

The guidelines manual

Process and methods

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Contents

1 Introduction	7
1.1 NICE guidance	7
1.2 Who this manual is for.....	8
1.3 NICE clinical guidelines	9
1.4 The development process for clinical guidelines	11
1.5 Updating the guidelines manual	19
2 The scope	21
2.1 Purpose of the scope	21
2.2 The scoping group.....	22
2.3 Stage 1: selecting key clinical issues and drafting the scope	23
2.4 Stage 2: checking the selected key clinical issues with stakeholders.....	32
2.5 Stage 3: consulting on the draft scope	34
2.6 Stage 4: finalising the scope after consultation	35
2.7 Amending the final scope after publication on the NICE website.....	36
3 The Guideline Development Group	37
3.1 Forming the GDG	37
3.2 Code of conduct and conflicts of interest.....	50
3.3 Identifying and meeting training needs.....	51
3.4 Running the GDG	52
3.5 Making group decisions and reaching consensus.....	55
3.6 Further reading	56
4 Developing review questions and planning the systematic review	58
4.1 Number of review questions	58
4.2 Developing review questions from the scope.....	58
4.3 Formulating and structuring review questions	59
4.4 Planning the systematic review	69
4.5 Further reading	71

5 Identifying the evidence: literature searching and evidence submission	72
5.1 Introduction	72
5.2 Searching for clinical evidence	72
5.3 Searching for economic evidence	79
5.4 Quality assurance of search strategies	81
5.5 Reference management software	81
5.6 Acquiring the full text of references.....	82
5.7 Documenting the search strategy	83
5.8 Timing of searches	84
5.9 Re-running searches	85
5.10 Calls for evidence from stakeholders.....	86
5.11 Additional requirements for service guidance	88
5.12 Further reading	89
6 Reviewing the evidence.....	91
6.1 Selecting relevant studies.....	91
6.2 Questions about interventions	93
6.3 Questions about diagnosis	103
6.4 Questions about prognosis	104
6.5 Using patient experience to inform review questions	105
6.6 Published guidelines.....	106
6.7 Further reading	107
7 Assessing cost effectiveness.....	110
7.1 The role of the health economist in clinical guideline development	110
7.2 Modelling approaches.....	115
7.3 Economic evidence and guideline recommendations	122
7.4 Further reading.....	124
8 Linking clinical guidelines to other NICE guidance	126
8.1 Technology appraisals	127

8.2	Interventional procedures	133
8.3	Public health guidance	136
8.4	Other NICE guidance	139
9	Developing and wording guideline recommendations	142
9.1	Interpreting the evidence to make recommendations	142
9.2	'Only in research' recommendations	147
9.3	Wording the guideline recommendations	147
9.4	Prioritising recommendations	160
9.5	Formulating research recommendations	161
9.6	Further reading	162
10	Writing the clinical guideline and the role of the NICE editors	164
10.1	Guideline structure	164
10.2	Style	168
10.3	The role of the NICE editors	170
11	The consultation process and dealing with stakeholder comments	173
11.1	Principles of responding to stakeholder comments	173
11.2	Consultation on the guideline	175
11.3	Considering a second consultation	176
12	Finalising and publishing the guideline	178
12.1	Editorial checks and review by NICE	178
12.2	Final steps	180
12.3	Launching and promoting the guideline	181
13	Implementation support for clinical guidelines	183
13.1	Needs assessment, support plan and tools	183
13.2	Developing the implementation tools	186
13.3	Publishing the implementation tools	188
13.4	Post-publication support	188
13.5	Working with national organisations	189

13.6 Other NICE implementation services and products	189
13.7 Further reading.....	190
14 Updating published clinical guidelines and correcting errors.....	192
14.1 Process and methods for reviewing the need to update a published guideline	192
14.2 Deciding whether to update a clinical guideline	198
14.3 Next steps.....	200
14.4 Exceptional updates	201
14.5 Presenting updates	202
14.6 Maintaining records	208
14.7 Correcting errors in published clinical guidelines	208
14.8 Further reading.....	209
Summary of main changes from the 2009 guidelines manual	211
Update information	217
About this manual	218

1 Introduction

This is not the current manual. From January 2015, guidelines were developed using [Developing NICE guidelines: the manual](#).

The National Institute for Health and Clinical Excellence (NICE) is the independent organisation responsible for providing national guidance on promoting good health and preventing and treating ill health. NICE guidance is developed using the expertise of the NHS and the wider healthcare community, including healthcare and other professionals, patients, service users and carers^[1], the academic world and the healthcare industry.

1.1 NICE guidance

NICE develops guidance across a number of [different areas](#) and on a range of topics.

All types of NICE guidance are developed using the best available evidence, and by involving stakeholders in a transparent and collaborative manner. Stakeholders include:

- national organisations that represent patients and carers
- national health and social care professional organisations
- the NHS
- organisations that fund or carry out research
- companies that have an interest in the guidance being developed.

1.1.1 Equality and social value judgements

NICE is committed to promoting equality, eliminating unlawful discrimination and actively considering the implications of its guidance for human rights. It aims to comply fully with the public sector equality duty as outlined in the Equality Act (2010) to:

- eliminate unlawful discrimination on the grounds of age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex or sexual orientation (the 'protected characteristics') in the way it carries out its functions and in its employment policies and practices **and**
- advance equality of opportunity between people who share a protected characteristic and people who do not share it **and**
- foster good relations between people who share a protected characteristic and people who do not share it.

NICE's revised equality scheme 2010–2013 sets out how it is meeting these obligations on equality and discrimination and what it still needs to do. The document Positively equal: a guide to addressing equality issues in developing NICE clinical guidelines provides further guidance on how equality issues are considered during guideline development.

All NICE guidance, and the procedures NICE uses to develop its guidance, follow the principles set out in Social value judgements: principles for the development of NICE guidance (second edition).

1.2 Who this manual is for

This guidelines manual explains how NICE develops and updates clinical guidelines. It provides advice on the technical aspects of clinical guideline development and the methods used. It is aimed primarily at staff at the National Collaborating Centres (NCCs) and the Internal Clinical Guidelines Programme within the Centre for Clinical Practice (CCP) at NICE^[2] that are commissioned by NICE to develop NICE clinical guidelines, and at members of the Guideline Development Groups (GDGs) that develop the individual guidelines (see table 1.1). It is also likely to be useful and of interest to a broader audience, including all guideline developers.

The advice in this manual draws on international guideline development methodology, and the experience and expertise of the clinical guidelines team in the CCP at NICE and the NCCs. It is based on internationally acceptable criteria of quality, as detailed in the Appraisal of Guidelines Research and Evaluation (AGREE II) instrument.

The structure of this manual follows the development of a NICE clinical guideline from inception through to publication. The clinical guideline development process is summarised in section 1.4.2, and an overview of the process for stakeholders, the public

and the NHS is provided in [appendix N](#). There is also information on the support provided by NICE to aid implementation of the guideline.

1.3 NICE clinical guidelines

NICE clinical guidelines are recommendations, based on the best available evidence, for the care of people by healthcare and other professionals. They are relevant to clinicians, health service managers and commissioners, as well as to patients and their families and carers.

Good clinical guidelines change the process of healthcare, improve outcomes for patients and ensure efficient use of healthcare resources. They can be used to develop standards for assessing the clinical practice of healthcare professionals, to educate and train healthcare professionals, to help patients make informed decisions, and to improve communication and shared decision-making between patients and healthcare professionals.

NICE clinical guidelines:

- set out the care that is suitable for most patients with a specific condition in the NHS in England and Wales^[3]
- aim to improve the quality of care
- assess the clinical and cost effectiveness of treatments and ways of managing a particular condition
- are developed using a process that takes account of the views of those who might be affected by the guideline (including healthcare and other professionals, patients and their carers, health service managers, NHS trusts, the public, government bodies and the healthcare industry)
- are based on the best available research evidence and expert consensus
- are developed using recognised methods that are robust and transparent
- may be used to inform the development of NICE quality standards.

Healthcare and other professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not

override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

1.3.1 Standard versus short clinical guidelines

Most NICE clinical guidelines are standard clinical guidelines, which cover broad aspects of clinical care and the management of specific conditions.

NICE short clinical guidelines address a smaller part of a care pathway. They allow the rapid development of guidance on aspects of care for which the NHS requires urgent advice.

The development of short clinical guidelines differs in some ways from that of standard clinical guidelines. Whereas an NCC oversees the development of most standard clinical guidelines, most short clinical guidelines are overseen by the Internal Clinical Guidelines Programme within CCP at NICE. Occasionally, NICE commissions an NCC to develop a short guideline. In all cases, a GDG is responsible for formulating the recommendations.

Implementation support is also provided for short clinical guidelines, following the same procedure as for standard clinical guidelines.

This manual describes the methods and processes used for developing standard clinical guidelines. Any differences between this and the process for developing short clinical guidelines are described in 'Guide to the short clinical guideline process' ([appendix M](#)).

1.3.2 Service guidance

Sometimes the Department of Health or the NHS Commissioning Board asks NICE to develop service guidance as part of the clinical guidelines programme. This service guidance is developed primarily for service commissioners rather than healthcare professionals, and focuses on the broad configuration and provision of clinical services. It addresses only interventions that are likely to have implications for the configuration of services (for example, the [Cancer service guidance](#) series).

NICE also agreed in 2009, as part of its programme of work to support the NHS quality and productivity agenda, to look increasingly for opportunities to make recommendations on service delivery within clinical guidelines. Broadly, these recommendations will fall into

the following categories:

- effectiveness and cost effectiveness of particular service models
- timing of an intervention and referral
- access to the service
- competencies required to achieve safe, clinically effective and patient-centred interventions.

The development process for NICE service guidance is largely the same as that for clinical guidelines. There may be a few differences in the composition of the GDG and the evidence base (see sections [3.1.1](#) and [5.11](#) respectively) for service guidance and for clinical guidelines that contain recommendations about service delivery.

1.4 The development process for clinical guidelines

The development time for a NICE clinical guideline (from the start of scoping to publication) is usually between 18 and 24 months for a standard guideline, and between 11 and 13 months for a short guideline.

1.4.1 Who is involved?

The various groups and individuals involved in developing clinical guidelines, and their key tasks during guideline development, are listed in table 1.1.

Table 1.1 Groups involved in clinical guideline development

	Keytasks
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<p>NICE</p>	<p>The Centre for Clinical Practice (CCP) at NICE commissions one of the NCCs to coordinate development of the clinical guideline</p> <p>For guidelines developed 'in house', the NICE Internal Clinical Guidelines Programme within the CCP develops the guideline with a GDG and carries out the tasks listed for NCCs below</p> <p>The CCP lead for the guideline (Director, Programme Director or Associate Director) signs off the scope</p> <p>The CCP works with the NICE Patient and Public Involvement Programme (PIIP) to provide an induction session for the GDG Chairs</p> <p>The Guidelines Commissioning Manager (GCM), technical team and CCP lead for the guideline support and advise the NCC during guideline development</p> <p>The CCP coordinates consultation on the draft guideline and collates consultation comments</p> <p>The GCM, technical team, CCP lead for the guideline and other NICE leads comment on the draft guideline</p> <p>The CCP reviews the final draft of the guideline and the responses by the NCC to stakeholder comments</p> <p>NICE's Guidance Executive approves ('signs off') the final guideline and confirms that the correct process has been followed for its development</p> <p>NICE publishes the NICE version of the guideline, the NICE pathway and 'Information for the public' (see section 1.4.3)</p> <p>The implementation programme at NICE develops implementation tools and may undertake a range of other activities to promote the uptake of a guideline (see section 1.4.3 and chapter 13)</p>
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<p>National Collaborating Centre (NCC)</p>	<p>Prepares the draft scope and revises the scope after consultation (see chapter 2)</p> <p>Prepares the workplan^[a]</p> <p>Helps run the stakeholder scoping workshop with the CCP at NICE (see chapter 2)</p> <p>Appoints and works with the GDG to develop the guideline (see chapter 3)</p> <p>Provides full technical and managerial support for the GDG (see chapter 3)</p> <p>Develops the review questions with the GDG (see chapter 4)</p> <p>Searches, assesses and synthesises the evidence (see chapters 3–7)</p> <p>Prepares the first draft of the guideline for consultation</p> <p>Compiles the responses to consultation comments on the draft guideline on behalf of the GDG</p> <p>Revises the guideline in response to comments received during the consultation and in accordance with NICE's review processes (see chapter 11)</p> <p>Publishes the final full guideline</p> <p>Advises NICE on issues concerning publication, dissemination, implementation and updating of the guideline</p>
<p>Guideline Development Group (GDG)</p>	<p>Contributes to preparing the scope (GDG Chair and Clinical Adviser only)</p> <p>Refines and agrees the review questions that will guide the search for evidence</p> <p>Discusses the evidence and draws conclusions</p> <p>Develops the guideline recommendations</p> <p>Responds to comments received during consultation and agrees on necessary changes to the guideline</p> <p>Works with NICE to develop the NICE pathway, 'Information for the public' and implementation tools (see chapters 10, 12 and 13)</p> <p>Supports and promotes uptake of the guideline</p>

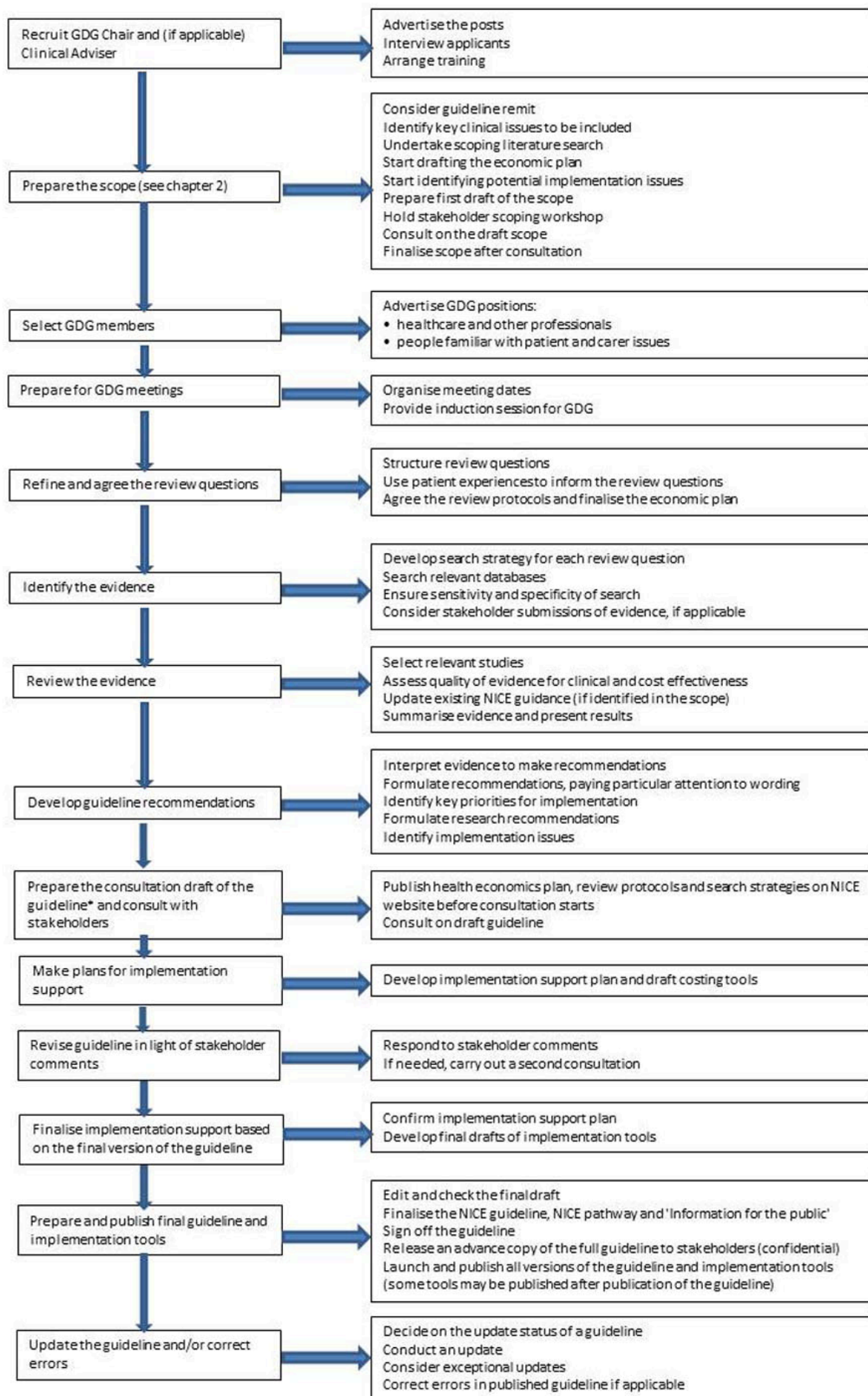
<p>Patient and Public Involvement Programme (PPIP) at NICE</p>	<p>Advises on patient and carer issues</p> <p>Identifies and approaches potential patient and carer stakeholder organisations for each clinical guideline</p> <p>Provides at least one member of the scoping group – the PPIP lead for the guideline (see section 2.2)</p> <p>Encourages and facilitates applications from patients and carers who are interested in becoming GDG members</p> <p>Advises, supports and provides training for patient and carer members of GDGs</p> <p>Comments on the draft guideline recommendations from a patient and carer perspective</p> <p>Works with NICE editors on drafting and signing off 'Information for the public'.</p>
<p>Stakeholders</p>	<p>Attend the stakeholder scoping workshop to discuss the scope of the guideline and the recruitment of GDG members</p> <p>Comment on the draft scope</p> <p>Respond to calls for evidence from the NCC (if they are made)</p> <p>Comment on the draft guideline</p> <p>Contribute to developing the implementation tools and may become involved in implementation activities</p> <p>Support and promote uptake of the guideline</p>
<p>^[a] The workplan sets out the development process for each guideline, and represents a formal agreement between the NCC and NICE. A workplan template is available on the NICE webboard for NCCs.</p>	

More information about key groups and individuals involved in clinical guideline development is given in [appendix N](#) and on the [NICE website](#).

1.4.2 Summary of the clinical guideline development process

Clinical guideline topics are referred from the Department of Health or the NHS Commissioning Board. The key stages in the development of NICE clinical guidelines are summarised in figure 1.1.

Figure 1.1 The clinical guideline development process



*The writing of the guideline is an iterative process that is ongoing throughout the development and consultation phases.

1.4.3 Publication and implementation of the clinical guideline

Four versions of each clinical guideline are published:

- The full guideline contains all the background details and evidence for the guideline, as well as the recommendations. This document is produced by the NCC or the NICE Internal Clinical Guidelines Programme.
- The NICE guideline contains only the recommendations from the full guideline, without the information on methods and evidence.
- The NICE pathway is a practical online resource for healthcare and other professionals that contains all the recommendations from a guideline, as well as any other NICE guidance that is directly relevant to the topic. It also contains links to implementation tools and to related NICE guidance and pathways.
- 'Information for the public' summarises the recommendations in the NICE guideline in everyday language for patients, their family and carers, and the wider public.

In addition to the different versions of the guideline, NICE also produces tools and may undertake a range of activities to support implementation. (See [chapter 13](#) for further information on implementation support.)

All versions of each clinical guideline, and the associated implementation tools, are published on the [NICE website](#).

1.4.4 Practical information

For any queries during the development of a clinical guideline, members of NCCs and GDGs should in the first instance contact the relevant Guidelines Commissioning Manager in the CCP at NICE.

NICE administers a 'webboard' for NCCs, which contains the following information and documents:

- declaration of interests forms

- 'The guidelines manual'
- guidelines templates (scope, full guideline, NICE guideline and short clinical guideline)
- writing guides
- documents relating to the GDG (for example, job descriptions and person specifications)
- minutes of meetings between NICE and the NCCs
- checklist about confidential information submitted by stakeholders.

As it becomes available, the following information about each clinical guideline can be found on the NICE website:

- the remit
- a list of registered stakeholders
- contact details of the NCC that is coordinating the development of the guideline
- details of the NICE project team
- members of the GDG
- a schedule for development of the guideline
- the consultation draft of the scope
- the final scope
- the equality impact assessment forms for the guideline completed at the scoping stage and before the guideline is signed off by NICE
- a table of stakeholder comments on the consultation draft of the scope and responses
- project history, and information on progress of the guideline
- health economics plan, review protocols and search strategies
- the consultation draft of the guideline
- a table of stakeholder comments on the consultation draft of the guideline and responses

- all versions of the published guideline
- tools to support implementation of the guideline.

1.5 Updating the guidelines manual

The formal process for updating this manual will begin 3 years after publication. In exceptional circumstances, and only if significant changes to the process of clinical guideline development are anticipated, this interval will be reduced to 2 years.

We welcome [comments on the content of this manual and suggested subjects for inclusion](#).

1.5.1 Interim updates

In some situations it may be necessary to make small changes to the clinical guideline development process before a formal update is due. These may be either minor insubstantial changes ('bug fixes'), or more significant changes for which formal consultation with stakeholders will be necessary. For small changes to be put in place without stakeholder consultation, they must fulfil all of the following criteria:

- no fundamental stage in the process is either added or removed
- no fundamental method, technique or step is either added or removed
- no stakeholders will obviously be disadvantaged
- the efficiency, clarity or fairness of the process or methodology will be improved.

Changes that meet all of these criteria will be published on the NICE website. 'The guidelines manual' will be updated, and changes from the previous version of the manual will be listed. Stakeholders in clinical guidelines under development at the time of the change will be notified if they are affected by the change. Stakeholders in newly commissioned guidelines will be advised to consult the website at the start of the project to familiarise themselves with the updated clinical guideline development process.

^[1] When the term 'patients and carers' is used in this manual, it is intended to include all lay people involved in developing NICE clinical guidelines. This includes people with specific conditions and disabilities and their family members (including parents for children and

young people under 16) and carers. It also includes employees of organisations representing the interests of patients and carers (for example, voluntary sector and non-governmental organisations). The term 'patients' is used as a general term to indicate a wide range of people who may be referred to differently elsewhere, such as service users of mental health services and healthy pregnant women. We also recognise that readers may use other terms such as 'consumer', 'user representative' or 'patient representative'.

^[2] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

^[3] NICE clinical guidelines are reviewed locally for their applicability to Northern Ireland (see [The Department of Health, Social Services and Public Safety website](https://www.nice.org.uk/terms-and-conditions#notice-of-rights)).

2 The scope

Topics for new clinical guidelines are referred to NICE by the Department of Health or the NHS Commissioning Board, and will usually be related to a topic in the library of quality standards for the NHS. The referral gives a remit that identifies the broad areas to be covered by the guideline, which is then translated into the scope for the guideline.

Preparing the scope is the first step in developing a clinical guideline, and determines the shape of the review work. It is conducted in four stages:

- Stage 1: selecting key clinical issues and drafting the scope ([section 2.3](#))
- Stage 2: checking the selected key clinical issues with stakeholders ([section 2.4](#))
- Stage 3: consulting on the draft scope ([section 2.5](#))
- Stage 4: finalising the scope after consultation ([section 2.6](#)).

This chapter describes what the scope is, the role of the scoping group and the process used to develop the scope at each stage.

2.1 Purpose of the scope

The purpose of the scope is to:

- provide an overview of what the clinical guideline will include, and what will not be covered
- identify the key clinical issues that must be included
- set the boundaries of the development work and provide a clear framework to enable the work to stay within the priorities agreed by NICE and the National Collaborating Centre (NCC) or the NICE Internal Clinical Guidelines Programme^[4] and the remit from the Department of Health or the NHS Commissioning Board
- ensure that equality issues are identified and considered
- inform the development of the detailed review questions (see [chapter 4](#)) and the search strategy (see [chapter 5](#)) from the key clinical issues

- provide information to healthcare and other professionals, stakeholders and the public about the expected content of the guideline
- ensure that the guideline will be of a reasonable size so that it can be developed within the specified time period.

The scope provides a framework within which to conduct the guideline development work. The title of the guideline (as given in the scope) needs to be considered very carefully so that it adequately reflects the content of the scope. The scope briefly describes the epidemiology relevant to the disease or condition, and defines the aspects of care that the guideline will cover in terms of the following:

- Populations to be included or excluded – for example, age groups or people with certain types of disease or condition. Equality groups that may merit specific consideration (for example, specific ethnic groups or people with learning disabilities) are identified.
- Healthcare setting – for example, primary, secondary or tertiary care.
- The different types of interventions and treatments to be included and excluded – for example, diagnostic tests, surgical treatments, medical and psychological therapies, rehabilitation and lifestyle advice. It is important that the scope is as specific as possible about the interventions the guideline is intended to cover.
- Topic-specific information and support for patients and carers.
- The main outcomes that will be considered.
- Defining links with other relevant NICE guidance, including guidance to be updated, guidance to be incorporated and other related guidance (see chapters [8](#) and [14](#)).

2.2 The scoping group

The scope is prepared by a scoping group, led by the NCC with input from the Guideline Development Group (GDG) Chair (and the GDG Clinical Adviser or topic specialist if there is one; see section 3.1.3) and NICE (including the Patient and Public Involvement Programme [PPIP] lead for the guideline). Box 2.1 shows the membership of the scoping group. The role of the group is to:

- identify the key clinical issues for inclusion and draft the scope

- revise the draft scope after the stakeholder scoping workshop
- prepare the draft scope for consultation
- respond to stakeholder comments
- finalise the scope after consultation.

Box 2.1 Members of the scoping group

NCC

- Director or senior staff member (Chair of scoping group)
- Project manager
- Information specialist
- Systematic reviewer
- Health economist

GDG

- Chair
- Clinical Adviser or topic specialist (if there is one)

NICE

- Guidelines Commissioning Manager (Centre for Clinical Practice [CCP]), plus staff providing technical support as necessary
- PPIP lead for the guideline

The scoping group meets (either face to face or by teleconference) before the stakeholder scoping workshop (see below), and again after the workshop to refine the draft scope for consultation. It also discusses and responds to comments received during consultation and finalises the scope for sign off by NICE.

2.3 Stage 1: selecting key clinical issues and

drafting the scope

This stage includes considering the remit from the Department of Health or the NHS Commissioning Board, identifying the key clinical issues for inclusion in the scope, searching the literature, considering any equalities issues and consulting with experts.

2.3.1 Considering the remit

The remit received by NICE forms the basis of the scope, and all issues specified by the remit are addressed in the scope. The remit may also be intended to support the subsequent development of a NICE quality standard. Sometimes NICE may request clarification on the remit and the topic. This may involve redefining the remit in order to specify the boundaries and the extent of the work.

2.3.2 Identifying the key clinical issues from the care pathway

This is a critical part of the process, because it determines the breadth and depth of the work. It involves identifying the most important aspects of care that the clinical guideline will cover. This ensures that the guideline focuses on areas in which the NHS most needs advice. Key clinical issues relate to the effectiveness and cost effectiveness of interventions or tests that are being considered for a given population.

To ensure that areas from the whole patient pathway for the condition are considered for inclusion in the scope, so that the guideline can inform the subsequent development of a NICE quality standard, a care pathway or similar analytical framework should be used. Draft review questions, which specify in some detail the particular interventions to be compared and the health outcomes of interest (see [chapter 4](#)), may be included in the scope. Key clinical issues should be as specific as possible, indicating the relevant population and the alternative strategies that are being considered. Examples of key clinical issues are shown in box 2.2.

Box 2.2 Examples of key clinical issues included in draft scopes for consultation

Issues relating to interventions

Issue relating to diagnosis

- CT for identifying patients with lung cancer who are suitable for curative surgery

Several criteria should be considered when identifying the key clinical issues (see box 2.3). The scoping group should ensure that it has taken equality issues into consideration when identifying the key clinical issues and drafting the scope (see section 2.3.5). The NCC (in discussion with the scoping group) should also consider the composition of the GDG at this stage (see [chapter 3](#)).

Box 2.3 Factors to consider when identifying key clinical issues and drafting the scope

Uncertainty or disagreement on best practice

Is there:

- variation in current practice?
- evidence suggesting that common practice may not be best practice?
- debate in the literature?

Potential to improve important health outcomes and/or make better use of health resources

- How many people are affected?
- What is the potential for health gain at acceptable cost?
- What is the potential for reducing ineffective practice?
- What is the potential for achieving cost savings with no, or limited, adverse impact on health?

Potential for avoiding unlawful discrimination and reducing health inequalities

- Consider possible inequalities relating to sex and gender, gender reassignment, pregnancy and maternity, race and ethnicity, disability, age, sexual orientation, marriage and civil partnership, religion or belief, and socioeconomic status.
- Are exclusions listed in the scope (for example, populations, treatments or settings) justified?
- Are there inequalities in prevalence, risk factors, severity or likely benefit that need to be addressed in the scope?

