making group decisions and reaching consensus*

See section 3.9 of developing NICE guidelines: the manual (2014).

4 *Identifying, prioritising and selecting topics*

The scope lists the first 8 topics that will be developed into antimicrobial prescribing guidelines. Further topics are identified using comments received from stakeholder organisations during consultation of the draft scope. The identified topics are prioritised for guideline development using the following criteria:

- the likely causative organisms are gram-negative bacteria (where resistance to treatment is more prevalent)

- people present in high numbers to health services
- management in practice is thought to be poor or variable
- there is a lack of existing NICE-accredited guidance
- the condition is self-limiting.

Additional topics may also be referred to NICE by the Department of Health, Public Health England or NHS England.

5 Developing review questions and planning the evidence review

See section 4 of Developing NICE guidelines: the manual (2014).

5.1 *Number of review questions*

See section 4.1 of Developing NICE guidelines: the manual (2014). In most cases a single review question will be formulated for each guideline.

5.2 *Developing review questions from the scope*

See section 4.2 of Developing NICE guidelines: the manual (2014).

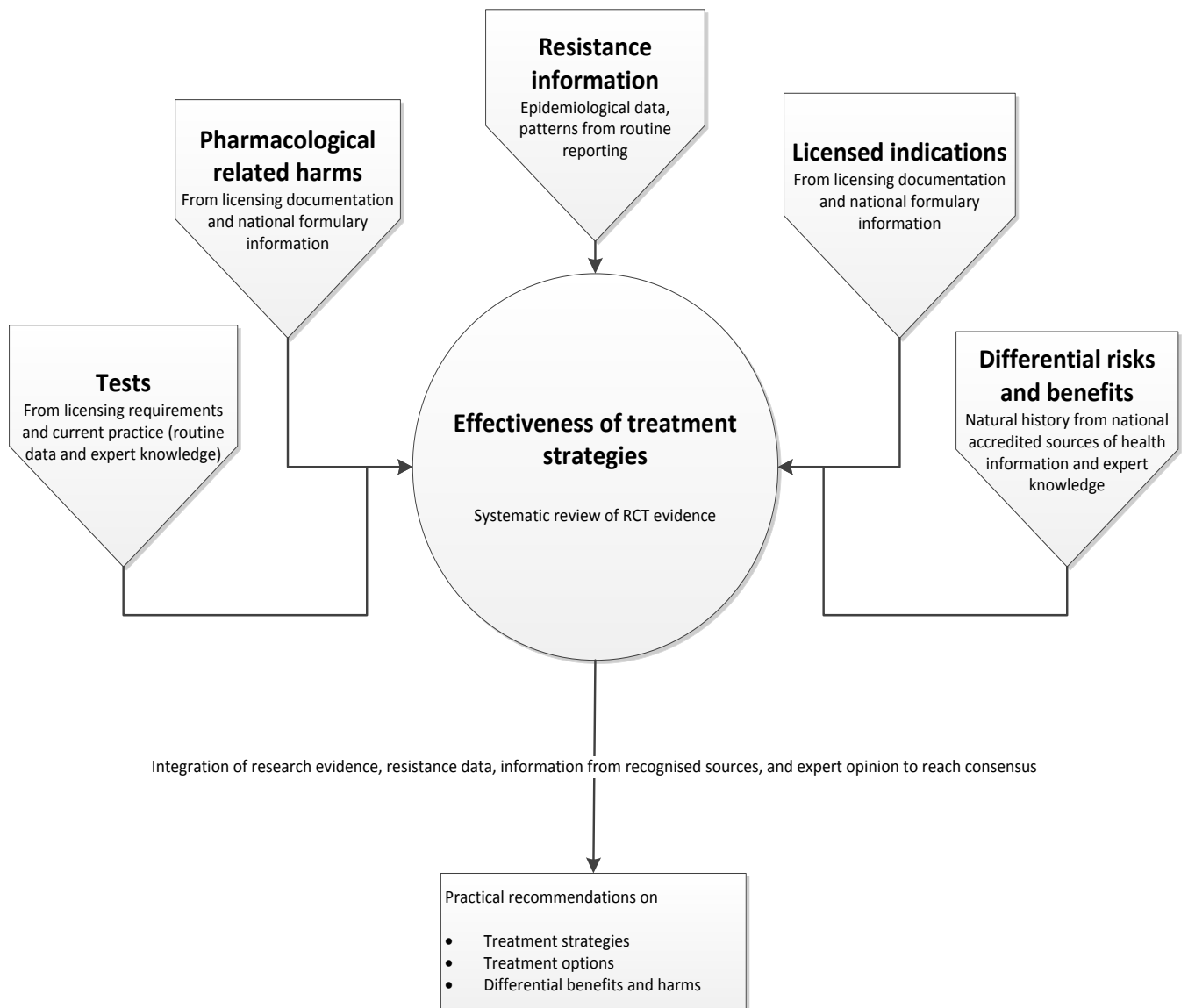
5.3 *Formulating and structuring different review questions*

See section 4.3 of Developing NICE guidelines: the manual (2014). Because antimicrobial prescribing guidelines will not consider cost utility analysis the review questions will not be structured to search for this type of evidence.