Likelihood that the guideline could contribute to change

- Is a new review of the evidence or an economic evaluation likely to reduce existing uncertainties?
- What is the potential for achieving consensus within the GDG and in the wider stakeholder community?

Other important factors

- Relationship with national policy and priorities.
- Need to update other NICE guidance.
- The existence of 'significant new medicines' (see [section 8.1.1](#))
- Consideration of the licensing status of drugs (see [section 9.3.6](#)).

2.3.2.1 Main outcomes

The scope includes a section listing the main outcomes of interest for the guideline. An exhaustive list is not required, although it should be possible to include some important disease/condition-specific outcomes. Health-related quality of life is a critical outcome and should always be included in the list. It is also desirable to specify any adverse effects of interventions that will be considered in the guideline. Overall survival will be an important outcome for many guidelines.

2.3.2.2 Complementary therapies

The effects of complementary and alternative therapies may be addressed in the guideline if such therapies are commonly used in the clinical area of interest. If commonly used complementary and alternative therapies are not to be covered in the guideline, this should be stated clearly in the scope.

2.3.3 The scoping search

A scoping search of the literature is important in order to identify previous clinical guidelines, health technology assessment reports, key systematic reviews and economic evaluations relevant to the guideline topic. This search should not aim to be exhaustive. It should be based on the need to reasonably inform the content of the scope as set out above. For guidelines that are updates of existing guidelines, the searches undertaken as part of the process for reaching a guideline review decision (see [section 14.1](#)) can be used to inform the searches required at the scoping stage.

Further searches to identify systematic reviews and economic evaluations will be necessary once the review questions have been finalised (see [chapter 5](#)).

Suggested sources for this scoping search are listed in box 2.4 (links are provided for sources that are freely available). Other sources may be used depending on the guideline topic. More information on literature searching is given in [chapter 5](#).

Box 2.4 Suggested sources for the scoping search (listed in alphabetical order)

- Clinical Evidence (BMJ Publishing Group)
- Cochrane Database of Systematic Reviews – CDSR (Cochrane Reviews)^a
- [COMET initiative website](#) (agreed sets of important outcomes)
- [DUETS](#) (UK Database of Uncertainties about the Effects of Treatments)
- Health Technology Assessment (HTA) Database (Technology Assessments)^b
- MEDLINE/MEDLINE In-Process
- [National Guideline Clearinghouse](#) (United States)
- NHS Economic Evaluation Database (NHS EED) (Economic Evaluations)^b and the Health Economic Evaluations Database (HEED), if subscribed to
- [NHS Evidence](#)
- [Turning Research into Practice](#) (TRIP database)
- Websites of [NICE](#) and the [National Institute for Health Research \(NIHR\) HTA Programme](#) for guidance and HTAs in development
- Websites of relevant professional bodies and associations that may have produced guidelines or reports (for example, British Thoracic Society for conditions relating to the lung)

For service delivery guidance:

- Health Management Information Consortium [HMIC] database

For information about patient or service user experience (including children and young people):

- [Healthtalk Online](#)
- [YouthHealthTalk](#)

Websites of relevant patient organisations that may report research on patients' views or experiences (NICE's PPIP can advise further).

^a Accessible via [the Cochrane Library](#). Database name in parentheses is that used in the Cochrane Library.

^b Accessible as part of [the Cochrane Library](#) and via the [Centre for Reviews and Dissemination](#) (CRD). The CRD website hosts the most up-to-date versions of the databases. Database names in parentheses are used in the Cochrane Library.

In addition to the results of the scoping search, the scoping group should consult the background documentation, if applicable. This may include briefing papers and documentation related to NICE clinical guideline review decisions (see [section 14.1](#)).

2.3.4 Preparing the draft scope

NICE has developed a template for preparing the draft scope that sets out the format and describes what should be included, along with notes on using the template. NCCs should use the up-to-date version of this template for preparing the scope. The template is available from NICE's webboard for NCCs and from the CCP at NICE.

References are not included in the scope, but the information specialist at the NCC should keep a detailed record of references used as a basis for the scope; these should be available on request.

2.3.5 Equality issues at the scoping stage

During development of the scope, due regard must be paid to considering and assessing any equality issues to establish:

- whether and to what extent the guideline is likely to be relevant to the promotion of equality and the elimination of unlawful discrimination
- whether and to what extent it would be proportionate to include particular equality issues in the scope.

Considerations will be reflected in the equality impact assessment (see [section 2.6.2](#)).

Further guidance on how to consider and assess equality issues at the scoping stage is given in the document [Positively equal: a guide to addressing equality issues in developing NICE clinical guidelines](#).

2.4 Stage 2: checking the selected key clinical

issues with stakeholders

It is essential to seek the views of experts in the field, stakeholders and organisations that represent the interests of people with the condition and their carers, to confirm that the key clinical issues identified by the scoping group are relevant and appropriate.

2.4.1 The stakeholder scoping workshop

Before the consultation on the draft scope, registered stakeholders are invited to a scoping workshop to discuss the key clinical issues identified by the scoping group. One person from each registered stakeholder organisation may attend. Organisations will be permitted to nominate more than one representative under some circumstances (for example, if an organisation represents the views of both professionals and patient groups) if space permits and with the prior agreement of NICE. People attend the workshop from their own perspective and do not represent the views of their stakeholder organisation, but should bring as wide a perspective of views as possible. Attendees, including representatives of relevant patient and carer organisations, should have specific knowledge of or experience in the topic area.

The stakeholder scoping workshop is in addition to the formal consultation on the scope. Stakeholder organisations should still submit comments in writing during consultation, as described in [section 2.5](#).

The objectives of the scoping workshop are to:

- obtain feedback on the selected key clinical issues
- identify which patient or population subgroups should be specified (if any)
- seek views on the composition of the GDG (see section 3.1.1)
- encourage applications for GDG membership.

At the workshop, the scoping group provides details about the scope, the timetable for guideline development, the guideline development process, the nature of stakeholder input into the guideline, and the processes for recruitment to the GDG and submission of evidence. This is followed by a structured discussion around the key clinical issues. The workshop is chaired by the CCP lead for the guideline (see [table 1.1](#)).

People attending the scoping workshop are sent an initial draft of the scope. This outlines the background to the guideline, groups and settings that will be covered, those that will not be covered, and the key clinical issues selected. This initial draft is intended as a starting point for discussion. The discussions and key themes that emerge from the scoping workshop are summarised by the NCC, with input from the GDG Chair, the Clinical Adviser (if there is one) and the Director or senior staff member of the NCC who is the Chair of the scoping group. This document is posted on the NICE website during consultation on the scope.

2.5 Stage 3: consulting on the draft scope

The scoping group considers the issues raised at the scoping workshop and refines the draft scope for consultation. The draft scope is edited by a NICE editor before consultation and may be modified by NICE after discussion with the scoping group. It is then posted on the NICE website for a 4-week period of public consultation. Comments are invited from registered stakeholder organisations. Comments will also be solicited from the Medicines and Healthcare products Regulatory Agency (MHRA) when the off-label use of drugs is included in the draft scope.

2.5.1 Stakeholder organisations

Organisations representing healthcare and other professionals, the NHS and patients and carers, as well as companies with an interest in a particular topic, can register as stakeholders for a particular clinical guideline. Registered stakeholder organisations comment on the draft scope (and, later, on the draft guideline – see [chapter 11](#)). [Appendix N](#) and the [NICE website](#) contain details about how to register as a stakeholder and how to contribute to the guideline development process.

Members of the scoping group and NICE's implementation adviser for the guideline (see [chapter 13](#)) routinely review the list of registered stakeholders to check whether any important organisations are missing. Stakeholders attending the stakeholder scoping workshop are also encouraged to identify potential stakeholders who are not registered.

2.6 Stage 4: finalising the scope after consultation

2.6.1 Dealing with stakeholder comments

The scoping group finalises the scope in the light of comments received. Stakeholders may ask for additional aspects of care to be included in the guideline, but this could make the development of the guideline unmanageable within the time permitted. Therefore the impact on overall workload needs to be considered before the scope is expanded in response to stakeholder comments. However, relevant suggestions that might make the guideline more useful, and so improve patient care, should not be ignored. This may entail removing other areas considered to be of lower priority. Suggestions clearly outside the original remit should not be included. If the scoping group considers that a request to expand the scope would mean that the guideline could not be completed on schedule, this should be discussed with NICE.

All stakeholder comments, and the actions taken by the scoping group and NICE in response to each comment, are clearly documented in a 'scope consultation table'. This is published on the NICE website with the final scope. The process for responding to stakeholder comments should follow the principles described in [section 11.1](#).

2.6.2 Equality impact assessment

Before the scope is signed off, an equality impact assessment (EIA) form is completed by the NCC and GDG Chair to demonstrate how equality issues have been identified and considered during scoping. The EIA form is reviewed and signed by the Chair of the scoping group (that is, the NCC Director or senior staff member) and the GDG Chair, and countersigned by the CCP lead for the guideline, before being posted on the NICE website. Further guidance on how to complete the EIA form is outlined in the document [Positively equal: a guide to addressing equality issues in developing NICE clinical guidelines](#).

2.6.3 Signing off the final scope

Subject to any amendments agreed by NICE, the revised scope and the responses to stakeholder comments are signed off by the CCP lead for the guideline.

Once the scope has been signed off, the GDG should not make changes without

consulting NICE, and this should be done only in exceptional circumstances.

The final scope and responses to stakeholder comments are posted on the NICE website.

2.7 Amending the final scope after publication on the NICE website

In exceptional circumstances the final scope that has been signed off and posted on the NICE website may need amending. For example, this might occur if a scope does not cover an important area of care. The decision on whether to amend the scope is made by NICE, based on advice from the NCC.

^[4] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

3 The Guideline Development Group

Convening an effective Guideline Development Group (GDG) is one of the most important stages in producing a NICE clinical guideline. The GDG agrees the review questions, considers the evidence and develops the recommendations. Membership of the GDG therefore needs to be multidisciplinary, comprising:

- healthcare and other professionals (both specialists in the topic and generalists)
- patients and/or carers
- the National Collaborating Centre (NCC) team.

The exact composition of the GDG should be tailored to the topic covered by the clinical guideline. It should reflect the range of stakeholders and groups whose professional activities or care will be covered by the guideline, and should include at least two members who have experience or knowledge of patient and carer issues.

During guideline development, people who are not members of the GDG but who have relevant expertise may be asked to attend meetings to take part in specific discussions (see section 3.1.7). Manufacturers of pharmaceutical products or medical devices are not represented on the GDG because of potential conflicts of interest; they have input into the guideline development process as stakeholders.

Members of the GDG are not permitted to submit comments as stakeholders during the consultation on the draft guideline (see [chapter 11](#)). If a GDG member is involved with a registered stakeholder organisation, they should not submit comments during the consultation on behalf of that organisation – someone else in the organisation should submit the comments.

This chapter describes the core elements of forming and running a GDG, including the appointment and role of the Chair and members.

3.1 Forming the GDG

The Chair and members of the GDG are appointed for the duration of a particular guideline's development. The Chair is appointed before the guideline scoping stage and is

a member of the scoping group. If there is a Clinical Adviser for the guideline, he or she is also appointed before scoping. Other GDG members are appointed after discussion about GDG membership at the stakeholder scoping workshop (see [section 2.4](#)).

3.1.1 The composition of the GDG

The composition of each GDG is described in a workplan that is prepared by the relevant NCC or the NICE Internal Clinical Guidelines Programme^[5] as part of its contractual agreement with NICE (the template is available from the NICE webboard for NCCs). The composition of the GDG is agreed by the Centre for Clinical Practice (CCP) lead for the guideline (see [table 1.1](#)). A workable size for a GDG is 13–15 people, including the NCC team. This balances the opportunity for individuals to contribute effectively with the need for a broad range of experience and knowledge. Members of the GDG should have sufficient expertise and credibility to command the respect of people within their field. The GDG has five key constituents:

- the Chair
- members from the healthcare professions ('healthcare professional members'; they may include a Clinical Adviser for the group), and from other professions where relevant
- patient and carer members
- technical members
- a project manager.

For some guideline topics, it may be important for the GDG to include an epidemiologist with knowledge of the subject. The GDG may also be supported by expert advisers (see [section 3.1.7.1](#)).

As far as possible, the GDG will have an appropriate balance with regard to the principles of [NICE's equality scheme](#).

Ideally, GDG members should be drawn from different parts of England, Wales and Northern Ireland (because guidelines apply to the NHS in England and Wales, and in Northern Ireland under special arrangements), but this will be influenced by the expertise available. For example, healthcare professional members (see [section 3.1.4](#)) may come from Scotland if they cannot be recruited from England, Wales or Northern Ireland.

All GDG members should be committed to developing the clinical guideline according to the processes set out in this manual, and to working within [NICE's equality scheme](#). They are expected to attend all GDG meetings (usually between 10 and 15).

New members should not usually be added to the GDG once the first GDG meeting has taken place, because this may disturb the group dynamic. If a GDG member becomes unable to fulfil their duties (for example, because of illness), the NCC may consider another recruitment process to replace that person, in discussion with NICE. If additional expertise is needed, the NCC should also discuss and agree this with NICE.

People are GDG members in their own right, and do not represent any particular organisation or group.

If service guidance is being developed (see [section 1.3.2](#)), or if a clinical guideline contains a service guidance component, additional members should be appointed to the GDG to reflect this. This might include input from:

- commissioning bodies in England (and local health boards in Wales, including specialist commissioning bodies)
- relevant clinical networks
- a chief executive or public health consultant with an interest in the topic.

Additional GDG members recruited for service guidance are subject to the same recruitment process as other GDG members (see below).

The following sections outline the roles of the GDG members and describe how the members should be appointed. Vacancies for GDG positions are posted on the [NICE website](#). In addition, other means are used to alert people to GDG vacancies, including circulating the information to all registered stakeholder organisations, liaising with the Royal Colleges (including their patient liaison groups), and using local networks. Templates for job descriptions and person specifications are available from NICE's webboard for NCCs, and from the CCP at NICE.

3.1.2 The GDG Chair

To work well, a GDG needs an effective Chair. The GDG Chair is a member of the scoping group (see [section 2.2](#)) and should therefore be recruited before work starts on the scope.

The Chair guides the GDG in terms of task (developing the guideline) and process (how the group works). The Chair also helps the GDG to work collaboratively, ensuring a balanced contribution from all members (see box 3.1).

The Chair may be a specialist in the guideline topic, but this is not essential because specialist knowledge can be provided by other GDG members.

Box 3.1 Key roles and functions of the GDG Chair

The Chair is required to attend an induction session (see [section 3.3.1](#)).

The Chair needs background knowledge about the guideline topic and NICE's clinical guideline development process.

To facilitate the working of the group, the Chair:

- sets up the rules for how the GDG operates, based on the principles set out in [section 3.4.1](#)
- assists with the planning of the GDG meetings
- establishes a climate of trust and mutual respect among members
- provides opportunities for all members to contribute to the discussions and activities of the group
- may meet individual GDG members outside GDG meetings.

In GDG meetings, the Chair:

- ensures that GDG members declare any new conflicts of interest that have arisen since their last declaration and handles any conflicts as they arise, in line with [NICE's policy](#)
- steers the discussions according to the agenda
- keeps the group discussion unified and avoids disruption by sub-conversations or dominance by any members
- encourages constructive debate, without forcing agreement
- prevents repetitive debate
- summarises the main points and key decisions from the debate
- signs off meeting minutes once approved by the GDG.

The Chair must ensure that [NICE's equality scheme](#) and [social value judgements document](#) are adhered to.

The Chair approves the draft full guideline and advises the NCC on responses to stakeholder comments.

3.1.2.1 Appointing the Chair

In accordance with NICE's policy [Appointments to guidance producing bodies advisory to NICE](#) (November 2006), the position of GDG Chair is advertised on the NICE website. It may also be advertised on the website of the NCC and/or the Royal College or professional body that hosts the NCC, and in other appropriate places identified by the NCC. The NCC informs the stakeholder organisations about the advertisement.

Applicants are required to submit a CV (including names and contact details of two referees), a completed declaration of interests form (available from NICE's webboard for NCCs), a completed equality monitoring form and a statement explaining how they meet the criteria laid out in the person specification. The Chair is appointed after interview by the selection panel, which should include the NCC Director (or senior colleague), the Director of the CCP (or delegate) and a non-executive director of NICE.

3.1.3 The Clinical Adviser

Where appropriate, a Clinical Adviser or topic specialist may be appointed. She or he is a member of the GDG with additional responsibilities, and works closely with the NCC team to provide expert topic-specific support. The Clinical Adviser is a member of the scoping group (see [section 2.2](#)), and is therefore appointed before work starts on the scope. The detailed responsibilities of the Clinical Adviser will differ depending on the guideline and the expert input required. These may include, for example, working with the systematic reviewer on the detail of the evidence reviews where expert topic-specific knowledge is needed, or checking the full guideline to ensure that clinical and technical terminology is correct.

3.1.3.1 Appointing the Clinical Adviser

The position of Clinical Adviser is advertised on the NICE website. It may also be advertised on the website of the NCC and/or the Royal College or professional body that hosts the NCC, and in other appropriate places identified by the NCC. NICE informs the stakeholder organisations about the advertisement.

Applicants are required to submit a CV (including names and contact details of two referees), a completed declaration of interests form (available from NICE's webboard for NCCs), a completed equality monitoring form and a statement explaining how they meet the criteria laid out in the person specification. The Clinical Adviser is appointed after

interview by the selection panel, which should include the NCC Director (or senior colleague), the Director of the CCP (or delegate) and a non-executive director of NICE.

3.1.4 Healthcare professional members

Healthcare professional members of the GDG should be recruited shortly after the stakeholder scoping workshop (see [section 2.4](#)). They should represent the perspective(s) of the healthcare professionals (and other professionals where relevant) involved in the care of patients affected by the guideline topic. They are on the GDG as healthcare professionals with appropriate knowledge and skills; detailed research expertise is not necessary, although an understanding of evidence-based medicine is essential. They are not expected to represent the views of their professional organisations.

A GDG has, on average, between six and eight healthcare professional members; the list of professions represented is agreed as part of the workplan between the NCC and NICE (the workplan template is available on the NICE webboard for NCCs).

The roles and responsibilities of the healthcare professional members of the GDG are shown in box 3.2.

Box 3.2 Key roles of healthcare professional members of the GDG

GDG members from the healthcare professions (and other professions where relevant) are expected to:

- agree the review questions, based on the key clinical issues in the scope
- contribute constructively to meetings and have good communication and team-working skills; this should include a commitment to the needs of patients and carers
- use their background knowledge and experience of the guideline topic to provide guidance to the NCC technical team in carrying out systematic reviews and economic analyses
- read all relevant documentation and make constructive comments and proposals at (and between) GDG meetings
- with other members of the GDG, develop recommendations based on the evidence reviews, or on consensus when evidence is poor or lacking
- advise on how to identify best practice in areas where research evidence is absent, weak or equivocal
- with other members of the GDG, consider implementation issues arising from recommendations, feed back to the implementation team at NICE and assist with the development of the implementation support tools (see [section 13.2](#))
- with other members of the GDG, approve the review protocols (see [section 4.4](#))
- with other members of the GDG, agree the minutes of GDG meetings.

They are not routinely expected to:

- review the evidence
- search the literature
- write the guideline.

3.1.4.1 Appointing healthcare professional members

Vacancies for healthcare professional members of the GDG are advertised on the NICE

website. They may also appear on the website of the NCC and/or the Royal College or professional body that hosts the NCC, and in other appropriate places identified by the NCC. NICE informs registered stakeholder organisations about the advertisement.

Applicants are required to submit a CV (including names and contact details of two referees), a completed declaration of interests form (available from NICE's webboard for NCCs) and a statement explaining how they meet the criteria laid out in the person specification. If they wish they can also complete an equality monitoring form. Members are selected by the Director of the NCC (or a delegated guideline lead if applicable) and the GDG Chair, and may be asked to attend an interview. Appointments will be subject to confirmation by the CCP lead for the guideline at NICE.

3.1.5 Patient and carer members

At least two members of each GDG should have experience and/or knowledge of issues that are important to patients and carers (the 'patient and carer members'). This is to ensure that patient and carer issues, as well as the views of healthcare professionals, inform the guideline development process. In general, patient and carer members will have direct experience of the condition as a patient, as a carer or family member, or as an officer or member of a patient or carer organisation or support group. They should be willing to reflect the experiences of a wide network of patients, rather than basing their views only on their own experience. They do not represent the views of any particular organisation. Healthcare professionals are well represented on GDGs, so patient and carer members usually do not have a healthcare professional background. Patient and carer members have equal status with other members of the GDG. Their specific roles are shown in box 3.3.

Box 3.3 Key roles of patient and carer members of the GDG

Patient and carer members carry out the same functions as other GDG members, but they are often able to offer specific expertise in:

- ensuring that review questions embrace patient as well as professional issues
- raising awareness of grey literature^[a] known to them (for example, patient surveys) that highlights patient issues that may inform the work of the GDG
- considering the extent to which published evidence has measured and taken into account outcome measures that patients consider important
- highlighting areas where patient preferences and patient choice may need to be acknowledged in the guideline
- ensuring that recommendations address patient issues and concerns
- ensuring that the guideline as a whole, and particularly the recommendations, are worded sensitively (for example, treating patients as people, not as objects of tests or treatments).

^[a] Grey literature is defined as reports that are not formally published or have limited distribution, such as institutional reports, and which may not be identified through the common bibliographic retrieval systems.

3.1.5.1 Appointing patient and carer members

Patients, carers and other members of the public can apply to become GDG members by responding to advertisements posted on the [NICE website](#). NICE's Patient and Public Involvement Programme (PPIP) contacts all registered patient and carer stakeholder organisations to alert them to these advertisements. However, a person does not need to be a member of a registered stakeholder organisation to apply. For further details, see [information on patient and public involvement](#).

- People who want to reply to the advertisement can download an application pack from the NICE website, which includes a 'mini job description' and a person specification to help them decide whether they have the experience and skills to make an effective contribution to the GDG. This pack can be sent by post on request.

- Applicants are asked to complete an application form describing how their skills and experience meet the specified requirements. They must also complete a declaration of interests form, and if they wish they can complete an equality monitoring form.
- Applications are sent to the PPIP, which can also offer advice and support during the application process, both to patient and carer organisations and to individual applicants.
- The PPIP forwards all applications to the NCC. Staff at the NCC and the GDG Chair shortlist applicants according to the criteria in the job description and person specification. The NCC interviews shortlisted applicants, either in person or by telephone, before making a final decision.
- The NCC is responsible for notifying successful and unsuccessful applicants.

3.1.6 NCC team

A core team from the NCC supports the GDG. This team usually includes the NCC Director, an information specialist, a lead systematic reviewer, a health economist and a project manager (the lead systematic reviewer may also act as project manager).

NCC staff who act as members of a GDG are voting members. However, to ensure that the NCC does not have too much influence in a vote, no more than three NCC staff members are allowed to vote on any one issue. For each vote, the NCC should decide which of its staff are the most appropriate to vote; these would normally be staff with particular knowledge of the issue under discussion.

3.1.6.1 Information specialist

The information specialist identifies the relevant literature that is used to answer the review questions developed by the GDG and the NCC team (see [chapters 4–6](#)). The role of the information specialist involves:

- contributing to the setting of review questions and review protocols
- designing and testing population and study design search filters (see [section 5.2.2.7](#))
- contributing to discussions among the NCC team and in GDG meetings as required, including deciding whether a search is needed and gathering key terms and synonyms

- identifying which databases should be searched
- drafting, refining and executing search strategies
- creating databases of the search results using reference management software (including removing duplicates), in preparation for sifting by a systematic reviewer (see [section 6.1](#))
- maintaining audit trails, including keeping a log of search results, rationales and strategies
- keeping track of which papers are ordered for which review question in the document delivery process.

In addition, the information specialist advises on issues such as copyright and licences, metadata, archiving and record management.

3.1.6.2 Systematic reviewer

The role of the systematic reviewer is to provide summarised tables of the evidence to inform other GDG members. This role involves:

- contributing to the setting of review questions and review protocols
- assessing and selecting published abstracts
- critical and quality appraisal of evidence using a validated system
- distilling evidence into tables
- synthesising evidence into statements
- maintaining comprehensive audit trails.

The systematic reviewer is a core member of the GDG, alongside the rest of the NCC team. He or she is crucial to the dissemination, presentation and debate of the evidence within the GDG.

3.1.6.3 Health economist

The role of the health economist is to inform the GDG about potential economic issues and to perform economic analyses. The health economist is a core member of the GDG, and

their role is described in more detail in [chapter 7](#).

3.1.6.4 Project manager

The project manager plays a crucial role in overseeing and facilitating the guideline development process.

3.1.7 Non-GDG members attending GDG meetings

People who are not members of the GDG may also attend GDG meetings, as either expert advisers or observers. They may be healthcare or other professionals, patients or carers, other experts, or NICE or NCC staff. They are expected to follow the code of conduct of the GDG and to sign the confidentiality agreement form (see [section 3.2](#)).

3.1.7.1 Expert advisers

If the GDG does not have sufficient knowledge or expertise to make recommendations in a particular area, it may call on 'expert advisers' – external experts who can provide additional evidence from their experience and specific expertise to help the GDG make decisions. These can include people with a patient and carer perspective. Expert advisers attend a GDG meeting because of their knowledge in a particular area. It is therefore important that they sit within the group and enter fully into any discussion. However, they are not full members of the GDG; they do not have voting rights, and they should not be involved in the final decisions or influence the wording of recommendations. They should submit a declaration of interests form before attending the GDG meeting.

3.1.7.2 Observers

An observer at a GDG meeting may be asked to sit apart from the group, and should enter into discussions only if invited to do so by the GDG Chair. Observers at GDG meetings may include members of NICE staff (for example, the Guidelines Commissioning Manager, the lead editor and the implementation lead). Observers who are not members of NICE staff or members of the NCCs are required to sign a declaration of interests form, and need the prior permission of the group to attend.

3.2 Code of conduct and conflicts of interest

3.2.1 Declaring interests

The NCC should consider any potential conflict of interest for any person applying to become a GDG member before making a decision on their appointment.

All GDG members and any individuals who have direct input into the guideline (including NCC and NICE staff, expert advisers and expert peer reviewers) should update their declaration of interests form before each GDG meeting. Any changes to a GDG member's declaration of interests should be recorded in the minutes of the GDG meeting (which are published on the NICE website). The Chair, in discussion with the NCC Director, should consider these in accordance with NICE policy.

Declarations of interests will be published in the final full guideline (see section 10.1).

3.2.2 Code of conduct and confidentiality

NICE has developed a code of conduct for GDG members and other people who attend GDG meetings. This code sets out the responsibilities of NICE and the GDG, and the principles of transparency and confidentiality (see appendix A1). On appointment, all GDG members are asked to sign a confidentiality form stating that they agree not to disclose any of the draft guideline recommendations before the public consultation begins (see appendix A2). This is to ensure that recommendations in the public domain have been agreed by all members of the GDG.

All people who see documents or who are party to discussions relating to a guideline before public consultation will be required to sign the confidentiality agreement form before becoming involved. The NCC should keep copies of signed forms.

3.2.3 Social value judgements and equality scheme

Before the GDG starts its work, the NCC should ensure that all GDG members have a copy of NICE's most recent report on social value judgements: Social value judgements: principles for the development of NICE guidance (2nd edition; 2008). They should also make sure that GDG members are aware of NICE's equality scheme and action plan.

3.2.4 Dealing with enquiries on GDG work

If GDG members are asked by external parties – including stakeholders or their professional organisation – to provide information about the work of the GDG, they should first discuss the request with the NCC or contact NICE (see [appendix A3](#)). They should declare this at the next GDG meeting and inform the NCC Director.

3.3 Identifying and meeting training needs

3.3.1 Chair

The person selected to perform the crucial role of GDG Chair may need support and training so that they can carry out their role effectively. He or she requires in-depth knowledge of the NICE clinical guideline development process and an understanding of group processes. The CCP provides a short induction session for GDG Chairs, in collaboration with the PPIP. Everyone who is appointed as a GDG Chair is required to attend one of these induction sessions. The induction covers the key tasks that the Chair is expected to perform. Box 3.4 outlines the content of the induction session.

Box 3.4 Content of the GDG Chair induction session

- Key principles for developing NICE clinical guidelines
- Formulating review questions
- Reviewing evidence
- Introduction to health economics
- Developing and wording recommendations
- Principles of facilitation
- NICE's equality scheme
- Declaring interests and dealing with conflicts of interest
- How the work of the GDG is planned and organised

In addition to the induction session, the NCC should identify and meet any additional training needs that a GDG Chair may have. For example, unless the Chair is an experienced facilitator, he or she may need additional training in this area – particularly in relation to the important role of ensuring that the views of patients and carers are given appropriate weight by the GDG. The NCC may consider a 'buddying' approach in which a new GDG Chair learns from someone with previous experience as a Chair.

3.3.2 Healthcare and other professional members

To work effectively, GDG healthcare and other professional members may need training and support in some technical areas of guideline development, such as systematic reviewing and health economics. The Chair and the NCC should be aware of the types of training that individual GDG members may need at the start of or during the guideline development process, so that they can provide the necessary support. Training for GDG healthcare and other professional members should be provided by the NCC at an early GDG meeting, and should include components similar to those outlined in box 3.4.

3.3.3 Patient and carer members

The PPIP at NICE offers dedicated training to all patient and carer members of the GDG. This training covers topics such as an introduction to health economics, critical appraisal, and developing recommendations from evidence. In addition, the training gives the patient and carer members the opportunity to learn from people who have been on previous GDGs.

The PPIP also gives a short presentation on the role of patient and carer members to the whole GDG at the first meeting.

3.4 Running the GDG

Running the GDG is the responsibility of the NCC, in consultation with the Chair. Core responsibilities for all meetings include:

- setting meeting dates, which should be done well in advance
- planning agenda items
- sending out papers

- keeping records of all meetings
- ensuring that all GDG members have a copy of the current guidelines manual.

A summary of the minutes of each GDG meeting is made available on the NICE website; this includes:

- where the meeting took place
- who attended
- apologies for absence
- declarations of interest of those in attendance, including actions and decisions made about any conflict of interest
- a list of the subjects discussed
- date, time and venue of next meeting.

Minutes of GDG meetings are posted on the NICE website during guideline development, before the guideline is published. Each set is approved by the GDG at the next meeting, and signed off by the GDG Chair and the NCC.

3.4.1 General principles

Because the GDG is multidisciplinary, its members will bring with them different beliefs, values and experience. All these perspectives should be valued and respected. Each member should have an equal opportunity to contribute to the guideline development process. It is important to check that the terminology that GDG members use is understood by all and clarified if needed. The Chair should ensure that there is sufficient discussion to allow a range of possible approaches to be considered, while keeping the group focused on the guideline scope and the timescale of the project.

3.4.2 Quorum

The quorum of the GDG will be 50% of appointed members. No business relating to the formulation of guideline recommendations may be conducted unless the meeting is quorate. If a member is excluded because of a conflict of interest and this causes membership to fall below the quorum, no business may be transacted.

Expert advisers (see section 3.1.7.1) are not appointed members of the GDG and do not count towards the quorum.

3.4.3 Meeting schedule

There are usually between 10 and 15 GDG meetings, held at approximately monthly intervals. Most are 1-day meetings, but some may take place over 2 days.

3.4.4 The first two GDG meetings

Specific aspects of the clinical guideline development process are covered in the first and second GDG meetings.

The first meeting should focus on providing information for GDG members on the following subjects:

- the process of clinical guideline development
- how systematic reviews are performed
- the role of health economics in decision-making
- how patient and carer members contribute
- the role of the GDG
- the role of individual members of the NCC team.

GDG members should also be made aware of and operate within the principles contained in the report [Social value judgements: principles for the development of NICE guidance and NICE's equality scheme](#).

Staff from the CCP and the PPIP at NICE will give presentations to explain how the elements of the clinical guideline development process fit together.

The second meeting should focus on agreeing the review questions, based on the scope. It may be helpful to establish an explicit framework that clarifies the objectives of the work, the specific tasks that need to be carried out and the timetable. This will enable the group to focus and to develop a working relationship that is structured and well defined. [Chapter 4](#) describes the process of developing review questions.

3.4.5 Working with NICE staff

At subsequent GDG meetings, the lead editor, implementation lead, costing lead and communications lead for the guideline from NICE may give presentations and/or provide information to explain their roles. The NICE leads will also ask for nominations for GDG members to work with them on the following aspects:

- the NICE pathway and 'Information for the public' – the GDG editorial nominees (see sections [10.3](#), [12.1](#) and [12.2](#))
- the implementation support tools – the GDG implementation support nominees and costing nominees (see [section 13.2](#))
- promoting the guideline (see [section 12.3](#)).

The roles of the various GDG nominees are described in more detail in the sections of this manual indicated above.

3.5 Making group decisions and reaching consensus

3.5.1 Reaching agreement

GDG members need to make collective decisions throughout the development of a clinical guideline. These include agreeing review questions ([chapter 4](#)), interpreting the evidence to answer these questions ([chapter 6](#)), and developing guideline recommendations ([chapter 9](#)). There are many different approaches to making group decisions, and there is no blueprint about which approach should be used in which circumstances. Also, because GDGs function in different ways to reflect their individual membership, it is difficult to be prescriptive about the approach that should be used.

In most cases, the GDG reaches decisions through a process of informal consensus. The role of the Chair is to ensure that each individual on the GDG is able to present their views, that assumptions can be debated and that the discussions are open and constructive. The GDG Chair needs to allow sufficient time for all members to express their views without feeling intimidated or threatened, and should check that all members of the group agree to endorse any recommendations. If the group cannot come to consensus in a particular area, this should be reflected in the wording of the recommendation.

Some GDGs may choose to use more formal voting procedures for certain decisions, but it is beyond the scope of this manual to offer guidance on when these should be used, or which of the many variants might be used. For example, a variation of the nominal-group technique was used by the National Clinical Guidelines Centre (NCGC) to agree key recommendations (known as 'key priorities for implementation') in a guideline. A summary of the methods used is presented in the full guideline [Chronic heart failure: national clinical guideline for diagnosis and management in primary and secondary care](#).

3.5.2 Using formal consensus methods outside the GDG

Exceptionally, if the literature search has found no evidence that addresses the review question, the GDG may identify best practice by using formal consensus methods (for example, the Delphi technique or the nominal-group technique). The use of these methods should be discussed on a case-by-case basis with the CCP at NICE. The final decision on whether these methods are warranted will be made by NICE. If it is decided that such methods may be used, the planning and methods should be clearly set out in a project plan and agreed by the CCP. The methods should also be described in the full guideline.

3.6 Further reading

Choudhry NK, Stelfox HT, Desky AS (2002) Relationships between authors of clinical practice guidelines and the pharmaceutical industry. *Journal of the American Medical Association* 287: 612–7

Eccles M, Grimshaw J, editors (2000) *Clinical guidelines from conception to use*. Abingdon: Radcliffe Medical Press

Elwyn G, Greenhalgh T, Macfarlane F (2001) *Groups: a guide to small groups*. In: *Healthcare, Management, Education and Research*. Abingdon: Radcliffe Medical Press

Hutchinson A, Baker R (1999) *Making use of guidelines in clinical practice*. Abingdon: Radcliffe Medical Press

National Institute for Health and Clinical Excellence (2006) [Appointments to guidance producing bodies advisory to NICE](#). London: National Institute for Health and Clinical Excellence

National Institute for Health and Clinical Excellence (2008) [Social value judgements](#):

principles for the development of NICE guidance, 2nd edition. London: National Institute for Health and Clinical Excellence

^[5] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

4 Developing review questions and planning the systematic review

At the start of guideline development, the key clinical issues listed in the scope need to be translated into review questions. In some instances, this may be done as part of the scoping process (see [chapter 2](#)). The review questions must be clear, focused and closely define the boundaries of the topic. They are important both as the starting point for the systematic literature review and as a guide for the development of recommendations by the Guideline Development Group (GDG). The development of the review questions should be completed soon after the GDG is convened.

This chapter describes how review questions are developed, formulated and agreed. It describes the different types of review question that may be used, and provides examples. It also provides information on how to plan the systematic review.

4.1 Number of review questions

The exact number of review questions for each clinical guideline depends on the topic and the breadth of the scope (see [chapter 2](#)). However, the number of review questions must be manageable for the GDG and the National Collaborating Centre (NCC) or the NICE Internal Clinical Guidelines Programme^[6] within the agreed timescale. For standard clinical guidelines that take 10–18 months to develop (from the time the scope is signed off to submission of the draft guideline), between 15 and 20 review questions is a reasonable number. This number is based on the estimate that, on average, it is feasible for a maximum of two systematic reviews to be presented at any one GDG meeting. However, review questions vary considerably in the number of relevant studies and the complexity of the question and analyses, and the numbers of questions given here are only a guide. For example, a single review question might involve a complex comparison of several treatment options with many individual studies. At the other extreme, a question might address the effects of a single intervention and have few relevant studies.

4.2 Developing review questions from the scope

Review questions should address all areas covered in the scope, and should not introduce new aspects not specified in the scope. They will contain more detail than, and should be

seen as building on, the key clinical issues in the scope.

Review questions are usually drafted by the NCC team. They should then be refined and agreed by all GDG members through discussions at GDG meetings. The different perspectives among GDG members will help to ensure that the right review questions are identified, thus enabling the literature search to be planned efficiently. On occasion the questions may need refining once the evidence has been searched; such changes should be documented.

Review questions then inform the development of protocols used by NCCs to detail how questions will be addressed.

4.2.1 Economic aspects

This chapter relates to the specification of questions for reviewing the clinical evidence. Evidence about economic aspects of the key clinical issues should also be sought from published economic evaluations and by conducting new modelling where appropriate. Methods for identifying and reviewing the economic literature are discussed in chapters [5](#) and [6](#); health economics modelling is discussed in chapter [7](#). When developing review questions, it is important to consider what information is required for any planned economic modelling. This might include, for example, information about quality of life, rates of adverse effects or use of health services.

4.3 Formulating and structuring review questions

A good review question is clear and focused. It should relate to a specific patient problem, because this helps to identify the clinically relevant evidence. The exact structure of the review question will depend on what is being asked, but it is likely to fall into one of three main areas:

- intervention
- diagnosis
- prognosis.

Patient experience is a component of each of these and should inform the development of a structured review question. In addition, review questions that focus on a specific element of patient experience may merit consideration in their own right.

4.3.1 Review questions about interventions

Usually, most review questions for a particular clinical guideline relate to interventions. Each intervention listed in the scope is likely to require at least one review question, and possibly more depending on the populations and outcomes of interest.

A helpful structured approach for developing questions about interventions is the PICO (population, intervention, comparator and outcome) framework (see box 4.1). This divides each question into four components:

- population (the population under study)
- intervention (what is being done)
- comparators (other main treatment options)
- outcome (measures of how effective the interventions have been).

Box 4.1 Features of a well-formulated review question on the effectiveness of an intervention using the PICO framework

Population: Which populations of patients are we interested in? How can they be best described? Are there subgroups that need to be considered?

Intervention: Which intervention, treatment or approach should be used?

Comparators: What is/are the main alternative(s) to compare with the intervention being considered?

Outcome: What is really important for the patient? Which outcomes should be considered? Examples include intermediate or short-term outcomes; mortality; morbidity and quality of life; treatment complications; adverse effects; rates of relapse; late morbidity and re-admission; return to work, physical and social functioning; resource use.

For each review question, the GDG should take into account the various confounding factors that may influence the outcomes and effectiveness of an intervention. They should also specify the healthcare setting for the question if necessary. To facilitate this process, outcomes and other key criteria that the GDG considers to be important should be listed. Once the review question has been framed, key words can be identified as potential search terms for the systematic review. Examples of review questions on the effectiveness

of interventions are presented in box 4.2.

Box 4.2 Examples of review questions on the effectiveness of interventions

For people with IBS (irritable bowel syndrome), are antimuscarinics or smooth muscle relaxants effective compared with placebo or no treatment for the long-term control of IBS symptoms? Which is the most effective antispasmodic?

(Adapted from: [Irritable bowel syndrome in adults: diagnosis and management of irritable bowel syndrome in primary care](#). NICE clinical guideline 61 [2008])

Which first-line opioid maintenance treatments are effective and cost-effective in relieving pain in patients with advanced and progressive disease who require strong opioids?

(Adapted from: [Opioids in palliative care](#). NICE clinical guideline 140 [2012]).

Review questions about drugs will usually only consider drugs with a UK marketing authorisation for some indication. Use of a drug outside its licensed indication (off-label use) may be considered if this use of the drug is common in the UK (see also [section 9.3.6.3](#)). Drugs with no UK marketing authorisation for any indication will not usually be considered in a guideline.

A review question relating to an intervention is usually best answered by a randomised controlled trial (RCT), because this is most likely to give an unbiased estimate of the effects of an intervention. Further information on the side effects of a drug may be obtained from other sources. Some advice on finding data on the adverse effects of an intervention is available in the [Cochrane handbook for systematic reviews of interventions](#).

There are, however, circumstances in which an RCT is not necessary to confirm the effectiveness of a treatment (for example, giving insulin to a person in a diabetic coma compared with not giving insulin) because we are sufficiently certain from non-randomised evidence that an important effect exists. This is the case only if all of the following criteria are fulfilled:

- An adverse outcome is likely if the person is not treated (evidence from, for example, studies of the natural history of a condition).

- The treatment gives a dramatic benefit that is large enough to be unlikely to be a result of bias (evidence from, for example, historically controlled studies).
- The side effects of the treatment are acceptable (evidence from, for example, case series).
- There is no alternative treatment.
- There is a convincing pathophysiological basis for treatment.

4.3.2 Review questions about diagnosis

Review questions about diagnosis are concerned with the performance of a diagnostic test or test strategy. A diagnostic test is a means of determining whether a patient has a particular condition (disease, stage of disease or subtype of disease). Diagnostic tests can include physical examination, history taking, laboratory or pathological examination and imaging tests.

Broadly, review questions that can be asked about a diagnostic test are of three types:

- questions about the diagnostic accuracy of a test or a number of tests individually against a comparator (the reference standard)
- questions about the diagnostic accuracy of a test strategy (such as serial testing) against a comparator (the reference standard)
- questions about the clinical value of using the test.

Questions about a diagnostic test consider the ability of the test to predict the presence or absence of disease. In studies of the accuracy of a diagnostic test, the results of the test under study (the index test[s]) are compared with those of the best available test (the reference standard) in a sample of patients. It is important to be clear when deciding on the question what the exact proposed use of the test is; for example, as an initial 'triage' test or after other tests.

The PICO framework described in the previous section is useful when formulating review questions about diagnostic test accuracy (see box 4.3). The healthcare setting of the test should be specified. The intervention is the test under investigation (the index test[s]), the comparison is the reference standard, and the outcome is a measure of the presence or absence of the particular disease or disease stage that the index test is intended to

identify (for example, sensitivity or specificity). The target condition that the test is intended to identify should be specified in the review question.

Box 4.3 Features of a well-formulated review question on diagnostic test accuracy using the PICO framework

Population: To which populations of patients would the test be applicable? How can they be best described? Are there subgroups that need to be considered?

Intervention(indextest[s]): The test or test strategy being evaluated.

Comparator: The test with which the index test(s) is/are being compared, usually the reference standard (the test that is considered to be the best available method to establish the presence or absence of the condition of interest – this may not be the one that is routinely used in practice).

Targetcondition: The disease, disease stage or subtype of disease that the index test(s) and the reference standard are being used to establish.

Outcome: The diagnostic accuracy of the test or test strategy for detecting the target condition. This is usually reported as test parameters, such as sensitivity, specificity, predictive values, likelihood ratios, or – where multiple cut-off values are used – a receiver operating characteristic (ROC) curve.

Examples of review questions on the accuracy of a diagnostic test are given in box 4.4. A review question relating to diagnostic test accuracy is usually best answered by a cross-sectional study in which both the index test(s) and the reference standard are performed on the same sample of patients. Case-control studies are also used to assess diagnostic test accuracy, but this type of study design is more prone to bias (and often results in inflated estimates of diagnostic test accuracy). Further advice on conducting reviews of diagnostic test accuracy can be found in the [Cochrane handbook for diagnostic test accuracy reviews](#).

Box 4.4 Examples of review questions on diagnostic test accuracy

Review question:

In children and young people under 16 years of age with a petechial rash, can non-specific laboratory tests (C-reactive protein, white blood cell count, blood gases) help to confirm or refute the diagnosis of meningococcal disease?

Formulation of question:

Population: All children and young people from birth up to their 16th birthday who have or are suspected of having bacterial meningitis or meningococcal septicaemia.

Index test(s): Non-specific laboratory tests (C-reactive protein, white blood cell count, blood gases).

Reference standard: Microscopy, lumbar puncture or clinical follow-up.

Outcomes: Event rates; prevalence; sensitivity; specificity; positive predictive value; negative predictive value.

(Adapted from: Bacterial meningitis and meningococcal septicaemia: management of bacterial meningitis and meningococcal septicaemia in children and young people younger than 16 years in primary and secondary care. NICE clinical guideline 102 [2010]).

Although the assessment of test accuracy is an important component of establishing the usefulness of a diagnostic test, the clinical value of a test lies in its usefulness in guiding treatment decisions, and ultimately in improving patient outcomes. 'Test and treat' studies compare outcomes of patients who undergo a new diagnostic test (in combination with a management strategy) with those of patients who receive the usual diagnostic test and management strategy. These types of study are not very common. If there is a trade-off between costs, benefits and harms of the tests, a decision-analytic model may be useful (see Lord et al. 2006).

Review questions aimed at establishing the clinical value of a diagnostic test in practice can be structured in the same way as questions about interventions. The best study design is an RCT. Review questions about the safety of a diagnostic test should also be structured in the same way as questions about interventions.

4.3.3 Review questions about prognosis

Prognosis describes the likelihood of a particular outcome, such as the progression of a

disease, or the survival time for a patient after the diagnosis of a disease or with a particular set of risk markers. A prognosis is based on the characteristics of the patient ('prognostic factors'). These prognostic factors may be disease-specific (such as the presence or absence of a particular disease feature) or demographic (such as age or sex), and may also include the likely response to treatment and the presence of comorbidities. A prognostic factor does not need to be the cause of the outcome, but should be associated with (in other words, predictive of) that outcome.

Prognostic information can be used within clinical guidelines to:

- provide information to patients about their prognosis
- classify patients into risk categories (for example, cardiovascular risk) so that different interventions can be applied
- define subgroups of populations that may respond differently to interventions
- identify factors that can be used to adjust for case mix (for example, in explorations of heterogeneity)
- help determine longer-term outcomes not captured within the timeframe of a clinical trial (for example, for use in an economic model).

Review questions about prognosis address the likelihood of an outcome for patients from a population at risk for that outcome, based on the presence of a proposed prognostic factor.

Review questions about prognosis may be closely related to questions about aetiology (cause of a disease) if the outcome is viewed as the development of the disease itself based on a number of risk factors. They may also be closely related to questions about interventions if one of the prognostic factors is treatment. However, questions about interventions are usually better addressed by controlling for prognostic factors.

Examples of review questions relating to prognosis are given in box 4.5.

Box 4.5 Examples of review questions on prognosis

Are there factors related to the individual (characteristics either of the individual or of the act of self-harm) that predict outcome (including suicide, non-fatal repetition, other psychosocial outcomes)?

(From: Self-harm: the short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care. NICE clinical guideline 16 [2004].)

For women in the antenatal and postnatal periods, what factors predict the development or recurrence of particular mental disorders?

(From: Antenatal and postnatal mental health: clinical management and service guidance. NICE clinical guideline 45 [2007].)

For people who are opioid dependent, are there particular groups that are more likely to benefit from detoxification?

(From: Drug misuse: opioid detoxification. NICE clinical guideline 52 [2007].)

A review question relating to prognosis is best answered using a prospective cohort study. A cohort of people who have not experienced the outcome in the review question (but for whom the outcome is possible) is followed to monitor the number of outcome events occurring over time. The cohort will contain people who possess or have been exposed to the prognostic factor, and people who do not possess or have not been exposed to it. The cohort may be taken from one arm (usually the control arm) of an RCT, although this often results in a highly selected, unrepresentative group. Case-control studies are not suitable for answering questions about prognosis, because they give only an odds ratio for the occurrence of the event for people with and without the prognostic factor – they give no estimate of the baseline risk.

4.3.4 Using patient experience to inform review questions

The PICO framework should take into account the patient experience. Patient experience, which may vary for different patient populations ('P'), covers a range of dimensions, including:

- patient views on the effectiveness and acceptability of given interventions ('I')
- patient preferences for different treatment options, including the option of foregoing treatment ('C')

- patient views on what constitutes a desired, appropriate or acceptable outcome ('O').

The integration of relevant patient experiences into each review question therefore helps to make the question patient-centred as well as clinically appropriate. For example, a review question that looks at the effectiveness of aggressive chemotherapy for a terminal cancer is more patient-centred if it integrates patient views on whether it is preferable to prolong life or to have a shorter life but of better quality.

It is also possible for review questions to ask about specific elements of the patient experience in their own right, although the PICO framework may not provide a helpful structure if these do not involve an intervention designed to treat a particular condition. Such review questions should be clear and focused, and should address relevant aspects of the patient experience at specific points in the care pathway that are considered to be important by the patient and carer members and others on the GDG. Such questions can address a range of issues, such as:

- patient information and support needs
- elements of care that are of particular importance to patients
- the specific needs of groups of patients who may be disadvantaged compared with others
- which outcomes reported in intervention studies are most important to patients.

As with the development of all structured review questions, questions that are broad in scope and lack focus (for example, 'what is the patient experience of living with condition X?') should be avoided. Examples of review questions relating to patient information and support needs are given in box 4.6.

Box 4.6 Examples of review questions on patient experience

What information and support should be offered to children with atopic eczema and their families/carers?

(From: Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years. NICE clinical guideline 57 [2007].)

What elements of care on the general ward are viewed as important by patients following their discharge from critical care areas?

(From: Acutely ill patients in hospital: recognition of and response to acute illness in adults in hospital. NICE clinical guideline 50 [2007].)

Are there cultural differences that need to be considered in delivering information and support on breast or bottle-feeding?

(From: Postnatal care: routine postnatal care of women and their babies. NICE clinical guideline 37 [2006].)

A review question relating to patient experience is likely to be best answered using qualitative studies and cross-sectional surveys, although information on patient experience is also becoming increasingly available as part of wider intervention studies.

4.3.5 Review questions about service delivery

Clinical guidelines may cover issues of service delivery. Examples of review questions relating to service delivery are given in box 4.7.

Box 4.7 Examples of review questions on service delivery

In patients with hip fractures what is the clinical and cost effectiveness of early surgery (within 24, 36 or 48 hours) on the incidence of complications such as mortality, pneumonia, pressure sores, cognitive dysfunction and increased length of hospital stay?

In patients with hip fracture what is the clinical and cost effectiveness of hospital-based multidisciplinary rehabilitation on functional status, length of stay in secondary care, mortality, place of residence/discharge, hospital readmission and quality of life?

What is the clinical and cost effectiveness of surgeon seniority (consultant or equivalent) in reducing the incidence of mortality, the number of patients requiring reoperation, and poor outcome in terms of mobility, length of stay, wound infection and dislocation?

(From: [Hip fracture: the management of hip fracture in adults](#). NICE clinical guideline 124 [2011].)

The most appropriate study design to answer review questions about service delivery is an RCT. However, a wide variety of methodological approaches and study designs have been used.

4.4 Planning the systematic review

For each systematic review, the systematic reviewer (with input from other technical staff at the NCC) should prepare a review protocol 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, as well as providing some protection against the introduction of bias. In addition, the review protocol should make it possible for the review to be repeated by others at a later date. A protocol should also make it clear how equality issues have been considered in planning the review work, if appropriate.

4.4.1 Structure of the review protocol

The protocol should be short (no longer than one page) and should describe any differences from the methods described in this guidelines manual ([chapters 5–7](#)), rather than duplicating the methodology stated here. It should include the components outlined in table 4.1.

Table 4.1 Components of the review protocol

Component	Description
Review question	The review question as agreed by the GDG.
Objectives	Short description; for example 'To estimate the effectiveness and cost effectiveness of...' or 'To estimate the diagnostic accuracy of...!'
Criteria for considering studies for the review	Using the PICO framework. Including the study designs selected.
How the information will be searched	The sources to be searched and any limits that will be applied to the search strategies; for example, publication date, study design, language. (Searches should not necessarily be restricted to RCTs.)
The review strategy	The methods that will be used to review the evidence, outlining exceptions and subgroups. Indicate if meta-analysis will be used and how it will be conducted.

The review protocol is an important opportunity to look at issues relating to equalities that were identified in the scope, and to plan how these should be addressed. For example, if it is anticipated that the effects of an intervention might vary with patient age, the review protocol should outline the plan for addressing this in the review strategy.

4.4.2 Process for developing the review protocol

The review protocol should be produced after the review question has been agreed by the GDG and before starting the review (that is, usually between two GDG meetings). The protocol should be approved by the GDG at the next meeting.

All review protocols should be included as appendices in the draft of the full guideline that is prepared for consultation (see also [chapter 10](#)). Any changes made to a protocol in the course of the work should be described. Review protocols will also be published on the NICE website 5–7 weeks before consultation on the guideline starts.

4.5 Further reading

Centre for Reviews and Dissemination (2009) [Systematic reviews: CRD's guidance for undertaking reviews in health care](#). Centre for Reviews and Dissemination, University of York

Cochrane Diagnostic Test Accuracy Working Group (2008) [Cochrane handbook for diagnostic test accuracy reviews, version 1.0.1](#) (updated March 2009). The Cochrane Collaboration

Higgins JPT, Green S, editors (2008) [Cochrane handbook for systematic reviews of interventions, version 5.1.0](#) (updated March 2011). The Cochrane Collaboration

Lord SJ, Irwig L, Simes RJ (2006) When is measuring sensitivity and specificity sufficient to evaluate a diagnostic test, and when do we need randomized trials? *Annals of Internal Medicine* 144: 850–5

National Institute for Health and Clinical Excellence (2011) [Diagnostics assessment programme manual](#). London: National Institute for Health and Clinical Excellence

Richardson WS, Wilson MS, Nishikawa J et al. (1995) The well-built clinical question: a key to evidence-based decisions. *American College of Physicians Journal Club* 123: A12–3

^[6] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

5 Identifying the evidence: literature searching and evidence submission

5.1 Introduction

The systematic identification of evidence is an essential step in clinical guideline development. Systematic literature searches undertaken to identify evidence of clinical and cost effectiveness should be thorough, transparent and reproducible. These searches will also minimise 'dissemination biases' (Song et al. 2000), such as publication bias and database bias, that may affect the results of reviews.

This chapter is aimed primarily at information specialists in the National Collaborating Centres (NCCs) and in NICE^[7]. It provides advice on the sources to search and on how to develop strategies for systematic literature searches to identify clinical and economic evidence. It also provides advice on other areas of information management that form an important part of the clinical guideline development process. These include using reference management software, acquiring the full text of articles and documenting the search process. Calls for submissions of evidence from stakeholders and undertaking baseline assessments of service activity (for service guidance) are also covered. The scoping search undertaken when drafting the scope of a clinical guideline is described in [section 2.3.3](#).

5.2 Searching for clinical evidence

5.2.1 Databases and other sources to search

The databases and other sources that should be searched to identify evidence of clinical effectiveness depend on the review question.

5.2.1.1 Core and subject-specific databases

The core databases listed in table 5.1 should be searched for every review question. Additional subject-specific databases and other resources may also need to be searched, depending on the subject area of the review question and the type of evidence sought.

Links are provided in table 5.1 for sources that are freely available.

Table 5.1 Databases that should be searched

Questiontype	Databases
<p>Review questions about interventions, diagnosis, prognosis^a, patient experience and service delivery</p>	<p><i>Coredatabases:</i></p> <p>MEDLINE/MEDLINE In-Process</p> <p>Embase</p> <p>Cochrane Database of Systematic Reviews – CDSR (Cochrane Reviews)^b</p> <p>Database of Abstracts of Reviews of Effects – DARE (Other Reviews)^c</p> <p>Cochrane Central Register of Controlled Trials – CENTRAL (Clinical Trials)^b</p> <p>Health Technology Assessment (HTA) database (Technology Assessments)^c</p> <p><i>Subject-specificdatabases(thislistisnotexhaustive):</i></p> <p>AMED (Allied and Complementary Medicine Database)</p> <p><u>The Campbell Collaboration Library of Systematic Reviews</u></p> <p>CINAHL (Cumulative Index to Nursing and Allied Health Literature)</p> <p><u>ERIC</u> (Education Resources Information Center)</p> <p><u>PEDro</u> (Physiotherapy Evidence Database)</p> <p>PsycINFO^d</p>

^a CDSR and DARE do not need to be searched for questions about prognosis.