5.4 *Evidence used to inform recommendations*

See section 4.4 of Developing NICE guidelines: the manual (2014). Figure 1 shows the evidence that will be used to inform recommendations on antimicrobial prescribing. Additional information from other sources (that is, not identified as part of the systematic evidence review) will also be included, such as data on safety and antimicrobial resistance.

Figure 1.



5.5 *Planning the evidence review*

See section 4.5 of *Developing NICE guidelines: the manual (2014)*. For each guideline evidence review, a review protocol is prepared that outlines the background, the objectives and the planned methods. This protocol will explain how the review is to be carried out and will help the reviewer to plan and think through the different stages.

6 Identifying the evidence: literature searching and evidence submission

See section 5 of Developing NICE guidelines: the manual (2014).

6.1 *Introduction*

See section 5.1 of Developing NICE guidelines: the manual (2014).

6.2 *Search protocols*

See section 5.2 of Developing NICE guidelines: the manual (2014).

6.3 *Sources*

See section 5.3 of Developing NICE guidelines: the manual (2014).

6.4 *Developing search strategies*

See section 5.4 of Developing NICE guidelines: the manual (2014). Where possible search strategies will be combined to cover more than 1 guideline.

6.5 *Calls for evidence from stakeholders*

See section 5.5 of Developing NICE guidelines: the manual (2014).

6.6 *Health inequalities and equality and diversity*

See section 5.6 of Developing NICE guidelines: the manual (2014).

6.7 *Quality assurance of the searches*

See section 5.7 of Developing NICE guidelines: the manual (2014).

6.8 *Reference management*

See section 5.8 of Developing NICE guidelines: the manual (2014). Eppi Reviewer will be used for this.

6.9 *Documenting the search*

See section 5.9 of Developing NICE guidelines: the manual (2014).

6.10 Re-running searches

See section 5.10 of Developing NICE guidelines: the manual (2014). In most cases it is unlikely that re-running of searches will be needed because of the short development time for antimicrobial prescribing guidelines.

7 Reviewing research evidence

See section 6 of Developing NICE guidelines: the manual (2014). The evidence is summarised into sections including effectiveness, safety, patient factors, resource impact and antimicrobial resistance.

7.1 Selecting relevant evidence

See section 6.1 of Developing NICE guidelines: the manual (2014).

A single search is carried out for several guidelines wherever possible. In these circumstances the search results will be sifted (see [section 6](#)) and will be categorised into the various topics. The included studies would usually sit within 1 guideline.

Safety information is also included for the medicines recommended in the guideline. Information is found from websites such as the Medicines and Healthcare products Regulatory Agency (MHRA) and the European Medicines Agency (EMA). In addition, explicit reference is made to information in the summary of product characteristics (if there is one) relating to precautions, warnings and undesirable effects, and also to published advice from the medicine regulators for medicines that are recommended (see [section 5.4](#)).

Specific information about antimicrobial resistance is also presented in the guideline where appropriate. Data, patterns and trends in resistance vary across the country and the degree or rate of change also varies. Information from the English Surveillance Programme for Antimicrobial Utilization and Resistance (ESPAUR) report and data from Public Health England will be included if available. Other national resistance data may be used, for example, Public Health England data such as, [antimicrobial resistance indicators](#) and the [second generation surveillance system](#) (see [section 5.4](#)). Resistance information and safety information are considered with the effectiveness evidence and are presented in the evidence review

and final guideline. Patient factors (such as having an informed choice, taste of medicine, route of medicine or frequency taken) are also taken into account during development of the guideline and are presented in the evidence review and final guideline.

Studies will be selected based on the review protocols (see [section 5.5](#)). Selected studies are further reviewed to prioritise and select the best available evidence. The following principles are used:

- studies are of direct relevance to UK practice
- more recently published studies from those that are included to obtain the most up-to-date information (for example, a systematic review published in 2016 would be prioritised over another published in 2008 if the same studies and outcomes were addressed)
- studies reporting patient-oriented outcomes (as given in the review protocol); studies reporting resistance patterns alone will not be prioritised
- higher quality evidence based on the hierarchy of evidence will be used (for example, a randomised control trial may not be selected if a systematic review which already includes this trial has been prioritised).