^b Accessible via [the Cochrane Library](#). Database names in parentheses are those used in the Cochrane Library. CENTRAL only needs to be searched when evidence from controlled trials is sought.

^c Accessible as part of [the Cochrane Library](#) and via the [Centre for Reviews and Dissemination \(CRD\)](#). The CRD website hosts the most up-to-date version of the databases. Database names in parentheses are those used in the Cochrane Library.

^d PsycINFO is searched as an additional core database by the NCC for Mental Health.

An awareness of the strengths and weaknesses of each database is important when undertaking a systematic literature search. The different databases index different journals, use different subject headings, cover different time periods and provide different amounts of bibliographic information. For example, Embase is considered to be stronger than MEDLINE in its coverage of the pharmacology, toxicology, drug research and psychiatric literature, but contains only selected coverage of the dental and nursing literature. On the other hand, MEDLINE contains a much better developed collection of scope notes for its subject heading (MeSH) terms, which can assist development of the search strategy. There will be overlap in the records retrieved from the different databases for a particular review question; the extent of this overlap for MEDLINE and Embase is reported as being between 10 and 87% depending on the topic (Lefebvre et al. 2008). Therefore cross-database searching, although time-consuming, is necessary in order to comprehensively identify evidence for clinical guideline development.

5.2.1.2 Other sources of information

The sources listed in table 5.2 – which include databases and websites – can provide useful information about ongoing research, patient experience, clinical audits and statistics to help guide Guideline Development Group (GDG) decision-making. This list is not intended to be exhaustive; the 'Searching for studies' chapter in the 'Cochrane handbook' offers a good overview and further examples of sources to search (Lefebvre et al. 2011).

Table 5.2 Other sources of information

Source	Website
--------	---------

International Standard Randomised Controlled Trial Number Register	www.controlled-trials.com/isrctn
International Clinical Trials Registry Platform (WHO)	http://apps.who.int/trialsearch/
IFPMA Clinical Trials Portal	http://clinicaltrials.ifpma.org
ClinicalTrials.gov (US National Institutes of Health service)	http://clinicaltrials.gov
UK Clinical Research Network (UKCRN) Study Portfolio database	http://public.ukcrn.org.uk/search
Web of Knowledge	www.isiwebofknowledge.com/
Conference Papers Index	www.csa.com/factsheets/cpi-set-c.php
The King's Fund	www.kingsfund.org.uk
DH-Data	http://ds.datastarweb.com/ds/products/datastar/sheets/dhss.htm
Hospital Episode Statistics	www.hesonline.nhs.uk
Patient Episode Database for Wales	www.wales.nhs.uk/sitesplus/922/page/50308
National or regional registers, for example cancer registers	Search by type of cancer to locate appropriate register
National or regional audits	Search by topic or geographical area for appropriate audit data.
Information about patient experiences	www.healthtalkonline.org www.youthhealthtalk.org
Surveys of patients' experiences	Search for relevant patient organisation websites; condition-specific or topic-specific as appropriate.

NCCs are not expected to routinely search other sources of information, and there is no requirement to hand search journals for studies.

5.2.2 How to search for clinical evidence

Many of the principles listed in this section are also relevant to searching for economic evidence (see [section 5.3](#)).

5.2.2.1 Devising an overall search strategy

Review questions can be broken down into different parts, which can then be used to devise a search strategy. For example, using the PICO (population, intervention, comparator and outcome) framework (see [box 4.1](#)), a search strategy can be constructed for terms relating to the population; this can be combined with terms relating to the interventions and comparators (if there are any) to be evaluated. It is important to remember that not all components of a review question will always be mentioned in the abstracts or subject headings of database records – in particular, outcomes are often not mentioned. Therefore it may not be advisable to include these components when developing a strategy. For guidelines that are being updated, previous strategies can be used to inform search strategy design.

5.2.2.2 Identifying search terms

Search strategies should usually consist of a combination of subject headings and 'free-text' terms from the titles and abstracts of relevant studies (see also [section 5.2.2.3](#)). Subject headings are used to identify the main theme of an article; however, not all conditions or diseases will have a subject heading, so it is important to use free-text terms too. When identifying subject headings it is important to include variations in thesaurus and indexing terms for each database; for example, MeSH in MEDLINE and the Cochrane Library, and Emtree in Embase. Free-text terms may include synonyms, acronyms, abbreviations, differences in terminology across national boundaries, different spellings, old and new terminology, brand and generic drug names, and lay and medical terminology. Misspellings or 'typos' may also affect a search, particularly with records in the process of being indexed, for which there may be only a title and no abstract or subject headings.

5.2.2.3 Sensitivity and precision

The key attributes of a search strategy are:

- **Sensitivity:** the number of relevant records retrieved by a search strategy as a proportion of the total number of relevant records (normally represented by a gold standard) (Jenkins 2004).
- **Precision:** the number of relevant records retrieved by a search strategy as a proportion of the total number of records retrieved (Jenkins 2004).

Both of these will be influenced by the time period covered and by the search terms used. Although it is important that searches for systematic reviews attempt to identify all the relevant literature, there needs to be a trade-off between conducting an exhaustive search that will need additional resources versus undertaking a more modest search that may miss some studies. Identifying key studies for a review question can assist in checking search sensitivity; such studies can also act as a guide to search terms.

5.2.2.4 Grouping review questions

It is useful to identify review questions that overlap and so can be grouped together for searching purposes. For example, questions about the most effective treatments for a condition may involve comparing several interventions. This may make it possible to carry out one search that covers all the interventions. Questions that have the population and intervention in common but a different comparator can be grouped together by identifying and combining search terms for the population and intervention only.

5.2.2.5 Limiting searches

Using certain parameters to limit searches can improve precision without unduly affecting sensitivity.

- **Date parameters.** These depend on the clinical guideline topic and on when the majority of the research was published. The date range for the search should be agreed by the GDG, in consultation with experts in the area. If relevant good-quality published systematic reviews exist (see [chapter 6](#)), additional searching may be limited to updating the reviews, covering the time period since the searches for the published reviews were conducted. However, existing reviews may not address all of the relevant outcomes, in which case new searches may be needed. Consider contacting authors of published reviews for updates, particularly for reviews found in the Cochrane Database of Systematic Reviews.

- Animal studies can be excluded from the search results in some databases. In Ovid, for MEDLINE the search strategy is:

1 Final search set

2 Exp Animals/ not Humans/

3 1 not 2.

- If a decision has been taken to limit a review to studies reported in English, the appropriate database limit function can be used to improve precision.
- Depending on the review question, it may be appropriate to limit searches to particular study designs. The best way to do this is to use an appropriate search filter rather than limiting searches by the publication type field (see sections 5.2.2.6 and 5.2.2.7).
- Sometimes it may be appropriate to limit searches by age. This can be useful to identify citations relating to children, but is often not necessary for those relating to adults. A search filter is listed on the InterTASC website (see section 5.2.2.7).
- Limiting searches by sex is not recommended.

5.2.2.6 Searching step-by-step by study design

For review questions on the effectiveness of interventions, it may be more efficient to search for systematic reviews, followed by randomised controlled trials (RCTs), followed by cohort or case-control studies. This will prevent unnecessary searching and review work. An absence of good-quality RCTs covering all the key outcomes may mean expanding the search to retrieve observational studies. The use of relevant search filters (see section 5.2.2.7) can help to identify study types and thus assist in this method of searching.

5.2.2.7 Search filters

Search filters can be used to make searching more efficient and effective by saving time and bringing consistency and focus to the searching process. Search filters may be developed using a range of research-based and non-research-based methods. The most reliable filters are likely to be those that describe explicit methods, including how the search terms were identified and combined, and how the performance of search strategies was tested using collections of relevant records (ideally different from the records used to

identify or extract the search terms) (Jenkins 2004). Research-based filters for finding RCTs and other study designs include the Cochrane Highly Sensitive Search Strategies for identifying RCTs in MEDLINE (Lefebvre et al. 2011) and filters developed by the McMaster University Hedges team for MEDLINE and Embase. The most comprehensive listing of available search filters can be found on the NICE [InterTASC Information Specialists' Sub-Group \(ISSG\) website](#), which lists filters by study design, database and interface.

When choosing a search filter, it is important to consider the age of the filter (to take account of changes such as indexing or interface changes), and whether it maximises sensitivity or precision. The most useful search filters for clinical guideline work are likely to be those for identifying specific study designs such as RCTs or economic evaluations.

5.3 Searching for economic evidence

The approach to searching for economic evidence should be systematic, but targeted to identify studies that are most relevant to current NHS practice and hence likely to inform GDG decision-making.

Two types of search might be required for economic evidence:

- First, a systematic search for economic evaluations relevant to the guideline and applicable to current NHS practice should be performed. This should cover all review questions with potential cost or resource implications and should not be limited to the modelling priorities identified in the economic plan. This search should be conducted by the information specialist, in consultation with the health economist.
- Additional searches may be necessary to identify other information required for economic modelling. This may include information about prognosis, adverse effects, quality of life, resource use or costs that is not always available from the clinical searches conducted for the guideline. The requirement for additional searches should be discussed by the information specialist and the health economist. (See [section 7.2.3](#) for more details about identifying model inputs, including searching for quality-of-life data.)

Much of the advice provided in section 5.2.2 about how to search for clinical evidence is relevant to systematic searches for economic evaluations.

5.3.1 Initial search to identify economic evaluations

The majority of the search for economic evaluations should be completed near the beginning of the guideline development process as an initial broad search. The first step is a search of a key health economics database using the patient population terms, as for the initial clinical background search. Other core databases should then be searched for the patient population terms with the addition of a published economics search filter.

A suggested strategy for searching for economic evaluations in the initial broad search is:

- NHS EED (NHS Economic Evaluation Database)^[8], and HEED (Health Economic Evaluations Database) if subscribed to – all years
- HTA database – all years.

This initial broad search should be extended to identify recent papers that have not yet been referenced in the economics databases, by searching MEDLINE (including MEDLINE In-Process) and Embase with a published economics search filter (see section 5.2.2.7), covering the most recent complete year.

Search filters to identify economic evaluations can maximise precision (for example, the economics search filters developed and validated as having high precision by the McMaster Hedges team) or sensitivity (for example, the CRD search filter developed to identify economic evaluations for NHS EED). Information specialists should use their judgement about whether maximising precision or sensitivity is more appropriate when selecting search filters to identify economic evidence (see sections 5.2.2.3 and 5.2.2.7).

Other subject-specific databases may be searched at this stage, at the discretion of the information specialist.

5.3.2 Further searches to identify economic evaluations

Further searches for economic evaluations may be needed for some review questions. The purpose of these searches is to try to ensure that all relevant economic evaluations are identified; some may not be retrieved by the initial search because of the inclusion criteria of the economics databases (for example, economic evaluations indexed in Embase have been sought for inclusion in NHS EED only since 2002). The need for additional searches and the criteria (such as date parameters) for any additional searches should be established by the health economist in consultation with the information specialist. As a

minimum, MEDLINE and Embase should be searched; additional databases should be searched as appropriate. It may also be worthwhile to use a highly sensitive economics search filter (for example, the CRD filter – see sections 5.2.2.7 and 5.3.1). The searches may be executed when required or alongside the clinical searches, depending on the preference of the health economist in consultation with the information specialist.

5.4 Quality assurance of search strategies

Efforts should be made to check the quality and accuracy of search strategies during the development of the clinical guideline. Although it will not usually be possible to check all strategies for every search, the following approaches can be used to ensure that the key studies are retrieved.

- Ask GDG members to identify key clinical studies or economic evaluations that are already published, in order to gather useful search terms.
- Check search strategies used in existing published systematic reviews.
- Run searches with and without certain search terms and assess the differences between the results obtained.
- Check the bibliographies of included studies to ensure that all relevant papers have been retrieved by the search strategy used.
- If relevant papers have not been retrieved by the search strategy, investigate and amend the strategy if appropriate.

5.5 Reference management software

Electronic records of the references retrieved by searches should be stored using reference management software such as EndNote, Reference Manager or ProCite. Records can be exported from bibliographic databases such as MEDLINE and imported automatically into the software using import filters. Details of references can also be added manually.

In addition to storing records of references, consideration should be given to using reference management software for the following:

- Coding the references with additional information, such as the source of the reference, the review question it was identified to answer, the study design and selection decisions. Coding should be determined and agreed by the NCC technical team before working with a reference management database to ensure consistency of use.
- Providing links to the full text of articles, where possible.
- Logging the ordering and/or receipt of articles.
- Keeping track of the printed copies of papers.
- Linking to word processing packages using output styles to facilitate the automatic generation of in-text citations and reference lists for the full version of the guideline.

5.6 Acquiring the full text of references

The full text of references can be obtained from several sources:

- Free online journal articles: many journals provide free access to some or all of their content. Several apply this to all material more than 1 or 2 years old; others provide access to particular types of articles only (for example, the British Medical Journal provides free access to all research articles). Individual articles can be purchased from the websites of most journals that do not allow free access, but this can be expensive.
- Some websites provide links to medical journal web pages with freely available articles. Two that are useful are [Free Medical Journals](#) and [Genamics JournalSeek](#).
- [NHS Evidence](#) and its Welsh equivalent, [NHS Wales e-Library for health](#), provide free access to some journals for all NHS staff and staff in organisations such as NICE and the NCCs that work exclusively for the NHS. An Athens log-in is needed to access journal content provided by NHS Evidence, which can be obtained by applying to the [Guidance Information Services team](#) at NICE.
- Free online reports: many institutions make their reports and guidelines freely available online, so it is worth checking the relevant websites.

- Libraries: many libraries that stock a wide range of journals, books and reports will have an inter-library loan or document delivery service. All will supply articles within copyright law and some will loan documents. There is usually a charge for this service, and for loans the cost of postage is usually extra. Some libraries provide articles at a reduced cost if an annual subscription is taken out. Three major libraries offering this level of service are the British Library, the British Medical Association (BMA) Library and the Royal Society of Medicine Library. A British Library account also allows users to pay for articles from other libraries that accept payment in this way. Some of the NCCs are based in, or associated with, a medical institution that has its own library.

5.7 Documenting the search strategy

An audit trail should be kept of the searches for both clinical and economic evidence that are conducted during the clinical guideline development process, so that the process for identifying the evidence is transparent and reproducible.

5.7.1 Internal documentation

The following information should be recorded for each search conducted during the clinical guideline development process:

- Details of the question for which the search was conducted.
- The names of the databases and database host systems used.
- The database coverage dates; for example, Ovid MEDLINE 1950 to February week 3 2012.
- The date on which the search was conducted.
- The search strategy (this should be stored in an easily accessible form such as Microsoft Word or ASCII plain text).
- Any limits applied to the search or to study designs searched for.
- The number of records retrieved from each database.
- A text file and/or database (from EndNote, Reference Manager or ProCite) of results.

Enough detail should be provided to allow searches to be repeated when the guideline

requires updating (see [section 14.1](#)).

5.7.2 Full guideline

A description of the searching process should be included in the methods section of the full version of the clinical guideline (see [section 10.1.1](#)). This should include:

- details of the scoping search (see [section 2.3.3](#))
- details of the development of the search strategies
- dates on which the searches were carried out, including any re-run searches (see [section 5.9](#))
- any limits placed on the type of evidence searched for and details of methodological search filters, if used
- names of the databases and database host systems and any other sources searched
- date or language limits applied to searches.

Search strategies will be published on the NICE website 5–7 weeks before consultation on the draft guideline starts, and will also be available to stakeholders during consultation. They should also be published at the same time as the final full guideline. It may be helpful to publish the search strategies for each literature search for all databases.

5.8 Timing of searches

Searches should be prioritised according to the clinical and economic evidence required for each GDG meeting. Additional searching time may be needed for guideline topics that involve a lot of pharmacological areas, for which there are likely to be large numbers of published papers. This should be taken into consideration early in the process and should be accounted for in the planning. Specific searches will need to be carried out for each of the review questions and the economic evidence that will be discussed at the planned GDG meetings.

5.9 Re-running searches

5.9.1 Clinical evidence

The searches undertaken to identify clinical evidence for each review question need to be re-run to identify any further evidence that has been published since the search was run initially. The final re-run of searches should be done 6–8 weeks before submission of the draft guideline to NICE. This can be done either by using database and website automatic alerting systems on each search or by executing re-runs of searches at one or two time points before the consultation.

Search strategies should be checked when re-running the search to ensure that all subject headings are still mapping to the appropriate heading, as these can change, and also to see if there are any new terms or headings that could be used (for example, MeSH headings are evaluated and can change annually). An awareness of how and when databases are indexed and updated should guide the re-run, because there may be times when indexing stops temporarily or when repetition of articles is more common. This can affect the value of re-running the search. It is worth noting that records identified by re-runs may not necessarily be 'new'. They may have been identified in the initial search in a different database that has a shorter indexing time lag, or they may have been identified in the same database but now have a revised entry date as a result of a revision of the indexing.

5.9.2 Economic evidence

As for clinical searches, economic evaluation literature searches should be re-run 6–8 weeks before submission of the draft guideline to NICE. The re-runs can be executed either question by question (that is, for the questions for which additional searches for economic evaluations were conducted) or, as a minimum, on the initial broad search only (see section 5.3.2). This will largely be determined by the requirements of the health economist. Re-runs of selective searches for model inputs may be repeated after guideline consultation, but only at the request of the health economist, who is able to determine whether there is time to incorporate any new information in a revised model (see also [section 7.2.3](#)). It is not usually necessary for the health economist to re-run other searches (for example, quality of life), but they should discuss this with the information specialist.

5.10 Calls for evidence from stakeholders

For some questions, the GDG and NCC staff may have good reason to believe that information exists that has not been found using standard searches. Examples include ongoing research in a field, if a technology is relatively new, studies that have been published only as abstracts (see [section 6.1.2](#)), data about the off-label use of drugs, data on adverse effects, economic models, and studies of the experiences of patients, carers or healthcare or other professionals.

In these situations, the NCC may call for evidence. This call goes to all registered stakeholders. It should specify the question being addressed and details of the type of evidence being sought, for example in terms of PICO framework and study design for questions of effectiveness. A call for evidence may be made at any point during development of a clinical guideline, and stakeholders should usually be given 4 weeks to respond. The NCC may choose not to issue any calls for evidence for a guideline.

If the NCC and GDG think it is likely that the regulatory authorities hold relevant data about a drug that has not been submitted in response to a call for evidence, they may approach the appropriate regulatory authority to release those data. This should be done through the Centre for Clinical Practice at NICE.

5.10.1 Confidential information

In addition to published studies, stakeholders may submit relevant unpublished data or studies in response to a call for evidence. When the NCC sends out a call for evidence, it should ask stakeholders that respond to complete a checklist that lists and identifies the location of all confidential information contained in their submission. This checklist is available from the NICE webboard for NCCs. The NCCs should keep the checklists for their records to ensure that the draft and final versions of the full guideline do not contain confidential information.

Box 5.1 summarises what may and may not be considered confidential by NICE.

Box 5.1 Information on what may and may not be considered confidential

Data that may be included as confidential include those that may influence share price values ('commercial in confidence') or are intellectual property ('academic in confidence'; that is, awaiting publication).

Confidential information should be kept to an absolute minimum; for example, just the relevant part of a sentence, a particular result from a table or a section of code.

NICE will not allow a whole study to be designated confidential. As a minimum, a structured abstract of the study or economic model will have to be made available for public disclosure during consultation on the guideline.

Results derived from calculations using confidential data will not be considered confidential unless releasing those results would enable back-calculation to the original confidential data.

In addition to completing the checklist, stakeholders should indicate the part of their submission that contains the confidential information, for example by using a highlighter pen on a hard copy, or the highlighter function in an electronic version. These markings should then be maintained on those sections so that the GDG knows which parts are confidential. When the draft and final versions of the full guideline are prepared for publication, the NCC should ensure that these sections are replaced by a note stating that confidential information has been removed, so that readers know exactly where confidential data have been used.

Following the principles in box 5.1, the amount of confidential information should be kept to a minimum. As a minimum, a summary should be publicly available by the time of the consultation on the guideline. NICE needs to be able to justify the recommendations in clinical guidelines on the basis of the evidence considered by the GDG. NICE and the NCC will therefore work with the data owners to agree a balance between confidentiality and transparency^[5].

5.10.2 Information not eligible for submission

Stakeholders are asked not to submit the types of evidence listed in box 5.2, as these will not be considered.

Box 5.2 Stakeholder material not eligible for consideration by the

GDG

Studies with weak designs if better designed studies are available

Promotional literature

Papers, commentaries and editorials that interpret the results of a published paper

Representations and experiences of individuals (unless assessed as part of a well-designed study or survey)

5.10.3 Documenting evidence from stakeholder submissions

Information received from stakeholders in response to a call for evidence should be entered into a reference management database (as described in [section 5.5](#)), and the details cross-checked against evidence identified through database searching. It should be assessed in the same way as published studies identified through the searches (see [section 6.2.1](#)).

5.11 Additional requirements for service guidance

In addition to evidence identified through routine literature searches, the GDG requires information describing the current configuration of clinical services, the level of activity and any significant regional variations. This will help the GDG to:

- identify the gaps between current clinical practice, service provision and patient experience and what the GDG concludes should be in place
- shape the guidance and formulate recommendations that are likely to have the greatest impact on the service as well as on clinical outcomes.

A detailed baseline assessment of service activity is needed, and should be conducted before the GDG starts work. This should be available for consideration early in the guideline development process, and ideally early enough to inform the scope. The following data sources might be used in providing an overall picture of service configuration and activity:

- hospital episode statistics (HES)
- patient episode data Wales (PEDW)

- national or regional registers (for example, cancer registers)
- national or regional clinical audits
- surveys of patients' experiences
- morbidity statistics from general practice.

5.12 Further reading

Centre for Reviews and Dissemination (2009) [Systematic reviews: CRD's guidance for undertaking reviews in health care](#). Centre for Reviews and Dissemination, University of York

Jenkins M (2004) Evaluation of methodological search filters – a review. *Health Information and Libraries Journal* 21: 148–63

Lefebvre C, Eisinga A, McDonald S et al. (2008) Enhancing access to reports of randomized trials published world-wide – the contribution of EMBASE records to the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library. *Emerging Themes in Epidemiology* 5: 13

Lefebvre C, Manheimer E, Glanville J (2011) Searching for studies. In: Higgins JPT, Green S, editors. [Cochrane handbook for systematic reviews of interventions, version 5.1.0](#) (updated March 2011). The Cochrane Collaboration.

Song F, Eastwood AJ, Gilbody S et al. (2000) Publication and related biases. *Health Technology Assessment* 4: 1–115

^[1] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

^[2] Accessible as part of the Cochrane Library and via the Centre for Reviews and Dissemination (CRD). The [CRD website](#) hosts the most up-to-date version of NHS EED.

^[3] For example, see the [Agreement between the Association of the British Pharmaceutical Industry \(ABPI\) and the National Institute for Health and Clinical Excellence \(NICE\) on](#)

guidelines for the release of company data into the public domain during a health technology appraisal.

6 Reviewing the evidence

Studies identified during literature searches (see [chapter 5](#)) need to be reviewed to identify the most appropriate data to help address the review questions, and to ensure that the guideline recommendations are based on the best available evidence. A systematic review process should be used that is explicit and transparent. This involves five major steps:

- writing the review protocol (see [section 4.4](#))
- selecting relevant studies
- assessing their quality
- synthesising the results
- interpreting the results.

The process of selecting relevant studies is common to all systematic reviews; the other steps are discussed below in relation to the major types of questions. The same rigour should be applied to reviewing fully and partially published studies, as well as unpublished data supplied by stakeholders.

6.1 Selecting relevant studies

The study selection process for clinical studies and economic evaluations should be clearly documented, giving details of the inclusion and exclusion criteria that were applied.

6.1.1 Clinical studies

Before acquiring papers for assessment, the information specialist or systematic reviewer should sift the evidence identified in the search in order to discard irrelevant material. First, the titles of the retrieved citations should be scanned and those that fall outside the topic of the guideline should be excluded. A quick check of the abstracts of the remaining papers should identify those that are clearly not relevant to the review questions and hence can be excluded.

Next, the remaining abstracts should be scrutinised against the inclusion and exclusion

criteria agreed by the Guideline Development Group (GDG). Abstracts that do not meet the inclusion criteria should be excluded. Any doubts about inclusion should be resolved by discussion with the GDG before the results of the study are considered. Once the sifting is complete, full versions of the selected studies can be acquired for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked should be excluded; those that meet the criteria can be assessed. Because there is always a potential for error and bias in selecting the evidence, double sifting (that is, sifting by two people) of a random selection of abstracts should be performed periodically (Edwards et al. 2002).

6.1.2 Conference abstracts

Conference abstracts can be a good source of information in systematic reviews. For example, conference abstracts can be important in pointing to published trials that may be missed, in estimating the amount of not-fully-published evidence (and hence guiding calls for evidence and judgements about publication bias), or in identifying ongoing trials that are due to be published. These sources of information are important in interpreting systematic reviews, and so conference abstracts should not be excluded in the search strategy.

However, the following should be considered when deciding whether to include conference abstracts as a source of evidence:

- Conference abstracts on their own seldom have sufficient information to allow confident judgements to be made about the quality and results of a study.
- It could be very time consuming to trace the original studies or additional data relating to the conference abstracts, and the information found may not always be useful.

Therefore:

- If sufficient evidence has been identified from full published studies, it may be reasonable not to trace the original studies or additional data related to conference abstracts.

- If there is a lack of or limited evidence identified from full published studies, the systematic reviewer may consider an additional process for tracing the original studies or additional data relating to the conference abstracts, in order to allow full critical appraisal and to make judgements on their inclusion in or exclusion from the systematic review.

6.1.3 Economic evaluations

The process for sifting and selecting economic evaluations for assessment is essentially the same as for clinical studies. Consultation between the information specialist, the health economist and the systematic reviewer is essential when deciding the inclusion criteria; these decisions should be discussed and agreed with the GDG. The review should be targeted to identify the papers that are most relevant to current NHS practice and hence likely to inform GDG decision-making. The review should also usually focus on 'full' economic evaluations that compare both the costs and health consequences of the alternative interventions and any services under consideration.

Inclusion criteria for filtering and selection of papers for review by the health economist should specify relevant populations and interventions for the review question. They should also specify the following:

- An appropriate date range, as older studies may reflect outdated practices.
- The country or setting, as studies conducted in other healthcare systems might not be relevant to the NHS. In some cases it may be appropriate to limit consideration to UK-based or OECD (Organisation for Economic Co-operation and Development) studies.
- The type of economic evaluation. This may include cost-utility, cost-benefit, cost-effectiveness, cost-minimisation or cost-consequence analyses. Non-comparative costing studies, 'burden of disease' studies and 'cost of illness' studies should usually be excluded.

6.2 Questions about interventions

These questions concern the relative effects of an intervention, as described in [section 4.3.1](#). The consideration of cost effectiveness is integral to the process of reviewing evidence and making recommendations about interventions. However, the quality criteria and ways of summarising the data are slightly different from those for

clinical effectiveness, so these are discussed in separate subsections.

6.2.1 Assessing study quality for clinical effectiveness

Study quality can be defined as the degree of confidence about the estimate of a treatment effect.

The first stage is to determine the study design so that the appropriate criteria can be applied in the assessment. A study design checklist can be obtained from the [Cochrane handbook for systematic reviews of interventions](#) (Higgins and Green 2011). Tables 13.2.a and 13.2.b in the Cochrane handbook are lists of study design features for studies with allocation to interventions at the individual and group levels respectively, and box 13.4.a provides useful notes for completing the checklist.

Once a study has been classified, it should be assessed using the methodology checklist for that type of study (see [appendices B–E](#)). To minimise errors and any potential bias in the assessment, two reviewers should independently assess the quality of a random selection of studies. Any differences arising from this should be discussed fully at a GDG meeting.

The quality of a study can vary depending on which of its measured outcomes is being considered. Well-conducted randomised controlled trials (RCTs) are more likely than non-randomised studies to produce similar comparison groups, and are therefore particularly suited to estimating the effects of interventions. However, short-term outcomes may be less susceptible to bias than long-term outcomes because of greater loss to follow-up with the latter. It is therefore important when summarising evidence that quality is considered according to outcome.

6.2.1.1 The GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to assessing the quality of evidence

The GRADE approach for questions about interventions has been used in the development of NICE clinical guidelines since 2009. For more details about GRADE, see the Journal of Clinical Epidemiology series, [appendix K](#) and the [GRADE working group website](#).

GRADE is a system developed by an international working group for rating the quality of evidence across outcomes in systematic reviews and guidelines; it can also be used to grade the strength of recommendations in guidelines. The system is designed for reviews

and guidelines that examine alternative management strategies or interventions, and these may include no intervention or current best management. The key difference from other assessment systems is that GRADE rates the quality of evidence for a particular outcome across studies and does not rate the quality of individual studies.

In order to apply GRADE, the evidence must clearly specify the relevant setting, population, intervention, comparator(s) and outcomes.

Before starting an evidence review, the GDG should apply an initial rating to the importance of outcomes, in order to identify which outcomes of interest are both 'critical' to decision-making and 'important' to patients. This rating should be confirmed or, if absolutely necessary, revised after completing the evidence review.

Box 6.1 summarises the GRADE approach to rating the quality of evidence.

Box 6.1 The GRADE approach to assessing the quality of evidence for intervention studies

In the GRADE system, the following features are assessed for the evidence found for each 'critical' and each 'important' outcome from a systematic review:

- study limitations (risk of bias): assessing the 'internal validity' of the evidence
- inconsistency: assessing heterogeneity or variability in the estimates of treatment effect across studies
- indirectness: assessing the degree of differences between the population, intervention, comparator for the intervention and outcome of interest
- imprecision (random error): assessing the extent to which confidence in the effect estimate is adequate to support a particular decision
- publication bias: assessing the degree of selective publication of studies.

Other considerations (for observational studies only):

- effect size
- effect of all plausible confounding
- evidence of a dose–response relationship.

The quality of evidence is classified as high, moderate, low or very low (see GRADE website for definitions).

The approach taken by NICE differs from the standard GRADE system in two ways:

- It also integrates a review of the quality of cost-effectiveness studies.
- It has no 'overall summary' labels for the quality of the evidence across all outcomes or for the strength of a recommendation, but uses the wording of recommendations to reflect the strength of the recommendation (see [section 9.3.3](#)).

6.2.2 Summarising and presenting results for clinical effectiveness

Characteristics of data should be extracted to a standard template for inclusion in an evidence table (see [appendix J1](#)). Evidence tables help to identify the similarities and differences between studies, including the key characteristics of the study population and interventions or outcome measures. This provides a basis for comparison.

Meta-analysis may be needed to pool treatment estimates from different studies. Recognised approaches to meta-analysis should be used, as described in the manual from NHS Centre for Reviews and Dissemination (2009) and in Higgins and Green (2011).

The body of evidence addressing a question should then be presented within the text of the full guideline as an evidence profile as described in the GRADE system (see [appendix K](#)). GRADEpro software can be used to prepare these profiles. Evidence profiles contain a 'quality assessment' section that summarises the quality of the evidence and a 'summary of findings' section that presents the outcome data for each critical and each important clinical outcome. The 'summary of findings' section includes a limited description of the quality of the evidence and can be presented alone in the text of the guideline (in which case full GRADE profiles should be presented in an appendix).

Short evidence statements for outcomes should be presented after the GRADE profiles, summarising the key features of the evidence on clinical effectiveness (including adverse events as appropriate) and cost effectiveness. The evidence statements should include the number of studies and participants, the quality of the evidence and the direction of estimate of the effect (see box 6.2 for examples of evidence statements). An evidence statement may be needed even if no evidence is identified for a critical or important outcome. Evidence statements may also note the presence of relevant ongoing research.

Box 6.2 Examples of evidence statements

Prostaglandin analogues versus beta-blockers for glaucoma – from [Glaucoma](#) (NICE clinical guideline 85; 2009):

- Moderate quality evidence from 12 studies with several thousand patients, showed that prostaglandin analogues are more effective than beta-blockers in reducing IOP from baseline at 6 to 36 months follow up, but the effect size is too small to be clinically effective.

Rehabilitation strategies/programmes after critical illness – from [Rehabilitation after critical illness](#) (NICE clinical guideline 83; 2009):

- One study with 126 patients presented moderate quality evidence that a 6-week supported self-help rehabilitation manual improved the recovery of patients' physical function 8 weeks and 6 months after ICU discharge.

Delayed versus immediate antibiotic prescribing strategy for acute otitis media – from [Respiratory tract infections – antibiotic prescribing](#) (NICE clinical guideline 69; 2008):

- Three studies with 773 children, presented high quality evidence that a delayed strategy reduced the consumption of antibiotics by 63% compared with an immediate prescribing strategy.

6.2.3 Indirect treatment comparisons and mixed treatment comparisons

NICE has a preference for data from head-to-head RCTs, and these should be presented in the reference case analysis if available. However, there may be situations when data from head-to-head studies of the options (and/or comparators) of interest are not available. In these circumstances, indirect treatment comparison analyses should be considered.

An 'indirect treatment comparison' refers to the synthesis of data from trials in which the interventions of interest have been compared indirectly using data from a network of trials that compare the interventions with other interventions. A 'mixed treatment comparison' refers to an analysis that includes both trials that compare the interventions of interest head-to-head and trials that compare them indirectly.

The principles of good practice for systematic reviews and meta-analyses should be carefully followed when conducting indirect treatment comparisons or mixed treatment comparisons. The rationale for identifying and selecting the RCTs should be explained, including the rationale for selecting the treatment comparisons that have been included. A clear description of the methods of synthesis is required. The methods and results of the individual trials should be documented. If there is doubt about the relevance of particular trials, a sensitivity analysis in which these trials are excluded should also be presented. The heterogeneity between the results of pairwise comparisons and inconsistencies between the direct and indirect evidence on the interventions should be reported.

There may be circumstances in which data from head-to-head RCTs are less than ideal (for example, the sample size may be small or there may be concerns about the external validity). In such cases, additional evidence from mixed treatment comparisons can be considered. In these cases, mixed treatment comparisons should be presented separately from the reference-case analysis and a rationale for their inclusion provided. Again, the principles of good practice apply.

When multiple options are being appraised, data from RCTs (when available) that compare each of the options head-to-head should be presented in a series of pairwise comparisons. Consideration may be given to presenting an additional analysis using a mixed treatment comparison framework.

When evidence is combined using indirect or mixed treatment comparison frameworks, trial randomisation should be preserved. A comparison of the results from single treatment arms from different randomised trials is not acceptable unless the data are treated as observational and appropriate steps are taken to adjust for possible bias and increased uncertainty.

Analyses using indirect or mixed treatment comparison frameworks may include comparator interventions (including placebo) that have not been defined in the scope of the guideline if they are relevant to the development of the network of evidence. The rationale for the inclusion and exclusion of comparator interventions should be clearly reported. Again, the principles of good practice apply.

Evidence from a mixed treatment comparison can be presented in a variety of ways. The network of evidence can be presented as tables. It may also be presented diagrammatically as long as the direct and indirect treatment comparisons are clearly identified and the number of trials in each comparison is stated.

If sufficient relevant and valid data are not available to include in meta-analyses of head-to-head trials, or mixed or indirect treatment comparisons, the analysis may have to be restricted to a qualitative overview that critically appraises individual studies and presents their results. The results of this type of analysis should be approached with particular caution.

Further information on evidence synthesis is provided by the [technical support documents developed by the NICE Decision Support Unit \(DSU\)](#).

6.2.4 Assessing study quality for cost effectiveness

Estimates of resource use obtained from clinical studies should be treated like other clinical outcomes and reviewed using the processes described above. Reservations about the applicability of these estimates to routine NHS practice should be noted in the economics evidence profile, in the same way as in a GRADE profile (see [section 6.2.1.1](#)), and taken into consideration by the GDG.

However, the criteria for appraising other economic estimates – such as costs, cost-effectiveness ratios and net benefits – are rather different, because these estimates are usually obtained using some form of modelling. In addition to formal decision-analytic models, this includes economic evaluations conducted alongside clinical trials. These usually require some external sources of information (for example, unit costs, health-state valuations or long-term prognostic data) and estimation procedures to predict long-term costs and outcomes. These considerations also apply to relatively simple cost calculations based on expert judgement or on observed resource use and unit cost data.

All economic estimates used to inform guideline recommendations should be appraised using the methodology checklist for economic evaluations ([appendix G](#)). This should be used to appraise unpublished economic evaluations, such as studies submitted by stakeholders and academic papers that are not yet published, as well as published papers. The same criteria should be applied to any new economic evaluations conducted for the guideline (see [chapter 7](#)).

The checklist ([appendix G](#)) includes a section on the applicability of the study to the specific question and the context for NICE decision-making (analogous to the GRADE 'directness' criterion). This checklist is designed to determine whether an economic evaluation provides evidence that is useful to inform GDG decision-making, analogous to the assessment of study limitations in GRADE.

The checklist includes an overall judgement on the applicability of the study to the guideline context, as follows:

- Directly applicable – the study meets all applicability criteria, or fails to meet one or more applicability criteria but this is unlikely to change the conclusions about cost effectiveness.
- Partially applicable – the study fails to meet one or more applicability criteria, and this could change the conclusions about cost effectiveness.
- Not applicable – the study fails to meet one or more applicability criteria, and this is likely to change the conclusions about cost effectiveness. Such studies would usually be excluded from further consideration.

The checklist also includes an overall summary judgement on the methodological quality of economic evaluations, as follows:

- Minor limitations – the study meets all quality criteria, or fails to meet one or more quality criteria but this is unlikely to change the conclusions about cost effectiveness.
- Potentially serious limitations – the study fails to meet one or more quality criteria, and this could change the conclusions about cost effectiveness.
- Very serious limitations – the study fails to meet one or more quality criteria, and this is highly likely to change the conclusions about cost effectiveness. Such studies should usually be excluded from further consideration.

The robustness of the study results to methodological limitations may sometimes be apparent from reported sensitivity analyses. If not, judgement will be needed to assess whether a limitation would be likely to change the results and conclusions.

If necessary, the health technology assessment checklist for decision-analytic models (Philips et al. 2004) may also be used to give a more detailed assessment of the methodological quality of modelling studies.

The judgements that the health economist makes using the checklist for economic evaluations (and the health technology assessment modelling checklist, if appropriate) should be recorded and presented in an appendix to the full guideline. The 'comments' column in the checklist should be used to record reasons for these judgements, as well as additional details about the studies where necessary.

6.2.5 Summarising and presenting results for cost effectiveness

Cost, cost effectiveness or net benefit estimates from published or unpublished studies, or from economic analyses conducted for the guideline, should be presented in an 'economic evidence profile' adapted from the GRADE profile (see [appendix K](#)). Whenever a GRADE profile is presented in the full version of a NICE clinical guideline, it should be accompanied by relevant economic information (resource use, costs, cost effectiveness and/or net benefit estimates as appropriate). It should be explicitly stated if economic information is not available or if it is not thought to be relevant to the question.

The economic evidence profile includes columns for the overall assessments of study limitations and applicability described above. There is also a comments column where the health economist can note any particular issues that the GDG should consider when assessing the economic evidence. Footnotes should be used to explain the reasons for quality assessments, as in the standard GRADE profile.

The results of the economic evaluations included should be presented in the form of a best-available estimate or range for the incremental cost, the incremental effect and, where relevant, the incremental cost-effectiveness ratio or net benefit estimate. A summary of the extent of uncertainty about the estimates should also be presented in the economic evidence profile. This should reflect the results of deterministic or probabilistic sensitivity analyses or stochastic analyses of trial data, as appropriate.

Each economic evaluation included should usually be presented in a separate row of the economic evidence profile. If large numbers of economic evaluations of sufficiently high quality and applicability are available, a single row could be used to summarise a number of studies based on shared characteristics; this should be explicitly justified in a footnote.

Inconsistency between the results of economic evaluations will be shown by differences between rows of the economic evidence profile (a separate column examining 'consistency' is therefore unnecessary). The GDG should consider the implications of any unexplained differences between model results when assessing the body of clinical and economic evidence and drawing up recommendations. This includes clearly explaining the GDG's preference for certain results when forming recommendations.

If results are available for two or more patient subgroups, these should be presented in separate economic evidence profile tables or as separate rows within a single table.

Costs and cost-effectiveness estimates should be presented only for the appropriate incremental comparisons – where an intervention is compared with the next most expensive non-dominated option (a clinical strategy is said to 'dominate' the alternatives when it is both more effective and less costly; see [section 7.3](#)). If comparisons are relevant only for some groups of the population (for example, patients who cannot tolerate one or more of the other options, or for whom one or more of the options is contraindicated), this should be stated in a footnote to the economic evidence profile table.

A short evidence statement should be presented alongside the GRADE and economic evidence profile tables, summarising the key features of the evidence on clinical and cost effectiveness.

6.3 Questions about diagnosis

Questions about diagnosis are concerned with the performance of a diagnostic test or test strategy (see [section 4.3.2](#)). Note that 'test and treat' studies (in which the outcomes of patients who undergo a new diagnostic test in combination with a management strategy are compared with the outcomes of patients who receive the usual diagnostic test and management strategy) should be addressed in the same way as intervention studies (see [section 6.2](#)).

6.3.1 Assessing study quality

Studies of diagnostic test accuracy should be assessed using the methodology checklist for QUADAS-2 (Quality Assessment of Studies of Diagnostic Accuracy included in Systematic Reviews) ([appendix F](#)). Characteristics of data should be extracted to a standard template for inclusion in an evidence table (see [appendix J2](#)). Questions relating to diagnostic test accuracy are usually best answered by cross-sectional studies. Case-control studies can also be used, but these are more prone to bias and often result in inflated estimates of diagnostic test accuracy.

There is currently a lack of empirical evidence about the size and direction of bias contributed by specific aspects of the design and conduct of studies on diagnostic test accuracy. Making judgements about the overall quality of studies can therefore be difficult. Before starting the review, an assessment should be made to determine which quality appraisal criteria (from the QUADAS-2 checklist) are likely to be the most important indicators of quality for the particular question about diagnostic test accuracy being addressed. These criteria will be useful in guiding decisions about the overall quality of

individual studies and whether to exclude certain studies, and when summarising and presenting the body of evidence for the question about diagnostic test accuracy as a whole (see section 6.3.2). Clinical input (for example, from a GDG member) may be needed to identify the most appropriate quality criteria.

6.3.2 Summarising and presenting results

No well designed and validated approach currently exists for summarising a body of evidence for studies on diagnostic test accuracy. In the absence of such a system, a narrative summary of the quality of the evidence should be given, based on the quality appraisal criteria from QUADAS-2 ([appendix F](#)) that were considered to be most important for the question being addressed (see section 6.3.1).

Numerical summaries of diagnostic test accuracy may be presented as tables to help summarise the available evidence. Meta-analysis of such estimates from different studies is possible, but is not widely used. If this is attempted, relevant published technical advice should be used to guide reviewers.

Numerical summaries and analyses should be followed by a short evidence statement summarising what the evidence shows.

6.4 Questions about prognosis

These questions are described in [section 4.3.3](#).

6.4.1 Assessing study quality

Studies that are reviewed for questions about prognosis should be assessed using the methodology checklist for prognostic studies ([appendix I](#)). There is currently a lack of empirical evidence about the size and direction of bias contributed by specific aspects of the design and conduct of studies on prognosis. Making judgements about the overall quality of studies can therefore be difficult. Before starting the review, an assessment should be made to determine which quality appraisal criteria (from the checklist in [appendix I](#)) are likely to be the most important indicators of quality for the particular question about prognosis being addressed. These criteria will be useful in guiding decisions about the overall quality of individual studies and whether to exclude certain studies, and when summarising and presenting the body of evidence for the question

about prognosis as a whole (see section 6.4.2). Clinical input (for example, from a GDG member) may be needed to identify the most appropriate quality criteria.

6.4.2 Summarising and presenting results

No well designed and validated approach currently exists for summarising a body of evidence for studies on prognosis. A narrative summary of the quality of the evidence should therefore be given, based on the quality appraisal criteria from appendix I that were considered to be most important for the question being addressed (see section 6.4.1). Characteristics of data should be extracted to a standard template for inclusion in an evidence table (see [appendix J3](#)).

Results from the studies included may be presented as tables to help summarise the available evidence. Reviewers should be wary of using meta-analysis as a tool to summarise large observational studies, because the results obtained may give a spurious sense of confidence in the study results.

The narrative summary should be followed by a short evidence statement summarising what the evidence shows.

6.5 Using patient experience to inform review questions

These questions are described in [section 4.3.4](#).

6.5.1 Assessing study quality

Studies about patient experience are likely to be qualitative studies or cross-sectional surveys. Qualitative studies should be assessed using the methodology checklist for qualitative studies ([appendix H](#)). It is important to consider which quality appraisal criteria from this checklist are likely to be the most important indicators of quality for the specific research question being addressed. These criteria may be helpful in guiding decisions about the overall quality of individual studies and whether to exclude certain studies, and when summarising and presenting the body of evidence for the research question about patient experience as a whole.

There is no methodology checklist for the quality appraisal of cross-sectional surveys.

Such surveys should be assessed for the rigour of the process used to develop the questions and their relevance to the population under consideration, and for the existence of significant bias (for example, non-response bias).

6.5.2 Summarising and presenting results

A description of the quality of the evidence should be given, based on the quality appraisal criteria from [appendix H](#) that were considered to be the most important for the research question being addressed. If appropriate, the quality of the cross-sectional surveys included should also be summarised.

Consider presenting the quality assessment of included studies in tables (see [table 1 in appendix H](#) for an example). Methods to synthesise qualitative studies (for example, meta-ethnography) are evolving, but the routine use of such methods in guidelines is not currently recommended.

The narrative summary should be followed by a short evidence statement summarising what the evidence shows. Characteristics of data should be extracted to a standard template for inclusion in an evidence table (see [appendix J4](#)).

6.6 Published guidelines

Relevant published guidelines from other organisations may be identified in the search for evidence. These should be assessed for quality using the AGREE II^[10] (Appraisal of Guidelines Research and Evaluation II) instrument (Brouwers et al. 2010) to ensure that they have sufficient documentation to be considered. There is no cut-off point for accepting or rejecting a guideline, and each GDG will need to set its own parameters. These should be documented in the methods section of the full guideline, along with a summary of the assessment. The results should be presented as an appendix to the full guideline.

Reviews of evidence from other guidelines that cover questions formulated by the GDG may be considered as evidence if:

- they are assessed using the appropriate methodology checklist from this manual and are judged to be of high quality
- they are accompanied by an evidence statement and evidence table(s)

- the evidence is updated according to the methodology for exceptional updates of NICE clinical guidelines (see [section 14.4](#)).

The GDG should create its own evidence summaries or statements. Evidence tables from other guidelines should be referenced with a direct link to the source website or a full reference of the published document. The GDG should formulate its own recommendations, taking into consideration the whole body of evidence.

Recommendations from other guidelines should not be quoted verbatim, except for recommendations from NHS policy or legislation (for example, Health and Social Care Act 2008).

6.7 Further reading

Altman DG (2001) Systematic reviews of evaluations of prognostic variables. *British Medical Journal* 323: 224–8

Balshem H, Helfand M, Schünemann HJ et al. (2011) GRADE guidelines: 3. Rating the quality of evidence. *Journal of Clinical Epidemiology* 64: 401–6

Brouwers M, Kho ME, Browman GP et al. for the AGREE Next Steps Consortium (2010) [AGREE II: advancing guideline development, reporting and evaluation in healthcare](#). *Canadian Medical Association Journal* 182: E839–42

Centre for Reviews and Dissemination (2009) [Systematic reviews: CRD's guidance for undertaking reviews in health care](#). University of York: Centre for Reviews and Dissemination

Chiou CF, Hay JW, Wallace JF et al. (2003) Development and validation of a grading system for the quality of cost-effectiveness studies. *Medical Care* 41: 32–44

Drummond MF, O'Brien B, Stoddart GL et al. (1997) Critical assessment of economic evaluation. In: *Methods for the economic evaluation of health care programmes*, 2nd edition. Oxford: Oxford Medical Publications

Eccles M, Mason J (2001) How to develop cost-conscious guidelines. *Health Technology Assessment* 5: 1–69

Edwards P, Clarke M, DiGuseppi C et al. (2002) Identification of randomized trials in systematic reviews: accuracy and reliability of screening records. *Statistics in Medicine* 21: 1635–40

Evers SMAA, Goossens M, de Vet H et al. (2005) Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. *International Journal of Technology Assessment in Health Care* 21: 240–5

Guyatt GH, Oxman AD, Schünemann HJ et al. (2011) GRADE guidelines: a new series of articles in the *Journal of Clinical Epidemiology*. *Journal of Clinical Epidemiology* 64: 380–2

Guyatt GH, Oxman AD, Akl EA et al. (2011) GRADE guidelines: 1. Introduction – GRADE evidence profiles and summary of findings tables. *Journal of Clinical Epidemiology* 64: 383–94

Guyatt GH, Oxman AD, Kunz R et al. (2011) GRADE guidelines: 2. Framing the question and deciding on important outcomes. *Journal of Clinical Epidemiology* 64: 395–400

Guyatt GH, Oxman AD, Vist G et al. (2011) GRADE guidelines: 4. Rating the quality of evidence – study limitations (risk of bias). *Journal of Clinical Epidemiology* 64: 407–15

Guyatt GH, Oxman AD, Montori V et al. (2011) GRADE guidelines 5: Rating the quality of evidence – publication bias. *Journal of Clinical Epidemiology* 64: 1277–82

Guyatt G, Oxman AD, Kunz R et al. (2011) GRADE guidelines 6: Rating the quality of evidence – imprecision. *Journal of Clinical Epidemiology* 64: 1283–93

Guyatt GH, Oxmand AD, Kunz R et al. (2011) GRADE guidelines 7: Rating the quality of evidence – inconsistency. *Journal of Clinical Epidemiology* 64: 1294–302

Guyatt GH, Oxman AD, Kunz R et al. (2011) GRADE guidelines 8: Rating the quality of evidence – indirectness. *Journal of Clinical Epidemiology* 64: 1303–10

Guyatt GH, Oxman AD, Sultan S et al. (2011) GRADE guidelines 9: Rating up the quality of evidence. *Journal of Clinical Epidemiology* 64: 1311–6

Harbord RM, Deeks JJ, Egger M et al. (2007) A unification of models for meta-analysis of diagnostic accuracy studies. *Biostatistics* 8: 239–51

Higgins JPT, Green S, editors (2011) [Cochrane handbook for systematic reviews of interventions. Version 5.1.0](#) (updated March 2011) [online]

Khan KS, Kunz R, Kleijnen J et al. (2003) Systematic reviews to support evidence-based medicine. How to review and apply findings of healthcare research. London: Royal Society of Medicine Press

Oxman AD, Guyatt GH (1992) A consumer's guide to subgroup analyses. *Annals of Internal Medicine* 116: 78–84

Philips Z, Ginnelly L, Sculpher M et al. (2004) Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technology Assessment* 8: iii–iv, ix–xi, 1–158

Schünemann HJ, Best D, Vist G et al. for the GRADE Working Group (2003) Letters, numbers, symbols and words: how to communicate grades of evidence and recommendations. *Canadian Medical Association Journal* 169: 677–80

Schünemann HJ, Oxman AD, Brozek J et al. for the GRADE Working Group (2008) Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. *British Medical Journal* 336: 1106–10

Scottish Intercollegiate Guidelines Network (2008) SIGN 50. A guideline developer's handbook, revised edition, January. Edinburgh: Scottish Intercollegiate Guidelines Network

Sharp SJ, Thompson SG (2000) Analysing the relationship between treatment effect and underlying risk in meta-analysis: comparison and development of approaches. *Statistics in Medicine* 19: 3251–74

Whiting PF, Rutjes AWS, Westwood ME et al. and the QUADAS-2 group (2011) QUADAS-2: A revised tool for the quality assessment of diagnostic accuracy studies. *Annals of Internal Medicine* 155: 529–36

^[10] For more details about AGREE II, see the [AGREE Enterprise website](#).

7 Assessing cost effectiveness

Health economics is about improving the health of the population through the efficient use of resources, so it necessarily applies at all levels, including individual clinical decisions. Clinicians already take resources and value for money into account when making clinical decisions; the incorporation of good-quality health-economic evidence into clinical guidelines can help to make this more consistent.

The Guideline Development Group (GDG) is required to make decisions based on the best available evidence of both clinical and cost effectiveness. This chapter describes the role of the health economist in the development of NICE clinical guidelines, and suggests possible approaches to considering economic evidence as part of the guideline development process. It also sets out the principles for conducting new economic modelling studies if there is insufficient evidence in the literature to assess the cost effectiveness of key interventions or services.

Guideline recommendations should be based on the estimated costs of the interventions or services in relation to their expected health benefits (that is, their 'cost effectiveness'), rather than on the total cost or resource impact of implementing them. Thus, if the evidence suggests that an intervention or service provides significant health benefits at an acceptable cost per patient treated, it should be recommended even if it would be expensive to implement across the whole population.

When implementing a guideline's recommendations, commissioners and trusts also need to know the resource and cost implications for their organisations. NICE undertakes a separate, but parallel, cost-impact analysis. This analysis is usually developed by the NICE costing analyst during the consultation period of the clinical guideline. Costing tools are published at the same time as the guideline, to allow organisations to estimate implementation costs (see [section 13.1.3](#)).

7.1 The role of the health economist in clinical guideline development

The health economist is a core member of the GDG alongside the rest of the National Collaborating Centre (NCC) or NICE Internal Clinical Guidelines Programme^[1] team, and should be involved from the beginning of scoping (see [chapter 2](#)). The health economist

should attend all GDG meetings.

Although the health economist has skills in economic analysis, the expertise of all of the GDG members will be necessary to ensure that economic evidence is underpinned by the most plausible assumptions and the best available clinical evidence. Similarly, the health economist may be able to provide input into the interpretation of clinical data and develop models to help assess overall health outcome.

The key role of the health economist in clinical guideline development is to:

- advise on economic issues
- review economic evaluations
- prioritise questions for further economic analysis
- collaborate with the systematic reviewer to develop evidence syntheses for input into economic models
- conduct economic evaluations
- liaise with the costing analyst at NICE to ensure consistency between the cost-effectiveness and cost-impact assessments.

The relative amounts of time spent by the health economist on each of these tasks will vary between guidelines. There are likely to be large differences between clinical guideline topics in the amount, relevance and quality of the economic literature. In some topic areas there may be high-quality data that can be used in economic models, whereas in other areas there will be little information.

Defining the economic priorities for each clinical guideline should start during scoping, and should proceed alongside development of the review questions. The NCC prepares an economic plan, which contains a preliminary overview of the relevant economic literature. The plan also identifies the initial priorities for further economic analysis and the proposed methods for addressing these questions (see section 7.1.3). It is prepared by the health economist in consultation with the rest of the NCC team and the GDG, and is discussed and signed off by NICE, usually within 3 months of the first GDG meeting. For short clinical guidelines the economic plan should be submitted to NICE 1 week after the first GDG meeting. The economic plan is likely to be modified during guideline development. For example, as the clinical evidence is reviewed it may become apparent that further

evaluation is not necessary for some aspects that were initially prioritised for economic analysis. Any key changes in the economic plan should be agreed between the NCC and NICE. A document listing the final areas prioritised for economic modelling and corresponding PICO (population, intervention, comparator and outcome) questions should be sent to NICE 5–7 weeks before consultation on the guideline so that it can be published on the NICE website. The rationale for the final choice of priorities for economic modelling should be explained in the full guideline.

The health economist should ensure that the economic model(s) developed for the guideline are sent to NICE and are available to stakeholders during consultation on the guideline. These models should be fully executable and clearly presented.

7.1.1 Advising on economic issues

The health economist should encourage the GDG to consider the economic consequences of the guideline recommendations as well as the clinical implications. A formal presentation outlining the basic principles of health economics is given at the first GDG meeting, and further presentations may be useful later in the guideline development process. It is particularly important that the GDG members understand that economic analysis is not simply a matter of estimating the consequences of a guideline recommendation in terms of use of resources, but is concerned with the evaluation of both costs and health benefits. GDG members also need to understand that economic evaluation should compare the costs and consequences of alternative courses of action. 'Cost of illness' or 'burden of disease' studies are not useful for decision-making when developing clinical guidelines.

Cost effectiveness is assessed in order to maximise health gain from available resources. If resources are used for interventions that are not cost effective, then less health gain is achievable across the whole population (that is, there is a greater 'opportunity cost').