When a study is not prioritised for inclusion based on the above principles, this is detailed (studies not prioritised) in an appendix.

7.2 *Assessing the quality of the evidence*

See section 6.2 of Developing NICE guidelines: the manual (2014). Safety information and information or data about antimicrobial resistance (see [section 7.1](#)) is not quality assessed as this is information or data is published by national bodies and regulators, such as from the Medicines and Healthcare products Regulatory Agency or European Medicines Agency.

7.3 *Equality and diversity considerations*

See section 6.3 of Developing NICE guidelines: the manual (2014).

7.4 Presenting and summarising evidence

The antimicrobial prescribing guideline will be presented in several forms and will include an evidence review, a guideline with recommendations (see [section 10](#)), and a visual summary of the recommendations.

Presentation of the evidence review

The evidence review will include a full overview of the evidence in addition to including information obtained from other sources (see [section 7.1](#)). The following sections are included in the evidence review:

- summary of the evidence (evidence statements) and a summary of included studies
- review of evidence for clinical effectiveness
- information on:
 - safety and tolerability
 - resistance
- other considerations, including:
 - resource impact
 - medicines adherence
- links to GRADE profiles in an appendix (if GRADE has been used).

The evidence is presented for each guideline.

Summary of included studies tables

A summary of included studies with key details of the study (reference [authors, date], study design, location and duration), population, intervention, comparator and outcome(s) is included for each evidence review instead of detailed evidence tables. Full references of the included studies can be found in the appendices of the evidence review.

Summarising and presenting results

See section 6.4 of *Developing NICE guidelines: the manual (2014)* for information about:

- summarising evidence

- summary tables
- other presentations of qualitative evidence
- synthesising qualitative evidence
- reporting 'bias' or variation
- evidence statements
- evidence statements if GRADE is used
- evidence statements if GRADE is not used
- evidence statements for qualitative data
- terminology of evidence statements
- reporting sparse, disparate qualitative evidence and narrative summaries.

Studies of interventions

See section 6.4 of Developing NICE guidelines: the manual (2014). It is unlikely that network meta-analysis and indirect treatment comparisons will be carried out. Other ways of summarising and illustrating the strength and direction of qualitative evidence about the effectiveness of an intervention may be used, such as forest plots or other graphical forms or a narrative summary of the evidence including quality overview will be presented.

Assessing the applicability of the evidence

See section 6.4 of Developing NICE guidelines: the manual (2014). The developer and committee need to judge the extent to which the evidence reported in the reviews is applicable to the areas for which it is developing recommendations. A body of evidence should be assessed to determine how similar the population(s), setting(s), intervention(s) and outcome(s) of the selected studies are to those outlined in the review question(s). The developer presents this assessment to the committee for review and comment.

Quantitative evidence statements

Examples of evidence statements about the effectiveness of specific interventions are given in Box 1.

Box 1 Example of evidence statements

A systematic review of RCTs ([King et al. 2015](#)) found that nasal saline for up to 28 days did not reduce the time to resolution of symptoms in adults (very low quality evidence). In the largest trial, in children aged 6 to 10 years, there were statistically significant reductions in nasal symptom scores, but these may not be clinically important (low quality evidence).

A systematic review of RCTs ([Zalmanovici Trestioreanu et al. 2013](#)) and 1 additional RCT ([Keith et al. 2012](#)) found that nasal corticosteroids (all doses assessed, with or without an antibiotic) for 14 to 21 days produced a statistically significant improvement in symptoms in adults and children aged 12 years and over compared with placebo (low to moderate quality evidence). However, it is not clear whether these statistically significant reductions in symptom scores are clinically important. The number needed to treat (NNT) was 15 for 1 additional person with acute sinusitis to have improved or resolved symptoms with nasal corticosteroids compared with placebo. Higher (twice daily) doses appeared to be more effective than lower (once daily) doses.

8 Taking account of resource impact

Antimicrobial prescribing guidelines will take into account the costs, consequences and resource impact associated with different courses of action but cost utility analysis will not be performed. Cost utility analysis is unlikely to aid decision making as the medicines being assessed are largely low cost generics with similar and established clinical effectiveness. Furthermore, the disutility associated with resistance, one of the key outcome measures, is likely to be very difficult to quantify. Where overall resource use between different options is similar, decisions will be driven primarily by effectiveness and other outcome data. Costs of antibiotics can vary over time based on manufacturer availability, use and stocks, however. This should be considered during development of the guideline and may support decisions about choice of antibiotic. Where there is uncertainty about the cost, a threshold analysis may be carried out.

Resource impact will be considered throughout guideline development, and particularly when changes to practice are being recommended. NICE's principles on social value judgements (see the entry on social value judgements in our glossary) must be taken into account alongside the clinical and cost effectiveness evidence in all decision making.