Within the context of the principles outlined in the document [Social value judgements: principles for the development of NICE guidance](#) (see also [section 1.1.1](#)), the GDG should be encouraged to consider recommendations for interventions that:

- are less effective than current practice but free up a substantial amount of resources that can be re-invested in the NHS **or**
- increase clinical effectiveness at an acceptable level of increased cost (see [section 7.3](#)).

The GDG members may find it useful if the health economist discusses with them other

economic concepts, such as incremental analysis, the NHS and personal social services (PSS^[12]) perspective, and measurement of health-related quality of life (HRQoL) and quality-adjusted life years (QALYs). The British Medical Journal has published a series of 'economics notes' describing other concepts that the health economist may wish to explore with the GDG (Raftery 1999–2001).

7.1.2 Reviewing economic evaluations

Identifying and examining published economic information that is relevant to the review questions is an important component of clinical guideline development. Processes for searching for, selecting, appraising and summarising economic evaluations are discussed in sections [5.3](#), [6.1.3](#), [6.2.4](#) and [6.2.5](#).

The general approach to reviewing economic evaluations should be systematic, but focused and pragmatic. If a high-quality economic analysis that addresses a key clinical issue and is relevant to current NHS practice has already been published, then further modelling by the health economist will probably not be necessary. This frees up time for modelling on other questions. However, many published economic evaluations will not be relevant; for example, costs in non-UK studies may differ from those in the NHS. Time should not be wasted on critically appraising studies that are not likely to provide useful information for guideline decision-making. Search strategies and inclusion and exclusion criteria for economic evaluations should be designed to filter out such papers (see [section 5.3](#)), and these strategies should be explained in the full guideline. The approach used should be explicitly stated in the full guideline and applied consistently.

7.1.3 Prioritising questions for further economic analysis

Only rarely will the health economic literature be comprehensive enough and conclusive enough that no further analysis is required. Additional economic analyses will usually be needed, in which case new analyses should be developed selectively, unless an existing analysis can easily be adapted to answer the question.

Close collaboration between the health economist and the rest of the GDG is essential early in the guideline development process to ensure that:

- the most important questions are selected for economic analysis
- the overall methodological approach is appropriate

- all of the important health effects and resource costs are included
- the clinical, epidemiological and resource evidence used is the best available and the assumptions are plausible
- the results of the analysis are interpreted appropriately and the limitations acknowledged.

It is acknowledged that the NCC has limited resources and time to construct new economic analyses. Therefore the complexity and number of new analyses will vary depending on what are considered priority areas and what information is required for robust decision making.

Economic analysis is potentially useful for any question in which one intervention or service is compared with another. This includes comparisons of methods for prevention, screening, risk assessment, diagnosis, monitoring, rehabilitation and follow-up, as well as treatment. It may also be appropriate for comparisons of different combinations or sequences of interventions, as well as individual components of the patient management algorithm. However, given the broad scope of many clinical guidelines, it will not be possible to conduct original analyses for every component. Selecting questions for further economic analysis, including modelling, should be a joint decision between the health economist and the other GDG members. Selection should be based on systematic consideration of the potential value of economic analysis across all key clinical issues.

An economic analysis will be more useful if it is likely to influence a recommendation, and if the health and financial consequences of the recommendation are large. The value of an economic analysis thus depends on:

- the overall 'importance' of the recommendation (which is a function of the number of patients affected and the potential impact on costs and health outcomes per patient)
- the current extent of uncertainty over cost effectiveness, and the likelihood that economic analysis will reduce this uncertainty.

For a particular question, new economic analyses may not be warranted if, for example, the clinical evidence is so uncertain that it is not possible to give even a rough estimate of cost effectiveness. Alternatively, the published evidence on cost effectiveness may be so reliable that further economic analysis would be superfluous. Economic analysis may also not be a priority if it is obvious that the resource implications are modest in relation to the expected health gains.

7.2 Modelling approaches

Economic evaluation will usually be conducted in the form of a cost-effectiveness analysis, with the health effects being measured using an appropriate non-monetary outcome indicator. In circumstances for which cost-effectiveness analysis is not appropriate, other validated methods may be used.

Cost-effectiveness analysis with the units of effectiveness expressed in cost per QALY gained (cost-utility analysis) is widely recognised as a useful approach for measuring and comparing the efficiency of different health interventions. QALYs are an overall measure of health outcome that weight the life expectancy of a patient with an estimate of their HRQoL (measured on a 0–1 scale). There are well documented methodological problems with QALYs, but this is also true of other approaches. The NICE technology appraisal programme (see [section 8.1](#)) uses the QALY approach. If suitable data are available, this approach should also be followed in clinical guideline development. If there are not sufficient data to estimate QALYs gained, an alternative measure of effectiveness may be considered for the cost-effectiveness analysis (such as life years gained or cases averted, or a more disease-specific outcome).

A cost-effectiveness analysis could be modelled around a single well-conducted randomised controlled trial, or by using decision-analytic techniques with probability, cost and health outcome data from a variety of published sources. For clinical guidelines there is often a trade-off between the range of new analyses that the health economist can conduct and the complexity of each piece of analysis. Simple methods may be used if these can provide the GDG with sufficient information on which to base a decision. For example, if an intervention is associated with better health outcomes and fewer adverse effects, then an estimate of cost may be all that is needed. Or a simple decision tree may provide a sufficiently reliable estimate of cost effectiveness. In other situations a more complex approach, such as Markov modelling or discrete event simulation, may be warranted.

Specific guidance on methods of cost-effectiveness analysis can be found in NICE's [Guide to the methods of technology appraisal](#). This includes a 'reference case', which specifies the methods considered by NICE to be the most appropriate for technology appraisals, and which is consistent with the NHS objective of maximising health gain from limited resources (see [table 7.1](#)). Economic analyses conducted for NICE clinical guidelines should usually follow this same reference case. Departures from the reference case may sometimes be appropriate in clinical guidelines, for example when there are insufficient

data to estimate QALYs gained. Any such departures must be highlighted in the full guideline and reasons given. Advice on how to implement the approaches described in NICE's [Guide to the methods of technology appraisal](#) is provided by the [technical support documents developed by the NICE Decision Support Unit \(DSU\)](#).

For the reference case, the perspective on outcomes should be all direct health effects on individuals, whether they are patients or others (principally carers). The perspective on costs should be that of the NHS and PSS. Some interventions or services may have a substantial impact on non-health outcomes or costs to other government bodies (for example, treatments to reduce illicit drug misuse may have the effect of reducing drug-related crime). Costs to other government bodies may be included if this has been specifically agreed with the Department of Health, usually before the referral of the topic. When non-reference-case analyses include these broader costs, explicit valuation methods are required. In all cases, these costs should be reported separately from the NHS and PSS costs. These costs should not be combined into an incremental cost-effectiveness ratio (ICER; where the QALY is the outcome measure of interest).

Productivity costs and costs borne by patients and carers that are not reimbursed by the NHS or social services should not usually be included in any analyses (see the [Guide to the methods of technology appraisal](#)).

The [Guide to the methods of technology appraisal](#) and accompanying technical support documents include other useful advice for health economists who are developing economic analyses for use in clinical guidelines.

Table 7.1 Summary of the reference case

This table is adapted from the consultation version of the NICE [Guide to the methods of technology appraisal](#), which is currently being updated (publication expected spring 2013).

Element of health technology assessment	Reference case
Defining the decision problem	The scope developed by NICE
Comparator	Interventions routinely used in the NHS, including those regarded as current best practice

Perspective on outcomes	All direct health effects, whether for patients or, when relevant, other people (principally family members or informal carers)
Perspective on costs	NHS and PSS
Type of economic evaluation	Cost–utility analysis with fully incremental analysis
Time horizon	Long enough to reflect all important differences in costs or outcomes between the technologies being compared
Synthesis of evidence on health effects	Based on a systematic review
Measuring and valuing health effects	Health effects should be expressed in QALYs. The EQ-5D is the preferred measure of HRQoL in adults.
Source of data for measurement of HRQoL	Reported directly by patients and/or carers
Source of preference data for valuation of changes in HRQoL	Representative sample of the UK population
Equity considerations	An additional QALY has the same weight regardless of the other characteristics of the people receiving the health benefit
Evidence on resource use and costs	Costs should relate to NHS and PSS resources and should be valued using the prices relevant to the NHS and PSS
Discounting	The same annual rate for both costs and health effects (currently 3.5%)
HRQoL, health-related quality of life; PSS, personal social services; QALY, quality-adjusted life year.	

7.2.1 General principles

Regardless of the methodological approach taken, the general principles described below should be observed. The health economist should carry out each economic analysis in collaboration with the rest of the GDG. Any variation from the principles outlined below

should be described and justified in the economic analysis.

Economic analyses should be explicitly based on the guideline's review questions. The economic analysis should compare all relevant alternatives for specified groups of patients. Any differences between the review question(s) and the economic analysis should be clearly acknowledged, justified and explained, with the approval of the GDG. The interventions or services included in the analysis should be described in sufficient detail to allow stakeholders to understand exactly what is being assessed. This is particularly important when calculating the cost effectiveness of services.

An economic analysis should be underpinned by the best-quality clinical evidence. The evidence should be based upon and consistent with that identified in addressing the guideline's review question. Sometimes the systematic reviewer will not have time to conduct an analysis (for example, a meta-analysis) for a key model parameter; in this case the health economist may conduct the analysis in collaboration with the rest of the GDG and NCC team. If clinical opinion is used in the cost-effectiveness analysis, this should be clearly stated and justified in the full guideline.

If existing models are being used or are informing the new analyses, the process of how these studies are being adapted or used to inform the new analyses should be outlined clearly.

The structure of the model should be discussed and agreed with the GDG early in development. Potential alternatives should be identified and considered for structural sensitivity analysis.

All cost-effectiveness analyses should be validated. The validation process should be outlined in the full guideline. Useful and practical validation methods could include:

- systematic checking of model formulae and inputs by a second modeller
- one-way and n-way sensitivity analyses (including null values and extreme values) (Krahn et al. 1997)
- ensuring that the model results are plausible and can be explained
- comparing clinical end points from the model with source materials.

If analyses are conducted to demonstrate external validity, the results should be reported. However, relevant data should not be omitted from inclusion to facilitate external validation

(for example, not including clinical trials so that they can be used for subsequent validation).

There should be the highest level of transparency in reporting methods and results. Conventions on reporting economic evaluations should be followed (see Drummond and Jefferson 1996). In particular, the following results should be presented:

- clinical end points from the analysis, such as life years gained, number of events and survival
- disaggregated costs
- total and incremental costs and QALYs for all options.

When comparing multiple mutually exclusive options, a fully incremental approach should be adopted that compares the treatments sequentially in rank order of effectiveness (or cost). Comparisons with a common baseline should not be used for decision-making.

7.2.2 Exploring uncertainty

Considerations of potential bias and limitations should be discussed by the GDG. Sensitivity analysis should be used to explore the impact of potential sources of bias and uncertainty on the results of the economic analysis.

Probabilistic sensitivity analysis is the preferred method for taking account of uncertainty arising from imprecision in model parameters. It allows the uncertainty associated with different parameters to be reflected simultaneously in the model results. Probabilistic methods also provide the best estimates of mean costs and outcomes in non-linear decision models where outputs are a result of a multiplicative function (for example, in Markov models). The choice of distributions used should be justified; for example, in relation to the available evidence or published literature. Options for presentation of the results of probabilistic sensitivity analysis include scatter plots and cost-effectiveness acceptability curves and frontiers.

If the health economist decides not to use probabilistic methods, this should be clearly stated and justified in the full guideline. The impact of parameter uncertainty should be thoroughly explored using deterministic sensitivity analysis.

Potential bias resulting from key structural assumptions should be explored through

deterministic sensitivity analyses, which test whether and how the model results in change under alternative plausible scenarios. Common examples of when this type of sensitivity analysis could be conducted are:

- when there is uncertainty about the most appropriate assumption to use for extrapolation of costs and outcomes beyond the trial follow-up period
- when there is uncertainty about how the pathway of care is most appropriately represented in the analysis
- when there may be economies of scale (for example, when appraising diagnostic technologies).

Deterministic sensitivity analysis should also be used to test the impact of potential bias resulting from the selection or exclusion of data sources for key model parameters.

Consideration can be given to including structural assumptions and the inclusion or exclusion of data sources in probabilistic sensitivity analysis. In this case the method used to select the distribution should be outlined in the full guideline (Jackson et al. 2011).

7.2.3 Identification and selection of model inputs

The NICE reference case ([table 7.1](#)) states that evidence on health effects should be obtained from a systematic review. Although it is desirable to conduct systematic literature reviews for other model inputs, this is time-consuming, and there is an opportunity cost in terms of both the health economist's and the information specialist's time. Therefore, before requesting additional literature searches from the information specialist, the health economist should explore pragmatic options for identifying inputs for economic analyses. This could include liaising with the systematic reviewer about using data from the studies identified in the clinical review. Alternatives could include asking GDG members and other experts for suitable papers or eliciting their opinions. If an additional literature search is necessary, the health economist should discuss this with the information specialist. If longer-term follow-up data are required, a literature search to identify cohort studies may be appropriate. It has been suggested (Cooper et al. 2007) that other search methods may be more efficient for identifying information for economic models. The report by Philips and co-workers (2004) is a useful guide to searching methods for economic models. When a systematic review is not possible, the health economist should use transparent processes for identifying other possible model inputs, assure their quality and justify their inclusion or exclusion.

Information on unit costs should be routinely obtained from national list prices such as the [NHS drug tariff](#), the PSSRU (Personal Social Services Research Unit) [Unit costs of health and social care](#) or [Department of Health reference costs](#). Information on costing can also be found in NICE's [Assessing cost impact: methods guide](#) and through discussion with the NICE costing analyst for the guideline. Some information about epidemiology or health service use might be better obtained from national statistics or databases than from studies in the literature.

As outlined in the updated NICE [Guide to the methods of technology appraisal](#) (publication expected spring 2013), the public list prices for technologies (for example, pharmaceuticals or medical devices) should be used in the reference-case analysis. When there are nationally available price reductions, for example for drugs procured for use in secondary care through contracts negotiated by the NHS Commercial Medicines Unit, the reduced price should be used in the reference-case analysis to best reflect the price relevant to the NHS. The Commercial Medicines Unit publishes information on the prices paid for some generic drugs by NHS trusts through its [Electronic Market Information Tool \(eMIT\)](#), focusing on drugs in the 'National Generics Programme Framework' for England. Analyses based on price reductions for the NHS will be considered only when the reduced prices are transparent and can be consistently available across the NHS, and if the period for which the specified price is available is guaranteed. When a reduced price is available through a patient access scheme that has been agreed with the Department of Health, the analyses should include the costs associated with the scheme. The health economist from the NCC is also encouraged to discuss the analyses with the appraisals team in the Centre for Health Technology Evaluation at NICE. For drugs that are predominantly prescribed in primary care, prices should be based on the Drug Tariff. In the absence of a published list price and a price agreed by a national institution (as may be the case for some devices), an alternative price may be considered, provided that it is nationally and publicly available.

HRQoL data are often needed for economic models. Many of the HRQoL search filters available are highly sensitive and so, although they identify relevant literature, they also detect a large amount of irrelevant literature. An initial broad HRQoL literature search may be a good option, but the amount of information identified may be unmanageable (depending on the key clinical issue being addressed). It may be more appropriate and manageable to incorporate a HRQoL search filter when executing additional searches for key clinical issues of high economic priority. The provision of HRQoL data should be guided by the health economist at an early stage in the guideline development process so that the information specialist can adopt an appropriate strategy. Two resources for identifying useful sources of utility data for economic modelling are the database of

preference weights on the [CEA \(Cost-Effectiveness Analysis\) Registry website](#) and the NICE Decision Support Unit technical support document [The identification, review and synthesis of health state utility values from the literature](#).

7.3 Economic evidence and guideline recommendations

For an economic analysis to be useful, it must inform the guideline recommendations. Cost effectiveness and clinical effectiveness should be discussed in parallel when formulating recommendations.

If there is strong evidence that one clinical strategy 'dominates' the alternatives (that is, it is both more effective and less costly), clearly this strategy should be recommended for appropriate patients. However, if, as is often the case, one strategy is more effective but also more costly, then the magnitude of the ICER should be considered. For example, the cost per QALY gained is calculated as the difference in mean cost divided by the difference in mean QALYs for one strategy compared with the next most effective alternative strategy.

If one intervention appears to be more effective than another, the GDG will have to decide whether the increase in cost associated with the increase in effectiveness represents reasonable 'value for money'. In doing so, it should make reference to the principles outlined in NICE's report [Social value judgements: principles for the development of NICE guidance](#). This states the following:

'NICE has never identified an ICER above which interventions should not be recommended and below which they should. However, in general, interventions with an ICER of less than £20,000 per QALY gained are considered to be cost effective. Where advisory bodies consider that particular interventions with an ICER of less than £20,000 per QALY gained should not be provided by the NHS they should provide explicit reasons (for example that there are significant limitations to the generalisability of the evidence for effectiveness). Above a most plausible ICER of £20,000 per QALY gained, judgements about the acceptability of the intervention as an effective use of NHS resources will specifically take account of the following factors.

- The degree of certainty around the ICER. In particular, advisory bodies will be more cautious about recommending a technology when they are less certain about the ICERs presented in the cost-effectiveness analysis.
- The presence of strong reasons indicating that the assessment of the change in the quality of life is inadequately captured, and may therefore misrepresent, the health gain.
- When the intervention is an innovation that adds demonstrable and distinct substantial benefits that may not have been adequately captured in the measurement of health gain.

As the ICER of an intervention increases in the £20,000 to £30,000 range, an advisory body's judgement about its acceptability as an effective use of NHS resources should make explicit reference to the relevant factors considered above. Above a most plausible ICER of £30,000 per QALY gained, advisory bodies will need to make an increasingly stronger case for supporting the intervention as an effective use of NHS resources with respect to the factors considered above.'

The [Guide to the methods of technology appraisal](#) outlines additional considerations that GDGs should take into account when developing recommendations. These include when to conduct a sensitivity analysis on the discount rate, and special considerations when examining a 'life-extending treatment at the end of life'.

The GDG's interpretations and discussions should be clearly presented in the 'Evidence to recommendations' sections of the full guideline. This should include a discussion of potential sources of bias and uncertainty. It should also include the results of sensitivity analyses in the consideration of uncertainty, as well as any additional considerations that are thought to be relevant.

7.3.1 In the absence of cost-effectiveness evidence

When no relevant published studies are found, and a new economic analysis is not prioritised, the GDG should make a qualitative judgement about cost effectiveness by considering potential differences in resource use and cost between the options alongside the results of the review of evidence of clinical effectiveness. The health economist should help the GDG to come to conclusions on the potential cost effectiveness of the interventions or services under consideration. This may include presenting information about unit costs and economic principles.

7.4 Further reading

Anderson R (2010) Systematic reviews of economic evaluations: utility or futility? *Health Economics* 19: 350–64

Briggs A, Claxton K, Sculpher K (2006) *Decision modelling for health economic evaluation*. Oxford: Oxford University Press

Centre for Reviews and Dissemination (2007) [NHS economic evaluation database handbook](#) [online].

Cooper NJ, Sutton AJ, Ades AE et al. (2007) Use of evidence in economic decision models: practical issues and methodological challenges. *Health Economics* 16: 1277–86

Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ. *British Medical Journal* 313: 275–83

Drummond MF, McGuire A (2001) *Economic evaluation in health care: merging theory with practice*. Oxford: Oxford University Press

Drummond MF, Sculpher MJ, Torrance GW et al. (2005) *Methods for the economic evaluation of health care programmes*, 3rd edition. Oxford: Oxford University Press

Eccles M, Mason J (2001) How to develop cost-conscious guidelines. *Health Technology Assessment* 5: 1–69

Jackson CH, Bojke L, Thompson G et al. (2011) A framework for addressing structural uncertainty in decision models. *Medical Decision Making* 31: 662–74

Krahn MD, Naglie G, Naimark D et al. (1997) Primer on medical decision analysis: Part 4 – Analyzing the model and interpreting the results. *Medical Decision Making* 17: 142–51

NICE Decision Support Unit (2011) Technical support document series [online]

Philips Z, Ginnelly L, Sculpher M et al. (2004) Review of good practice in decision-analytic modelling in health technology assessment. *Health Technology Assessment* 8: 1–158

Raftery J, editor (1999–2001) Economics notes series. *British Medical Journal* [online]

^[1] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

^[12] Department of Health definition: PSS – personal social services describes care services for vulnerable people, including those with special needs because of old age or physical disability and children in need of care and protection. Examples are residential care homes for the elderly, home help and home care services, and social workers who provide help and support for a wide range of people.

8 Linking clinical guidelines to other NICE guidance

As the amount of NICE guidance increases, there will be more topics that span the different work programmes at NICE.

- Clinical guidelines focus on the management of a particular disease or condition.
- Technology appraisal guidance focuses on the clinical and cost effectiveness of one or more technologies, such as new drugs, surgical procedures and medical devices.
- Interventional procedures (IP) guidance covers the safety and efficacy of interventional procedures used for diagnosis or treatment.
- Public health guidance deals with promoting good health and preventing ill health.
- Medical technologies guidance covers the efficacy and cost effectiveness of new or innovative medical technologies.
- Diagnostics guidance covers the efficacy and cost effectiveness of new diagnostic technologies.
- NICE has been asked to develop social care guidance, but at the time this manual was updated, the specific details of this programme were not known. Therefore details about links to social care guidance are not provided here.

The Centre for Health Technology Evaluation (CHTE) at NICE develops technology appraisal, interventional procedures, medical technologies and diagnostics guidance. Public health guidance is the responsibility of the Centre for Public Health Excellence (CPHE). Details of the development processes and methods for other programmes can be found on the [NICE website](#).

The scoping stage of clinical guideline development should identify topics from other programmes that are relevant to the guideline being developed (see [chapter 2](#)).

This chapter deals with the approaches to be taken when:

- guidance from another programme has already been published and requires incorporation into a clinical guideline
- NICE asks a Guideline Development Group (GDG) to update an existing piece of guidance in a clinical guideline
- a relevant piece of guidance from another programme is being developed concurrently.

8.1 Technology appraisals

NICE publishes two types of technology appraisals:

- The single technology appraisal (STA) process is designed specifically for the rapid appraisal of a single technology with a single indication. Most of the relevant evidence for an STA is supplied by the manufacturer or sponsor of the technology. NICE commissions an [independent academic centre](#) to technically review the evidence submission and prepare an Evidence Review Group (ERG) report.
- The multiple technology appraisal (MTA) process considers the clinical and cost effectiveness of one or more technologies. Evidence for an MTA is derived from a number of sources, including an assessment carried out by an independent academic or other research group (the Assessment Group), evidence provided by the consultees to the appraisal process (including manufacturers), and the participation of selected clinical specialists and patient experts.

[Process guides for technology appraisals](#) are available on the NICE website.

8.1.1 Significant new medicines

A first assessment of a significant new medicine or a significant licence extension for an existing medicine is usually carried out as a technology appraisal. It can be carried out in a clinical guideline only when this has been agreed by both the Department of Health and the manufacturer. If a significant new medicine is identified during the scoping of a guideline, the National Collaborating Centre (NCC) or NICE Internal Clinical Guidelines Programme^[13] should alert the Guidelines Commissioning Manager (GCM), who will liaise with the relevant work programmes within NICE.

8.1.2 A previously published technology appraisal

When the topic of a newly commissioned clinical guideline covers an area for which there are one or more previously published technology appraisals, there are four possible approaches:

- The technology appraisal guidance is incorporated verbatim into the clinical guideline.
- The clinical guideline cross-refers to the technology appraisal guidance.
- The technology appraisal guidance is updated through the relevant technology appraisal process.
- The technology appraisal guidance is updated through the clinical guideline development process (see section 8.1.3).

When technology appraisal guidance is incorporated into a clinical guideline, the technology appraisal guidance remains in existence alongside the guideline. The funding direction (which states that the NHS provides funding and resources for drugs and treatments that have been recommended by NICE technology appraisals, normally within 3 months from the date that NICE publishes the guidance) remains in place for the recommendations in the technology appraisal guidance.

Before a decision to incorporate or update a technology appraisal is made, the appraisals team needs to prepare a technology appraisal review proposal. There are two reasons for this:

- new evidence may indicate that the appraisal should be updated as a technology appraisal rather than within a clinical guideline (see also section 8.1.3) **or**
- if technology appraisal guidance is incorporated into a clinical guideline, the technology appraisal will usually be placed on the static list (see the [technology appraisal process guides](#)).

Developing a review proposal involves consulting with the relevant stakeholders for the technology appraisal. It is essential that relevant technology appraisals that are considered suitable for incorporation into a clinical guideline are identified as early as possible in guideline development, preferably in the early stages of scoping (see [chapter 2](#)).

When recommendations from a published technology appraisal are incorporated into a

clinical guideline, they should usually be reproduced unchanged. Under exceptional circumstances where suggested changes to recommendation wording are proposed (for example, if the appraisal recommendation covers both primary and secondary care, but the guideline recommendation is concerned with secondary care only), the proposed change to the wording must be discussed with the NICE appraisals team and agreed by NICE's Guidance Executive. This should be done on a case-by-case basis.

8.1.2.1 Guideline question covering a different population or drug indication compared with published technology appraisal guidance

Sometimes a clinical guideline may address a question that relates to a drug for which there is technology appraisal guidance, but covers different population groups or drug indications. In these cases the GDG should apply methodologies comparable with those used in the technology appraisal for assessing the evidence of clinical and cost effectiveness. The final recommendations in the guideline for these groups or indications may be different from the technology appraisal recommendations if there is evidence of differing safety, clinical effectiveness or cost effectiveness for those populations or drug indications.

8.1.3 Updating technology appraisal guidance in a clinical guideline

Planning the update of a technology appraisal is described in the technology appraisal process guides. The NCC becomes a commentator for the appraisal review proposal, which allows it to have formal input into the process of updating the appraisal.

It is anticipated that technology appraisal guidance will only rarely be updated in a clinical guideline. A technology appraisal is likely to be suitable for updating in the context of a clinical guideline only if all of the following conditions are met (see [NICE's policy on updating technology appraisals in clinical guidelines](#)).

- The technology falls within the scope of the guideline.
- There is no proposed change to an existing patient access scheme or flexible pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement.

- There is no new evidence that is likely to lead to significant changes in the clinical or cost effectiveness of a technology.
- The technology is well established and embedded in the NHS. Evidence that a technology is not well established or embedded may include the following:
 - spending on the technology for the indication that was the subject of the appraisal continues to rise
 - there is evidence of unjustified variation across the country in access to the technology
 - there is plausible and verifiable information to suggest that the availability of the technology is likely to be reduced if the funding direction were removed
 - the technology is excluded from the payment by results (PbR) tariff.
- Stakeholder opinion, expressed in response to consultation on a review proposal for the technology appraisal, is broadly supportive of the proposal.

The final decision on whether an existing technology appraisal is to be updated in a clinical guideline will be taken by NICE's Guidance Executive, before the workplan for the guideline is signed off.

When technology appraisal guidance is updated and changed in a clinical guideline, the original appraisal will be withdrawn when the guideline is published. The funding direction associated with the technology appraisal will no longer apply. Similarly, any existing patient access scheme that was agreed as part of the technology appraisal for the particular indication will no longer apply (unless there is a commitment by the manufacturer to continue the scheme).

Early planning is essential to identify how the NCC will undertake any updates of technology appraisals within a clinical guideline. The steps that should be taken are described below.

8.1.3.1 Call for evidence

When planning the clinical guideline, the NCC should consider whether any data exist that are not in the public domain but are likely to be of use in updating the technology appraisal. If so, the NCC should issue a call for evidence from stakeholders, using the procedures described in [section 5.10](#).

8.1.3.2 Economic modelling

If there is significant new clinical evidence or a change in costs since the original technology appraisal guidance was published, the NCC will need to conduct an economic evaluation to determine whether a change in the guidance is appropriate. In exceptional circumstances, it may not be apparent that an economic analysis is necessary until the clinical evidence has been reviewed and discussed by the GDG. Nevertheless, the NCC health economist should start planning for this work at an early stage. The intended approach to cost-effectiveness analysis for technology appraisal updates should be included in the economic plan and discussed with the GDG and NICE (see [section 7.1](#)).

Assessments of cost effectiveness for updates of technology appraisals in clinical guidelines should follow the principles described in [section 7.2](#). The approach should be similar to that used in the original technology appraisal (as described in the 'Evidence and interpretation' section of the appraisal guidance document for MTAs or the 'Manufacturer's submission' section for STAs). Any differences in approach must be justified on the basis of changes in the evidence base or the decision context (such as a broader range of comparators in the guideline).

The NCC may sometimes consider that an assessment of cost effectiveness can best be done by updating an existing model (for example, the model provided by the Assessment Group for the original technology appraisal or a model submitted by a manufacturer or sponsor). If so, this should be discussed with the Centre for Clinical Practice (CCP) at NICE during development of the economic plan.

8.1.4 Concurrent development of a clinical guideline and a technology appraisal

When a technology appraisal is being developed at the same time as a related clinical guideline, there are three important aspects to consider, in order to ensure that the final recommendations in the guideline and the appraisal are complementary and consistent:

- timing
- exchange of information
- publication of recommendations.

8.1.4.1 Timing

The development of related clinical guidelines and technology appraisals will normally be coordinated so that the published appraisal recommendations can be incorporated into the consultation draft of the guideline. Details of the timelines should be agreed between the NCC and the guidelines and appraisals teams at NICE.

8.1.4.2 Exchange of information

Information exchange is mutually beneficial to the Appraisal Committee (which is responsible for formulating technology appraisal guidance) and the GDG, and the GDG needs to be aware of progress in related appraisal topics. The following mechanisms have therefore been put in place.

- A member of the NICE appraisals team will be invited to an early GDG meeting to outline the relevant technology appraisal process (MTA or STA). Differences between the appraisal and clinical guideline development processes, the opportunities for input from the GDG to the appraisal process and the status of the ongoing relevant appraisals will be discussed.
- A member of the NICE appraisals team will advise the GDG on the integration of the appraisal into the guideline, and will be invited to attend GDG meetings as appropriate.
- The GDG will act as a commentator for the relevant appraisal (see [technology appraisal process guides](#)).
- The GDG Chair (or a delegate) and the NCC Director (or a delegate) will act as links with the technical lead for the appraisal. They will attend the Appraisal Committee meetings when relevant. GDG members attending NICE Appraisal Committee meetings should update their declaration of interests before each meeting. NICE will conduct a review of declarations of interests before selecting GDG representatives to attend Appraisal Committee meetings. Guidance for GDG members on attendance at NICE Appraisal Committee meetings is provided in [appendix A4](#).
- For MTAs, the NCC health economist for the clinical guideline and the Assessment Group for the technology appraisal should work together to ensure that the economic models for the guideline and the appraisal are consistent.

- For STAs, the health economist for the clinical guideline should familiarise themselves with the manufacturer's model and the critique of the model in the Evidence Review Group report.

8.1.4.3 Publication of recommendations

The GDG must not publish its own recommendations in a clinical guideline in areas already covered in the scope of any relevant ongoing technology appraisal. This also applies to areas covered in existing published technology appraisals unless NICE has agreed that the technology appraisal guidance will be updated in the clinical guideline (see section 8.1.3).

If technology appraisal recommendations have not been finalised at the time of guideline consultation, the guideline should cross-refer to the appraisal consultation document.

8.2 Interventional procedures

8.2.1 Published interventional procedures guidance

IP guidance differs from other NICE guidance in that it addresses the safety and efficacy of interventions, not their clinical and cost effectiveness. (For more details see the [Interventional procedures programme process guide](#).)

Any published IP guidance that is relevant to the guideline should be identified during the scoping phase of a clinical guideline. There are two approaches, depending on whether the recommendation in the IP guidance is for 'normal' or 'special' arrangements for clinical governance, consent and audit or research. As clinical guidelines focus on placing established treatments in the care pathway, they will generally only include IP guidance that recommends 'normal' arrangements.

8.2.1.1 Procedures with recommendations for 'normal' arrangements

There are two possible scenarios, depending on whether the IP guidance merits a review question.

Review question not justified

If the scoping group for a guideline decides that IP guidance for which 'normal'

arrangements are recommended is relevant to its clinical guideline but will not justify a review question, the IP guidance will simply be referred to in the 'Related NICE guidance' section of the guideline. The NCC will not search for new evidence on procedures that are not incorporated into a review question. However, if in the course of their search for evidence the NCC finds new relevant evidence on that procedure, they will inform the IP Programme at NICE.

Review question justified

If the scoping group for a guideline considers that a procedure published under 'normal' arrangements for IP guidance is likely to justify a review question, this will be highlighted in the draft scope for the guideline. During consultation on the scope, the IP programme will consult its specialist advisers for the procedure to ascertain whether it is emerging as standard NHS practice. CCP and the IP programme will then draft a joint paper for NICE Guidance Executive describing the intention to address the clinical and cost effectiveness of the intervention in the guideline, the justification for this decision and what is currently known about the availability of new evidence. At this stage any indications within the IP guidance that are outside the scope of the guideline will also be highlighted to Guidance Executive.

Assuming that the intervention is included in the final scope, the NCC will consider the clinical and cost effectiveness of the procedure using the usual methods for clinical guidelines (see chapters [6](#) and [7](#)).

When the GDG has had the opportunity to review the evidence and consider its recommendation(s), CCP and the IP programme will inform Guidance Executive of the implications of the draft guideline recommendations for the IP guidance.

Normally the IP guidance will remain active. This is because the IP guidance relates to the efficacy and safety of the procedure, and so the clinical guideline and the IP guidance address different questions. Thus IP guidance remains current even if recommendations on efficacy and safety are supplemented by a clinical guideline recommendation on the clinical and cost effectiveness of a procedure for one or some indications. IP guidance may also contain more detailed information about the procedure that may be of value to patients and clinicians. Importantly, the IP guidance may also specify conditions for use of the procedure; for example that the surgeon should have training, or that the procedure should be carried out within the context of a multidisciplinary team. The clinical guideline will include a cross-reference to the IP guidance, and a note referring to the clinical

guideline will be inserted on the NICE webpage for the IP guidance.

In circumstances when there is considerable uncertainty about the clinical or cost effectiveness of a procedure, the GDG may decide to make an 'only in research' recommendation relating to the generation of additional evidence on relative clinical or cost effectiveness of the procedure (see [section 9.2](#)). The decision to make this type of recommendation for a procedure where IP guidance has been published under 'normal' arrangements will be taken by the GDG in consultation with NICE. This decision will be made on a case-by-case basis, and will require the CCP and IP teams to present an agreed paper to NICE Guidance Executive.

8.2.1.2 Procedures with recommendations for 'special' arrangements

If, in the opinion of the GDG, a procedure with recommendations for 'special' arrangements has become part of mainstream practice and falls into the subject area of a review question, the GDG will formally notify the procedure to the IP Programme to allow for potential review of the IP guidance. If on re-assessment the procedure's status is changed to 'normal' arrangements, the NCC will consider its clinical and cost effectiveness (see [section 8.2.1.1](#)). If the procedure retains its 'special' arrangements status (because of concerns about its safety, or because the long-term efficacy is unknown and important), the IP guidance should be listed in the 'Related NICE guidance' section of the clinical guideline.

8.2.1.3 IP guidance published with other recommendations

Sometimes IP guidance will recommend that a procedure should only be carried out in research, or that it should not be used. These recommendations are made if the IP Advisory Committee considers the evidence to be either insufficient or indicative that the intervention is unsafe and/or not effective, and so it is unable to recommend even conditional use. A recommendation not to use a procedure will be made if there is no evidence of efficacy and/or safety, or evidence of a lack of efficacy and/or safety. A 'research only' recommendation will be made if the evidence on the procedure shows that there are important uncertainties. The evidence base for such procedures usually reflects the fact that they are not established procedures. As such, they would not normally form part of a review question in a clinical guideline.

8.2.2 Concurrent development of a clinical guideline and IP

guidance

The NCC will check the IP guidance publication list for both published and 'in development' guidance during the guideline development phase. If a clinical guideline is already in development when a relevant notification is received, the IP Programme will pass the finalised scope(s) for the relevant procedure(s) to the CCP at NICE. This will allow appropriate planning and cross-referencing between the two programmes.

If IP guidance in development has not been finalised at the time of the guideline consultation, the IP consultation document is listed in the 'Related NICE guidance' section of the guideline.

8.2.3 New IP referral

When a newly notified procedure has been scoped and it has been agreed that it will be assessed by the IP Programme, and a clinical guideline is already being developed in this area, the IP Programme team will inform the NCC and the NICE GCM that the notified procedure is relevant to the guideline, but the procedure will not form part of the clinical guideline.

8.3 Public health guidance

NICE public health guidance aims to reduce the risk of developing a disease or condition, and to promote a healthy lifestyle.

Where NICE has published a clinical guideline or public health guidance and a new piece of work is commissioned in a related area, careful thought needs to be given to avoiding unnecessary duplication. The detailed processes for doing this are covered in the update to [The NICE public health guidance development process](#) (third edition September 2012).

The Department of Health or the NHS Commissioning Board may ask NICE to develop new combined guidance on both the prevention and clinical management of a condition. A referral for combined guidance is managed jointly by the CCP and the Centre for Public Health Excellence (CPHE). Examples include the prevention and management of obesity, and the prevention, early identification and management of alcohol use disorders in adults and adolescents.

8.3.1 Coordination

Two separate groups or committees at NICE are involved in developing the guidance:

- The Public Health Advisory Committee (PHAC) for the prevention and/or early identification of a condition – the CPHE manages the Committee.
- The GDG for clinical management – the NCC manages the GDG and reports to the GCM in the CCP.

On occasion it may be appropriate to form one joint development group, for example for updating combined guidance.

A joint steering group is established from the outset to coordinate the work and to monitor progress. The group is likely to include the following people:

- CPHE Associate Director, lead analyst and project manager
- NCC Director and project manager
- CCP GCM
- PHAC Chair
- GDG Chair(s)
- a representative of the Patient and Public Involvement Programme (PPIP) at NICE.

The steering group meets at the beginning of the process and may meet every 6 months during guidance development to review progress. One of the key tasks is to decide whether the prevention and management aspects will be published as an integrated piece of guidance or as two separate pieces of guidance (public health guidance and a clinical guideline).

8.3.2 Scoping

When the remit is received from the Department of Health or the NHS Commissioning Board, the steering group identifies key areas that will be covered in the scopes, and outlines areas of responsibility. Some issues may need to be discussed jointly by the two development groups (see section 8.3.3).

It is desirable to appoint a joint Chair for the two development groups. The Chair should have a good understanding of both public health and clinical issues. If it is not possible to appoint a joint Chair, the steering group is responsible for communication between the two groups.

Two scopes are developed: one on prevention and/or early identification, and one on clinical management. The draft scopes are consulted on at the same time and, if possible, a joint stakeholder scoping workshop is arranged. The list of stakeholders should normally be merged. The final scopes are agreed by the steering group, and should clearly define the issues that will be addressed under prevention and those that will be addressed under clinical management. All prioritised topics must be covered in either the prevention scope or the clinical management scope. Stakeholder comments are responded to separately by the CPHE and the NCC scoping groups, but the steering group meets to agree consistency between responses.

8.3.3 Group members and the development process

Early in the process (preferably during scoping), the steering group ratifies the decisions made about membership of the GDG (the PHACs are standing advisory committees) and makes a final decision on whether there should be overlapping membership. The development groups work to a joint timetable, but follow the processes and methods set out by the CCP and CPHE respectively. Although the PHAC and GDG meetings are held separately, it is helpful if there is at least one joint meeting during development to ensure consistency and to avoid overlaps or gaps.

8.3.4 Consultation, the editorial process and publication

The draft clinical guideline and public health guidance are normally consulted on at the same time, using the usual consultation processes of the CCP and CPHE respectively. Stakeholder comments are categorised as relating to prevention or clinical management, or as joint comments. Responses are drafted by each project management team in the CPHE and the NCC, and discussed by the joint steering group before being finalised by the two groups.

It is important that there is early discussion with the steering group and with the editorial and communications teams at NICE about how the final guidance is presented. The editorial team should agree the proposed format with the two development groups early in the process, and should also agree the proposed recommendations after editing at a joint

meeting with the two groups if possible. The two parts of the guidance are published at the same time as a pair.

8.4 Other NICE guidance

Two further programmes have been developed at NICE, within the CHTE. These are the Medical Technologies Evaluation Programme and the Diagnostics Assessment Programme. These programmes develop guidance on innovative medical devices and diagnostics, normally at an early stage in their use in the NHS.

The interactions between these new guidance programmes and other NICE guidance programmes are at a relatively early stage. NICE has implemented systems for liaison across programmes to support the efficient development of consistent, implementable guidance.

8.4.1 Medical technologies guidance

Medical technologies guidance considers a single medical device or diagnostic technology that provides at least equivalent clinical outcomes for equivalent or reduced cost, compared with technologies in current use.

The [Medical Technologies Evaluation Programme \(MTEP\) process and methods guides](#) are available on the NICE website.

8.4.1.1 Published medical technologies guidance

If the guideline scoping group identifies a key clinical issue for the guideline where there is published medical technologies guidance, the CCP will discuss with the MTEP team how this will be approached within the guideline during consultation on the guideline scope. The CCP and the MTEP will write a joint paper for NICE Guidance Executive describing the proposed approach.

Assuming that the topic remains in the final scope, the CCP will brief the MTEP of the GDG's views as soon as the draft recommendations are available. The CCP and the MTEP will then decide on the relationship between the recommendations for the different programmes, consulting Guidance Executive if appropriate.

8.4.1.2 Concurrent development of a clinical guideline and medical technologies guidance

The NCC will check the medical technologies guidance publication list for both published and 'in development' guidance during the guideline development phase. If a clinical guideline is already in development when a relevant notification is received, the MTEP will pass the finalised scope(s) for the relevant procedure(s) to the CCP at NICE. This will allow appropriate planning and cross-referencing between the two programmes.

If medical technologies guidance in development has not been finalised at the time of the guideline consultation, the medical technologies consultation document should be listed in the 'Related NICE guidance' section of the guideline.

8.4.1.3 New MTEP referral

When a newly notified technology has been scoped and it has been agreed that it will be assessed by the MTEP, and a clinical guideline is already being developed in this area, the MTEP team will inform the NCC and the NICE GCM that the notified procedure is relevant to the guideline, but the technology will not form part of the clinical guideline.

8.4.2 Diagnostics guidance

Diagnostics guidance helps to ensure that the NHS is able to adopt clinically and cost-effective diagnostic technologies rapidly and consistently.

The programme assesses all types of measurements and tests that are used to evaluate a patient's condition, such as physiological measurements, laboratory tests, pathology tests, imaging tests and endoscopy. Diagnostic technologies may be used for various purposes, such as diagnosis, clinical monitoring, screening, treatment triage, assessing stages of disease progression and risk stratification.

Diagnostics guidance considers one or more diagnostic technologies that are claimed to provide improved clinical outcomes at additional cost, compared with diagnostics in current use. The aim of the evaluation is to consider whether the products under consideration are cost-effective.

The [NICE Diagnostic Assessment Programme manual](#) is available on the NICE website.

8.4.2.1 Published diagnostics guidance

If the guideline scoping group identifies a key clinical issue for the guideline where there is published diagnostics guidance, the CCP will discuss with the Diagnostic Assessment Programme (DAP) team how this will be approached within the guideline during consultation on the guideline scope. The CCP and the DAP will write a joint paper for NICE Guidance Executive describing the proposed approach.

Assuming that the topic remains in the final scope, the CCP will brief the DAP of the GDG's views as soon as the draft recommendations are available. The CCP and the DAP will then decide on the relationship between the recommendations for the different programmes, consulting Guidance Executive if appropriate.

8.4.2.2 Concurrent development of a clinical guideline and diagnostics guidance

The NCC will check the diagnostics guidance publication list for both published and 'in development' guidance during the guideline development phase. If a clinical guideline is already in development when a relevant notification is received, the DAP will pass the finalised scope(s) for the relevant diagnostics to the CCP at NICE. This will allow appropriate planning and cross-referencing between the two programmes.

If diagnostics guidance in development has not been finalised at the time of the guideline consultation, the diagnostics consultation document should be listed in the 'Related NICE guidance' section of the guideline.

8.4.2.3 New DAP referral

When a newly notified diagnostic has been scoped and it has been agreed that it will be assessed by the DAP, and a clinical guideline is already being developed in this area, the DAP team will inform the NCC and the NICE GCM that the notified diagnostic is relevant to the guideline, but it will not form part of the clinical guideline.

^[13] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

9 Developing and wording guideline recommendations

Many users of clinical guidelines do not have time to read the full document, and may want to focus only on the recommendations. It is therefore vital that recommendations are clear, can be understood by people who have not read the full guideline, and are based on the best available evidence of clinical and cost effectiveness. This chapter addresses key areas in developing guideline recommendations:

- interpreting the evidence to make recommendations
- wording the recommendations
- prioritising recommendations for implementation
- formulating research recommendations.

These processes are at the heart of the work of the Guideline Development Group (GDG). However, they are not straightforward and it may not be easy for the GDG to reach agreement. Consensus techniques may need to be used within the GDG (see [section 3.5](#)).

9.1 Interpreting the evidence to make recommendations

The GDG must decide what the evidence means in the context of the review questions and economic questions posed, and decide what recommendations can usefully be made to healthcare and other professionals.

In the full guideline, the aim should be to show clearly how the GDG moved from the evidence to the recommendation. This is done in a section called 'evidence to recommendations' so that it can be easily identified. This section may also be a useful way to integrate the findings from several evidence reviews that are related to the same recommendation(s).

Underpinning this section is the concept of the 'strength' of a recommendation (Schünemann et al. 2003). This takes into account the quality of the evidence but is

conceptually different. Some recommendations are 'strong' in that the GDG believes that the vast majority of healthcare and other professionals and patients would choose a particular intervention if they considered the evidence in the same way that the GDG has. This is generally the case if the benefits clearly outweigh the harms for most people and the intervention is likely to be cost effective. However, there is often a closer balance between benefits and harms, and some patients would not choose an intervention whereas others would. This may happen, for example, if some patients are particularly averse to some side effect and others are not. In these circumstances the recommendation is generally weaker, although it may be possible to make stronger recommendations about specific groups of patients.

For all recommendations, a general principle of NICE clinical guidelines is that patients should be informed of their choices and be involved in decisions about their care. Patients may choose not to accept the advice to have the most cost-effective intervention, or they may opt for a treatment that has the same or lower long-term health and personal social service costs if, for example, they feel that its side effects are more tolerable. There might be little evidence of differences in cost effectiveness between drugs within a class, and the clinician and patient might choose between these drugs on the basis of side-effect profile. However, it is not usually possible to offer patients interventions that are above NICE's threshold for cost effectiveness (see [section 7.3](#)) because the opportunity cost of that course of action has been judged to be too great (see [section 7.1.1](#)).

The GRADE system (see [section 6.2.1.1](#)) allocates labels or symbols to represent the strength of a recommendation. NICE has chosen not to do this, but instead to reflect the concept of strength in the wording of the recommendation (see [section 9.3.3](#)). The GDG's view of the strength of a recommendation should be clear from its discussions, as reported in the full guideline.

The following points will need to be covered in the discussions and can also be used as a framework for reporting those discussions.

9.1.1 Relative value placed on the outcomes considered

Often more outcome data are available than are actually used in decision-making. It is therefore important to have explicit discussion of which outcomes are considered important for decision-making (including consideration of the perspective of the decision-makers) when developing review protocols (see [section 4.4](#)), and of what relative importance was given to them. This might be done informally (for example, 'death was

considered the most important outcome') or formally (for example, by the use of utility weights).

This discussion should be clearly separated from discussion of how this will play out when the evidence is reviewed, because there is a potential to introduce bias if outcomes are selected on the basis of the results. An example of this would be choosing only outcomes for which there were statistically significant results.

It may be important to note outcomes that were not considered to be important for decision-making, and why (such as surrogate outcomes if longer-term, more relevant outcomes are available). If the same set of outcomes is used for a number of review questions, it might be more efficient to record this information once and then refer back to it.

9.1.2 Trade-off between clinical benefits and harms

A key stage in moving from evidence to recommendations is weighing up the magnitude and importance of the benefits and harms of an intervention. This may be done qualitatively (for example, 'the evidence of a reduction in mortality outweighed a small increase in side effects'), or quantitatively using a decision model.

9.1.3 Trade-off between net health benefits and resource use

If there are net health benefits from an intervention, there should be an explanation of how the implications of resource use were considered in determining cost effectiveness. Again, this may be informal, or may be more formal and include the use of economic modelling. If there is no clear evidence of net health benefit, cost and resource use could be discussed here.

9.1.4 Quality of the evidence

There should be discussion of how the presence, likely magnitude and direction of potential biases and uncertainty in the clinical and economic evidence have influenced the recommendation, and why. This should reflect the judgement on the quality of the evidence as described in the GRADE profile and the NICE economic profile. Lower-quality evidence makes it more difficult to justify a strong recommendation in general, although there may be exceptions to this. For example, evidence on the frequency of adverse effects is often of low quality, but a strong recommendation might be made not to use a

particular drug thought to have teratogenic effects in women of child-bearing potential.

The discussion of uncertainty may include consideration of whether the uncertainty is sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation.

9.1.5 Other considerations

If the 'evidence to recommendations' section combines consideration of several possible interventions, it may include discussion of the position of an intervention within a pathway of care.

This is also the appropriate place to note how the GDG's responsibilities under equalities legislation and [NICE's equality scheme](#) have been discharged in reaching the recommendation(s). This covers inequalities related to age, disability, gender reassignment, marriage and civil partnership, race, religion or belief, sex and sexual orientation and socioeconomic status. The GDG will need to consider whether:

- the evidence review has addressed areas identified in the scope as needing specific attention with regard to equalities issues
- criteria for access to an intervention might be discriminatory, for example through membership of a particular group, or by using a test that might discriminate unlawfully
- people with disabilities might find it impossible or unreasonably difficult to receive an intervention
- guidance can be formulated so as to promote equalities, for example by making access more likely for certain groups, or by tailoring the intervention to specific groups.

Before the guideline is signed off, an equality impact assessment (EIA) form is completed by the National Collaborating Centre (NCC) or the NICE Internal Clinical Guidelines Programme^[14] and the GDG to demonstrate how equality issues have been identified and considered during development. The EIA form is signed by the NCC Director and GDG Chair, and countersigned by the Centre for Clinical Practice (CCP) lead for the guideline, before being posted on the NICE website. Further guidance on how to complete the EIA form is outlined in the document [Positively equal: a guide to addressing equality issues in developing NICE clinical guidelines](#).

It may be useful to briefly discuss the extent of change in practice that will be needed to implement a recommendation, and the possible need for carefully controlled implementation with, for example, training programmes or demonstration projects.

9.1.6 Challenges in formulating recommendations

There are many reasons why it can be difficult for a GDG to reach a decision about a recommendation. The evidence base is always imperfect, and so there is always a degree of judgement by the GDG. There may be very little, or no, good-quality evidence that directly addresses the review question the GDG has posed. In this situation, there are several options to consider:

- The GDG may wish to look at evidence that is likely to be more at risk of bias than the evidence they had hoped to find. For example, if the GDG had set out to collect only randomised trials for a question of effectiveness, but found none, they might consider looking for good-quality non-randomised studies. However, there is a risk that considerable time and effort is spent finding and reviewing studies that are likely to be biased and so are hard to interpret. This approach should be pursued only if there is reason to believe that it will help the GDG to formulate a recommendation.
- The GDG may wish to extrapolate from high-quality evidence in a related area, for example in a largely similar patient group or for a closely related intervention. The GDG will need to make its approach explicit, stating the basis it has used for extrapolating from the data and the assumptions that have been made. This will need to include consideration of the plausibility of the assumptions. This approach is unlikely to be helpful if the evidence is derived from a question that is too different from the review question, or if the evidence is not of the highest quality.

- The GDG may consider basing a recommendation on its view of current most cost-effective practice. Formal consensus techniques may be used to elicit opinions from the GDG, although NICE does not recommend a particular approach. Importantly, it is not usually appropriate to involve stakeholders from outside the GDG in this process, as they will be offering opinions on recommendations without having seen the evidence considered by the GDG; in addition, stakeholders will not have agreed to adhere to the principles underlying NICE's decisions on recommendations. This approach would also allow some stakeholders input to the decision-making process that other stakeholders will not have. GDGs should therefore be particularly cautious about using and interpreting the results of such exercises involving stakeholders outside the GDG, and should discuss any proposed use with NICE. The final decision on whether such work with external stakeholders is warranted will be made by NICE.

When formulating recommendations, there are likely to be instances when members of the GDG disagree about the content of the final guideline. Formal consensus methods can be used for agreeing the final recommendations (see [section 3.5](#)). Whatever the approach used, there should be a clear record of the proceedings and how areas of disagreement have been handled. This may be summarised in the full guideline.

9.2 'Only in research' recommendations

If evidence of effectiveness is either lacking or too weak for reasonable conclusions to be reached, the GDG may recommend that particular interventions are used within the NHS only in the context of research. Factors that will be considered before issuing such recommendations include the following:

- The intervention should have a reasonable prospect of providing benefits to patients in a cost-effective way.
- The necessary research can realistically be set up or is already planned, or patients are already being recruited.
- There is a real prospect that the research will inform future NICE guidance.

9.3 Wording the guideline recommendations

Writing the recommendations is one of the most important steps in developing a clinical guideline. Many people read only the recommendations, so the wording must be concise,

unambiguous and easy to translate into clinical practice. Each recommendation, or bullet point within a recommendation, should contain only one main action.

The wording of recommendations should be agreed by the GDG, and should:

- focus on the action that needs to be taken
- include what readers need to know
- reflect the strength of the recommendation
- emphasise the involvement of the patient (and/or their carers if needed) in decisions on treatment and care
- use plain English where possible and avoid vague language
- follow NICE's standard advice on recommendations about drugs, waiting times and ineffective interventions.

The rest of this section explains these points in more detail. The lead editor for the guideline from NICE can advise on the wording of recommendations.

9.3.1 Focus on the action

Recommendations should begin with what needs to be done. When writing recommendations, keep in mind a reader who is saying, 'What does this mean for me?'. Recommendations should be as specific as possible about the exact intervention being recommended and the group of people for whom it is recommended (see also section 9.3.2).

Use direct instructions because they are clearer and easier to follow. Most recommendations should be worded in this way. Assume you are talking to the healthcare professional who is working with the patient at the time.

Examples

- Record the person's blood pressure every 6 months.
- Ask people in high-risk groups whether they have symptoms.

- Carry out and record a focused baseline assessment for people with faecal incontinence to identify the contributory factors.

Exceptions

- Recommendations about service organisation, or if the audience is not the healthcare professional. For example: 'Care should be provided by a multidisciplinary team.'
- Recommendations that a specific type of healthcare professional should carry out an intervention. For example: 'An occupational therapist should assess the patient's needs.'
- Recommendations that use 'must' or 'must not' (see [section 9.3.3.1](#)).

Start with a verb describing what the reader should do, such as 'offer', 'measure', 'advise', 'discuss', 'ask about' (see sections 9.3.3 and 9.3.4 for advice on the choice of verb).

Examples

- Advise pregnant women to limit their intake of oily fish to two portions a week.
- Perform surgery within 48 hours of symptom onset.
- Offer relaxation techniques for managing pain, sleep problems and comorbid stress or anxiety.

Exceptions

- Sometimes it is clearer to start with details of the patient group or other details, particularly if recommending different actions for slightly different circumstances or to make the sentence structure simpler. For example: 'If surgery is an option, refer the patient to a specialist surgeon to discuss the risks and benefits.'

9.3.2 Include what readers need to know

Recommendations should contain enough information to be understood without reference to the evidence or other supporting material. But do not add unnecessary details, because recommendations are more likely to be followed if they are clear and concise.

- Define any specialised terminology that is used in the recommendations. Avoid using abbreviations unless your audience is likely to be more familiar with the abbreviation than with the term in full. If abbreviations are essential, define them at first mention and in a glossary.
- Define the target population if it is not obvious from the context. Often it is necessary to define the population only in the first of a group of recommendations, if it is clear that the subsequent recommendations in that section relate to the same population.
- Include cross-references to other recommendations in the guideline if necessary to avoid the need to repeat information such as treatment regimens.
- Do not include reasons justifying the recommendation unless this will increase the likelihood that it will be followed – for example, if it involves a change in usual practice or needs particular emphasis.
- Include only one main action in each recommendation or bullet point.

9.3.3 Reflect the strength of the recommendation

The description of the process of moving from evidence to recommendations in [section 9.1](#) indicates that some recommendations can be made with more certainty than others. This concept of the 'strength' of a recommendation should be reflected in the consistent wording of recommendations within and across clinical guidelines. There are three levels of certainty:

- recommendations for interventions that must (or must not) be used
- recommendations for interventions that should (or should not) be used
- recommendations for interventions that could be used.