Where cost information is presented this is obtained from:

- [NHS Drug Tariff](#) (price at which NHS reimburses medicines, updated monthly)
- [Drugs and pharmaceutical electronic market information](#) (eMIT) (for medicines predominantly used in secondary care)

- [Dictionary of medicines and devices](#) (DM+D) (lists medicines and devices with information from the same sources as the Drug Tariff [[NHS Business Services Authority](#)] so mainly useful for devices, updated weekly)
- [MIMS](#) (may be needed for new medicines, where costs are not available elsewhere)
- [British national formulary](#) (BNF) or [BNF for children](#) (BNFc).

9 Linking to other guidance

See section 8 of Developing NICE guidelines: the manual (2014). Related published or in development NICE guidelines will be identified when the review protocol for the topic is being agreed.

9.1 *Linking to other NICE guidance*

See section 8.1 of Developing NICE guidelines: the manual (2014).

9.2 *Guidance from other developers*

See section 8.2 of Developing NICE guidelines: the manual (2014).

10 Developing and wording recommendations and writing the guideline

The guideline contains the committee's recommendations along with an evidence review and any relevant committee discussions. The evidence review includes:

- background and context for the guideline – such as the need for the guideline, epidemiology (if relevant), current practice and the policy context
- the evidence – details of the evidence, any analysis and any gaps in the evidence
- a summary of generic and specific issues considered
- information about the most challenging changes in practice and suggestions that may help users of the guideline address these.
- GRADE tables
- summary of included studies

The evidence review will be presented as a pdf accessible from the guideline homepage.

10.1 *Interpreting the evidence to make recommendations*

See section 9.1 of Developing NICE guidelines: the manual (2014). See also [section 8](#) of this guide.

10.2 *Wording the recommendations*

See section 9.2 of Developing NICE guidelines: the manual (2014).

10.3 *Recommendations on medicines, including off-label use of licensed medicines*

See section 9.2 of Developing NICE guidelines: the manual (2014). Dosages and treatment durations of medicines will be recommended where this is known as this is important in managing antimicrobial resistance.

10.4 *Highlighting areas for future consideration in quality standard development*

See section 9.3 of developing NICE guidelines: the manual (2014).

10.5 *Formulating research recommendations*

See section 9.4 of Developing NICE guidelines: the manual (2014).

10.6 *Presenting the evidence and the recommendations*

For publication, the committee's recommendations in the form of a guideline will be published online along with:

- a visual summary of the guideline recommendations
- any recommendations for future research
- a summary of evidence (derived from the evidence review document).

10.7 *Incorporating the guideline recommendations into NICE Pathways*

See section 9.5 of Developing NICE guidelines: the manual (2014).

11 The validation process for draft guidelines, and dealing with stakeholder comments

See section 10 of Developing NICE guidelines: the manual (2014).

12 Finalising and publishing the guideline

See section 11 of Developing NICE guidelines: the manual (2014).

12.1 *Releasing an advance copy to stakeholders*

Embargoed copies of the final guideline are not shared with stakeholders who commented at consultation, in confidence 2 weeks before publication due to the frequency and number of guideline outputs.

12.2 *Publication*

The guideline, visual summary, evidence review and NICE Pathway along with consultation stakeholder comments and responses are published on the NICE website at the same time.

13 Resources to support implementation

See section 12 of Developing NICE guidelines: the manual (2014). Resources that have been designed to support implementation of the guidelines can be endorsed by NICE. Information about NICE's [endorsement programme](#) can be found on the NICE website.

14 Ensuring that published guidelines are current and accurate

See section 13 of Developing NICE guidelines: the manual (2014). In addition, the English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) produces an annual report outlining current trends in antimicrobial prescribing and resistance patterns and any other relevant national resistance data. When this report is published annually an assessment will be carried out to determine if any guideline recommendations need reviewing and updating.

15 Updating guidelines

See section 14 of Developing NICE guidelines: the manual (2014). Any updates will be carried out by the committee (see [section 3](#)). Where an existing guideline recommendation needs updating, replacing or standing down, this will be highlighted during development and will be considered by NICE's [Guidance Executive](#) (see section 11 of Developing NICE guidelines: the manual (2014)).

16 About this interim process

The interim process for antimicrobial prescribing guidelines: managing common infections provides a high-level overview of the process for developing the guidelines and is aligned with [Developing NICE guidelines: the manual](#) which explains the processes and methods used to develop and update NICE guidelines.

References for each chapter can be found in developing NICE guidelines: the manual (2014). The process will be updated periodically and the principles will be incorporated into [Developing NICE guidelines: the manual when this is next revised](#).