The NICE guideline includes a standard section about how wording reflects the strength of recommendations.

9.3.3.1 Recommendations for interventions that must or must not be used

Recommendations that an intervention must or must not be used are usually included only if there is a legal duty to apply the recommendation, for example to comply with health and safety regulations. In these instances, give a reference to supporting documents.

These recommendations apply to all patients.

However, occasionally the consequences of not following a recommendation are so serious (for example, there is a high risk that the patient could die) that using 'must' (or 'must not') is justified. Discuss this with the Guidelines Commissioning Manager at NICE, and explain in the recommendation the reason for the use of 'must'.

If using 'must', word the recommendation in the passive voice ('an intervention must be used') because the distinction between 'should' and 'must' is lost when the recommendation is turned into a direct instruction.

Examples

- Ultra-rapid detoxification under general anaesthesia or heavy sedation (where the airway needs to be supported) must not be used. This is because of the risk of serious adverse events, including death.
- Gloves used for direct patient care:
 - must conform to current EU legislation (CE marked as medical gloves for single use) **and**
 - should be appropriate for the task.

9.3.3.2 Recommendations for interventions that should or should not be used – 'strong' recommendations

For recommendations on interventions that 'should' be used, the GDG is confident that, for the vast majority of people, the intervention (or interventions) will do more good than harm, and will be cost effective.

Use direct instructions for recommendations of this type where possible (see section 9.3.1), rather than using the word 'should'. Use verbs such as 'offer', 'refer', 'advise' and 'discuss'.

Example

- Offer bariatric surgery as a first-line option (instead of lifestyle interventions or drug treatment) to adults with a BMI of more than 50 kg/m².

Use similar forms of words (for example, 'Do not offer...') for recommendations on interventions that should not be used because the GDG is confident that they will not be of sufficient benefit for most patients.

Example

- Do not offer antibiotic prophylaxis against infective endocarditis to people at risk undergoing dental procedures.

If an intervention is strongly recommended but there are two or more options with similar cost effectiveness, and the choice will depend on the patient's values and preferences, a 'should' recommendation can be:

- combined with a 'could' recommendation (see section 9.3.3.3), for example by using wording such as 'Offer a choice of drug A or drug B' **or**
- followed by a 'could' recommendation, for example 'Offer drug treatment. Consider drug A or drug B.'

9.3.3.3 Recommendations for interventions that could be used

For recommendations on interventions that 'could' be used, the GDG is confident that the intervention will do more good than harm for most patients, and will be cost effective. However, other options may be similarly cost effective, or some patients may opt for a less effective but cheaper intervention. The choice of intervention, and whether to have the intervention at all, is therefore more likely to vary depending on a person's values and preferences, and so the healthcare professional should spend more time considering and discussing the options with the patient. It may be possible to make 'strong' recommendations for subgroups of people with different values and preferences. NICE's report [Social value judgements: principles for the development of NICE guidance](#) (2nd edition; 2008) states the following:

'Although NICE agrees that respect for autonomy and individual choice are important for the NHS and its users, this should not mean that NHS users as a whole are disadvantaged by guidance recommending interventions that are not clinically and/or cost-effective.'

Use direct instructions for recommendations of this type where possible (see section 9.3.1), rather than using the word 'could'.

Use 'consider' to indicate that the recommendation is less strong than a 'should' recommendation.

Examples

- Consider combination chemotherapy to treat patients with advanced breast cancer for whom a greater probability of response is important and who understand and are likely to tolerate the additional toxicity.
- Consider carbamazepine and oxcarbazepine but be aware of the risk of exacerbating myoclonic or absence seizures.

Do not use 'consider offering', because of potential confusion with the wording of strong recommendations. Also, it might be misinterpreted to mean that a healthcare professional may consider offering an intervention without discussing it with the patient.

To minimise confusion, only use 'consider' to indicate the strength of a recommendation. Avoid other possible uses of 'consider'. For example, if a particular clinical sign or symptom should make a healthcare professional think about a diagnosis, use 'be aware of the possible diagnosis...', 'explore a diagnosis of...' or similar, rather than 'consider a diagnosis of'. Use 'take other factors into account' or similar, instead of 'consider other factors'. 'Assess' and 'think about' are other possible alternatives to 'consider'.

9.3.4 Emphasise the patient's involvement

To emphasise the patient's role in decision-making and the need for them to consent to treatment, generally use verbs such as 'offer', 'consider' and 'discuss' in recommendations, rather than 'prescribe' or 'give'. As described above, 'consider' is used for recommendations on interventions that could be used, and implies that more discussion will be needed.

Use 'people' or 'patients' rather than 'individuals', 'cases' or 'subjects'. Where possible, use 'people' rather than 'patients' for people with mental health problems or chronic conditions. 'Service users' can be used for people with mental health problems if 'patients' is the only alternative. Do not use 'patients' in relation to healthy pregnant women.

9.3.4.1 Recommendations about patient-centred care

The NICE guideline includes a standard section on patient-centred care that covers

informed consent and taking into account the patient's individual needs. This section also cross-refers to NICE guidance on [patient experience in adult NHS services](#), which covers subjects such as treating the person as an individual, communication, information and shared decision-making. NICE has also produced guidance on [service user experience in adult mental health](#), which is cross-referred to in guidelines on mental health. The patient experience and service user experience guidance can be cross-referred to in recommendations, but specific recommendations should not be made on issues covered in that guidance unless there are particular reasons to do so that relate to the guideline topic. Examples include:

- if there are issues relating to provision of information to patients, or to patients' support needs, that are specific to the condition covered by the guideline
- if certain drugs are prescribed 'off-label' (see [section 9.3.6.3](#)) and more detailed forms of consent than usual are required from patients.

9.3.5 Use plain English

In general, follow the principles of effective writing as described in the 'Writing for NICE' booklet, which is available on the NICE webboard for NCCs.

Avoid vague words and phrases, such as 'may' and 'can', or general statements such as 'is recommended', 'is useful/helpful', 'is needed' and 'treatment options include'. Instead, use an active verb that tells readers what they should do, and indicates the strength of the recommendation.

Examples

- Instead of 'an intervention may be offered', say 'consider the intervention'.
- Instead of 'an intervention is recommended', say 'offer the intervention'.
- Instead of 'an intervention is helpful', say 'offer the intervention' or 'consider the intervention' (see [section 9.3.3](#)).

'Appropriate' is often redundant: for example 'give appropriate advice', because we would never recommend giving inappropriate advice.

9.3.6 Recommendations on drugs, including off-label use

Guideline developers should follow NICE's standard procedure when referring to drugs. This includes using standard wording when off-label use of drugs is recommended.

9.3.6.1 Use generic names

Give the recommended international non-proprietary name (rINN), as listed in the [British national formulary](#) (BNF). Usually, only the generic name is needed. Occasionally (for example, if referring to a specific preparation or device), the proprietary name may be given in parentheses at first mention. Do not give the manufacturer's name.

9.3.6.2 Do not give dosages

Readers are expected to refer to the summary of product characteristics (SPC) for details of dosages. Include dosage information only if there is evidence that a particular drug is often prescribed at the wrong dosage, or there is clear evidence about the effectiveness of different dose levels. If off-label use is being recommended and there is no relevant dosage information in the BNF, include details of the dosage regimen in the full guideline. SPCs can be found in the [Electronic Medicines Compendium](#).

9.3.6.3 Off-label use

Make it clear if the recommended use is outside the drug's licensed indication ('off label').

Recommendations are usually about the uses of drugs (often referred to as the licensed indications) for which the drug regulatory authority has granted a marketing authorisation, either in the UK or under the European centralised authorisation procedure. However, there are clinical situations when the use of a drug off-label may be judged by the prescriber to be in the best clinical interests of the patient. Off-label use may be recommended if the clinical need cannot be met by a licensed product and there is a sufficient evidence base and/or experience of using the drug to demonstrate its safety and efficacy to support this. Off-label prescribing is particularly common in pregnant women and in children and young people (see below), as these groups have often been excluded from clinical trials during drug development. When prescribing a drug off-label, the prescriber should follow relevant professional guidance (for example, the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#)) and make a clinical judgement, taking full responsibility for the decision for the patient under

his or her direct care. In addition, the patient (or those with authority to give consent on their behalf) should be made fully aware of these factors and provide informed consent, which should be documented by the prescriber.

A licensed drug is accompanied by an SPC, which describes the indications, cautions and contraindications for a drug based on an assessment of safety, quality and efficacy by the regulatory authority. The NCC and GDG should check recommended uses against the licensed indications listed in the SPC, and include a footnote if the drug does not have a UK marketing authorisation for the use being recommended. The footnote should make it clear that the drug is not licensed for the stated use.

This standard wording for the footnote captures the above points:

- At the time of publication ([month year]), [name of drug] did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

Additional information can be added as needed – for example, if off-label use is recommended and the drug is commonly used in UK clinical practice, a phrase such as 'Although this use is common in UK clinical practice' can be added. Other examples of footnote wording are shown in box 9.1. In cases where the SPC for a drug specifically mentions a caution or contraindication for its use but the GDG wishes to recommend the drug, this should be stated clearly in the recommendation or footnote. The evidence that the GDG has considered in reaching the conclusion that use in these circumstances can be justified should be clearly set out in the full guideline.

If a guideline includes recommendations for off-label use of drugs, the introduction to the NICE version should include standard wording (as in the NICE guideline template) about the responsibilities of the prescriber and the need to follow relevant professional guidance (for example, the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#)).

If there is no information on dosage regimens available in a recognised source (such as the BNF), the NCC should document dosage information in the full guideline and alert the NICE implementation team to ensure that this is disseminated to prescribers.

Prescribing drugs outside their licensed indication to children and young people

In certain circumstances drugs are prescribed to children and young people outside their licensed indications (off-label use) because the clinical need cannot be met by licensed drugs; for example, for an indication not specified in the marketing authorisation, or administration of a different dose. The Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) has issued a policy statement on the use of unlicensed drugs and the use of licensed drugs for unlicensed applications in children and young people. This states clearly that such use is necessary in paediatric practice and that doctors are legally allowed to prescribe drugs outside their licensed indications where there are no suitable alternatives and where use is justified by a responsible body of professional opinion (Joint Royal College of Paediatrics and Child Health/Neonatal and Paediatric Pharmacists Group Standing Committee on Medicines 2010).

Therefore, where there is no alternative treatment and only where there is a sufficient evidence base and/or experience of using the drug to demonstrate its safety and efficacy, a clinical guideline may recommend use of a drug outside its licensed indications for treating a child or young person. It is expected that prescribers will use the SPC to inform their prescribing decisions for individual patients, and they should be able to justify using a drug outside its licensed indications. Informed consent should be obtained from the child and/or their parent or guardian as appropriate and documented.

Footnotes for recommendations addressing off label-use of drugs in children and young people should follow the format described above and in box 9.1.

Box 9.1 Examples of footnotes to guideline recommendations about the off-label use of drugs

Where use is outside the licensed indication:

At the time of publication (August 2011), spironolactone did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

[Adapted from: [Hypertension: clinical management of primary hypertension in adults](#). NICE clinical guideline 127 (2011).]

Vaginal PGE₂ has been used in UK practice for many years in women with ruptured membranes. However, the SPCs (July 2008) advise that in this situation, vaginal PGE₂ is either not recommended or should be used with caution, depending on the preparation (gel, tablet or pessary). Healthcare professionals should refer to the individual SPCs before prescribing vaginal PGE₂ for women with ruptured membranes. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

[Adapted from: [Induction of labour](#). NICE clinical guideline 70 (2008).]

Where the SPC mentions a specific caution or contraindication:

Metformin is used in UK clinical practice in the management of diabetes in pregnancy and lactation. Clinical experience supports its effectiveness and safety but this is not currently reflected in the SPC. The SPC (March 2008) advises that when a patient plans to become pregnant and during pregnancy, diabetes should not be treated with metformin but insulin should be used to maintain blood glucose levels. For use of metformin in these situations, the prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Good practice in prescribing medicines – guidance for doctors](#) for further information.

[Adapted from: [Diabetes in pregnancy: management of diabetes and its complications from pre-conception to the postnatal period](#). NICE clinical guideline 63 (2008).]

9.3.7 Recommendations on waiting times and ineffective interventions

Guideline developers should follow NICE's standard advice for recommendations on waiting times. It is also acceptable to make recommendations that advise stopping the use of an ineffective intervention.

9.3.7.1 Waiting times and other policies set by other bodies

Avoid giving targets for waiting and referral times: refer to relevant targets set by the Department of Health or the Welsh Government, and where possible direct readers to the relevant document rather than including the target in the recommendation. This is because policy can change, making a guideline that includes such targets out of date. If no target exists, recommendations may include a maximum time if the GDG considers this to be essential.

Sometimes a recommendation will need to specify a waiting time, referral time or time of intervention because this relates to the safety and/or effectiveness of a clinical intervention. In this case, check that the recommendation does not conflict with relevant targets set by the Department of Health or the Welsh Government and ensure that the clinical reason for specifying the time is made clear.

9.3.7.2 Ineffective interventions

Recommend stopping ineffective interventions: state explicitly if particular treatments or activities should not be carried out or should be stopped (see box 9.2).

Box 9.2 Example of a recommendation about stopping ineffective practice

Do not routinely offer pharmacological or mechanical VTE prophylaxis to patients with cancer having oncological treatment who are ambulant.

[From: [Venous thromboembolism: reducing the risk](#). NICE clinical guideline 92 (2010).]

9.3.8 Using tables in recommendations

Do not use tables to summarise several actions in one recommendation. Such summaries

make it more difficult to link the recommended actions to the evidence summaries. A recommendation may include a small table to improve clarity; for example, to present information that should be shared with patients, or if the information is most easily understood when tabulated. An example is shown in box 9.3.

Box 9.3 Example of a table within a recommendation

Use predicted 6-month mortality to categorise the risk of future adverse cardiovascular events as follows:

Predicted 6-month mortality	Risk of future adverse cardiovascular events
1.5% or below	Lowest
>1.5 to 3.0%	Low
>3.0 to 6.0%	Intermediate
>6.0 to 9.0%	High
over 9.0%	Highest

[From: [Unstable angina and NSTEMI: the early management of unstable angina and non-ST-segment-elevation myocardial infarction](#). NICE clinical guideline 94 (2010).]

9.4 Prioritising recommendations

NICE's standard clinical guidelines can cover large clinical areas and, as a result, often contain a considerable number of recommendations relevant to the many review questions. The GDG will need to identify a subset of these recommendations as key priorities for implementation. These may be used to guide implementation activities (see [chapter 13](#)) and may be useful in the subsequent development of NICE quality standards. The number of recommendations prioritised in this way will vary depending on the guideline, but is normally between 5 and 10. There is no 'ranking' within this set of recommendations.

Key priorities for implementation are usually those that are likely to do at least one of the following:

- have a high impact on outcomes that are important to patients

- have a high impact on reducing variation in care and outcomes
- set challenging but achievable expectations of health services
- focus on key infrastructural and clinical requirements for high-quality care
- include actions that are measurable
- lead to more efficient use of NHS resources
- promote patient choice
- promote equality.

In addition, the GDG should attempt to identify recommendations that are particularly likely to benefit from support from NICE's implementation programme. Criteria overlap with those above, but include whether a recommendation:

- relates to an intervention that is not part of routine care
- requires changes in service delivery
- requires retraining of staff or the development of new skills and competencies
- highlights the need for practice to change
- affects and needs to be implemented across a number of agencies or settings (complex interactions)
- may be viewed as potentially contentious, or difficult to implement for other reasons.

There should be a clear record of which criteria were considered particularly important by the GDG for each prioritised recommendation. This should be reported in a short paragraph in the full guideline.

9.5 Formulating research recommendations

The GDG is likely to identify areas in which there are uncertainties or where robust evidence is lacking. NICE has published a [Research recommendations process and methods guide](#), which details the approach to be used across NICE's guidance-producing programmes to identify key uncertainties and associated research recommendations.

For standard clinical guidelines where there may be many hundreds of uncertainties, it will not be possible to document every uncertainty in detail. Similarly, although GDGs could write research recommendations for dealing with each uncertainty, this is not likely to be feasible. Therefore the GDG should select up to five key research recommendations for inclusion in the NICE version of the guideline; more research recommendations may be listed in the full guideline. Further information about how these should be derived can be found in the research recommendation process and methods guide.

9.6 Further reading

Brown P, Brunnhuber K, Chalkidou K et al. (2006) How to formulate research recommendations. *British Medical Journal* 333: 804–6

Claxton K, Sculpher MJ (2006) Using value of information analysis to prioritise health research: some lessons from recent UK experience. *Pharmacoeconomics* 24: 1055–68

Glasziou P, Del Mar C, Salisbury J (2003) Evidence-based medicine workbook. London: British Medical Journal Books

[Guideline Implementability Appraisal \(GLIA\)](#) [online]

Joint Royal College of Paediatrics and Child Health/Neonatal and Paediatric Pharmacists Group Standing Committee on Medicines (2010) [The use of unlicensed medicines or licensed medicines for unlicensed applications in paediatric practice](#) [online]

Lord SJ, Irwig L, Simes RJ (2006) When is measuring sensitivity and specificity sufficient to evaluate a diagnostic test, and when do we need randomized trials? *Annals of Internal Medicine* 144: 850–5

Sackett DL, Straus SE, Richardson WS (2000) Evidence-based medicine: how to practice and teach EBM, 2nd edition. Edinburgh: Churchill Livingstone

Schünemann HJ, Best D, Vist G et al. for the GRADE Working Group (2003) Letters, numbers, symbols and words: how to communicate grades of evidence and recommendations. *Canadian Medical Association Journal* 169: 677–80

Scottish Intercollegiate Guidelines Network (2002) SIGN 50. A guideline developer's handbook. Edinburgh: Scottish Intercollegiate Guidelines Network

^[14] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

10 Writing the clinical guideline and the role of the NICE editors

At the end of guideline development, four versions of the guideline are published. These are:

- the full guideline
- the NICE guideline
- the NICE pathway (all of the recommendations summarised in a web-based interactive pathway, with links to related guidance)
- 'Information for the public' (for patients, carers and the public).

The National Collaborating Centre (NCC) or the NICE Internal Clinical Guidelines Programme^[15], with the Guideline Development Group (GDG), writes the full guideline and the NICE guideline. The NICE editors are responsible for the NICE pathway and 'Information for the public', working with the NCC and GDG (see sections [10.3](#), [12.1](#) and [12.2](#) for more details).

This chapter describes the key principles for writing guidelines and what each version should include. The role of the NICE editors is also described.

10.1 Guideline structure

10.1.1 The full guideline

The full guideline contains all the recommendations, together with details of the methods used and the evidence underpinning the recommendations. It should specify the date of publication of the version of the guidelines manual that was used for developing the guideline.

The most recent version of the full guideline template and notes on how to use it are posted on the NICE webboard for NCCs. The content should include the following:

- A title page, funding, disclaimer and copyright information, and a contents page.
- A summary section containing:
 - GDG membership
 - a foreword (optional)
 - key priorities for implementation
 - an algorithm of the care pathway (optional)
 - a list of all the recommendations
 - a list of all the research recommendations
 - a list of the other versions of the guideline
 - if the guideline is an update, details of what has been updated (see [section 14.5](#)).
- A short overview section discussing the need for the guideline, its aim, scope and expected audience and a section on patient-centred care.
- A short methods section that cross-refers to the guidelines manual wherever possible and makes clear where and why there have been any deviations from the methods described in the manual.
- If relevant to the guideline, an epidemiology chapter consisting of a formal review of epidemiology data, including data from disease registries. It should not include general background or 'scene-setting'.

- Chapters dealing with the review questions and the evidence that led to the recommendations, each with the following content:
 - An introduction to the chapter.
 - The review question(s) in PICO (population, intervention, comparator[s] and outcome) format (see [chapter 4](#)) or a summary protocol.
 - A brief introduction to the review question if there is more than one question in the chapter (optional).
 - The clinical evidence review using summary GRADE profiles (see [section 6.2.1.1](#) and [appendix K](#)), including a summary of economic studies. If it is not possible to apply GRADE to the evidence, it may be presented in another suitable format; for example, narrative summaries.
 - The network meta-analysis (if this has been done for the review question).
 - The health economic evidence review and/or summary of the model.
 - Evidence statements (short text summaries of the evidence on clinical and cost effectiveness).
 - An 'evidence to recommendations' discussion: a structured summary of GDG discussions on the trade-off between benefits and harms, and consideration of economic evidence, in relation to policy, making clear the justification for the recommendation(s) (see [section 9.1](#)).
 - The recommendation(s).
 - The research recommendation(s) (if applicable).
- References.
- Glossary and abbreviations.

- Appendices, which should include:
 - a list of the contributors
 - declarations of interest
 - the scope
 - review questions and PICO tables
 - clinical and health economic review protocols
 - details of search strategies (see [chapter 5](#))
 - summary of numbers of studies identified
 - excluded studies
 - evidence tables (these may be presented on a CD-ROM) (see [appendix J](#))
 - forest plots
 - full GRADE profiles
 - full economic report
 - prioritisation of research recommendations (see [section 9.5](#))
 - if the guideline is an update, a table summarising the proposed changes to the original recommendations (see [section 14.5](#)).
 - anything else specific to the guideline, such as questionnaires, charts or examples of software.

10.1.2 The NICE guideline

The NICE guideline presents the recommendations without the evidence underpinning them. The length of the NICE guideline will therefore depend on the number of recommendations in the full guideline.

When preparing the NICE guideline, NCC staff should enter text directly into NICE's Word template. The most recent version of the NICE template and notes on how to use it are posted on the NICE webboard for NCCs.

The main information included in the NICE guideline is:

- a brief introduction explaining why the guideline is needed and the key issues it will address, and including information about off-label drug use if applicable
- a standard section on patient-centred care that covers general issues such as informed consent and taking into account the patient's individual needs
- a standard section about the strength of recommendations
- key priorities for implementation
- the recommendations
- brief details of the scope
- up to five research recommendations, and an explanation of why each of these is important (see [section 9.5](#))
- a list of related NICE guidance
- details of GDG membership
- if the guideline is an update, details of what has been updated (see [section 14.5](#)).

Background information is not usually included with the recommendations in the NICE guideline. Occasionally, a brief summary may be given if the information is essential for understanding or implementing the recommendations. Any background information that is included should be in the form of a short introductory paragraph to the relevant section, not as part of the recommendations themselves. The NICE guideline should not include descriptions of GDG commentary. NCCs should liaise with the NICE lead editor if they feel that background information needs to be included in the NICE guideline.

10.2 Style

Detailed instructions for writing guideline recommendations are given in [section 9.3](#).

When preparing the recommendations and the NICE guideline, NCC staff should follow the 'NICE style guide' and 'Writing for NICE' (both available from the NICE webboard for NCCs). It is advisable to also follow the 'NICE style guide' for the full guideline.

The full guideline and the NICE guideline should be written in a style that can be understood by non-specialist healthcare practitioners and by anyone who has a good knowledge of the guideline topic but is not a trained clinician (for example, a patient with the condition who has in-depth knowledge of the disease and treatment options). Plain English should be used, and unnecessary jargon avoided. The NICE editorial team can advise on this.

10.2.1 Bulleted lists

Bulleted lists are a useful way of:

- simplifying and clarifying a series of points
- dealing with repetition
- dealing with complex paragraph structures.

A bulleted list should be used rather than a numbered one, unless there is a good reason to use numbers. This is because a numbered list can imply a ranking or preference that may not be intended.

10.2.2 Tables and figures in the full guideline

Tables should be easy to understand and have clear, informative titles. Footnotes should be included only if they are essential for readers to understand the table. Comparisons within the table should compare like with like.

Tables should be numbered sequentially and should be cited in the text, but information in a table should not be repeated in the text. Figures should also be numbered sequentially.

Tables or figures from another source may be reproduced only if written permission has been obtained, usually from the publisher. It must be stated in the full guideline that such permission has been received.

10.2.3 Abbreviations

Abbreviations should be used sparingly, and in accordance with the 'NICE style guide'. If a term appears only a few times, it is usually better not to abbreviate it. However, if general readers will be more familiar with the abbreviation, or if the full term is long, the

abbreviation may be used throughout the guideline. All abbreviated terms should be defined at first use. The full guideline may be downloaded in sections, so abbreviations should be redefined at first use in each section. A list of abbreviations should be included in the full guideline.

10.2.4 Algorithm

The full version of the guideline may contain an algorithm that shows the care pathway and summarises the recommendations. The algorithm may form the basis of the NICE pathway (see section 10.3.2).

The algorithm should be uncluttered and follow a logical sequence. Arrows should mostly flow from top to bottom. Each decision should flow from the question that precedes it. It will usually be necessary to produce the algorithm in several sections – for example, covering diagnosis, initial management and long-term management.

If appropriate, recommendations may be summarised in other ways, such as in tables or boxes.

The algorithm should only summarise the recommendations; it must not include any information that is not in the recommendations.

10.3 The role of the NICE editors

One person from the NICE editorial team is designated as the lead editor for a particular clinical guideline, although other members of the team will also work on the guideline. The lead editor works with the NCC and members of the GDG before, during and after consultation (see also [chapter 12](#)), and has a formal responsibility for NICE's publications – that is, the NICE version of a clinical guideline, the NICE pathway and 'Information for the public'. The lead editor and other members of the editorial team work on these products to ensure that:

- they conform to NICE's requirements in terms of style and format
- the recommendations are unambiguous
- the information is clear and appropriate for the intended audience.

This section summarises the main work that the editors do.

10.3.1 Editing of guideline recommendations

The lead editor advises the NCC and GDG on recommendation wording during guideline development, and carries out detailed editing of the recommendations before the consultation draft of the guideline is submitted to NICE.

After consultation, the lead editor will usually attend the GDG meeting at which stakeholder comments and changes to the guideline are discussed. They can advise on the wording of the recommendations at this meeting, and will edit the recommendations in detail after the meeting.

10.3.2 The NICE pathway

NICE pathways are a practical online resource for healthcare professionals to use on a day-to-day basis. A pathway presents recommendations from a clinical guideline in a set of interactive topic-based diagrams. It contains all the recommendations from the guideline as well as any other NICE guidance that is directly relevant to the topic (for example, quality standards and technology appraisal guidance). It also contains links to implementation tools and to related NICE guidance and pathways.

The NICE pathway is produced by the lead editor, working closely with the NCC and nominated members of GDG (see section 10.3.4).

10.3.3 'Information for the public'

'Information for the public' (formerly called 'Understanding NICE guidance') summarises the guideline recommendations in everyday language, and is aimed at patients, their families and carers, and the wider public. It does not describe the condition or interventions in detail.

It may be used by hospitals and other organisations in the NHS, and by patient and carer organisations, to develop their own information.

'Information for the public' is written by the lead editor, working closely with the NCC, nominated members of the GDG (see section 10.3.4) and the Patient and Public Involvement Programme (PPIP) lead.

10.3.4 Involvement of the GDG with the NICE pathway and

'Information for the public'

During the guideline development process, each GDG is asked to nominate two or three members who will work closely with the lead editor on the NICE pathway and 'Information for the public'. Ideally these GDG editorial nominees should include at least one clinician for the pathway, and at least one patient and carer member for 'Information for the public'. The role of the nominees is to:

- attend an editorial meeting (see below)
- gather the views of GDG members on key issues concerning the NICE pathway and 'Information for the public'
- check for clinical accuracy, answer queries and check revisions on behalf of the GDG.

The editorial meeting usually takes place during consultation on the guideline. The GDG editorial nominees, the GDG Chair and at least one staff member from the NCC (such as the project manager) are invited. Also present from NICE are the lead editor, the Guidelines Commissioning Manager (who chairs the meeting) and sometimes the PPIP lead. The main aim of this meeting is to discuss drafts of the NICE pathway and 'Information for the public', which are circulated in advance. The wording of the guideline recommendations may also be discussed.

^[15] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

11 The consultation process and dealing with stakeholder comments

Consultation with stakeholders, which lasts 6 weeks for standard clinical guidelines, is an integral part of the NICE clinical guideline development process. Comments received from stakeholders are a vital part of the quality-assurance and peer-review processes, and it is important that they are addressed appropriately. This chapter advises staff in National Collaborating Centres (NCCs) and the NICE Internal Clinical Guidelines Programme^[16] on responding to stakeholder comments following consultation.

This chapter also includes information on what to expect during the consultation process. Circumstances in which a second consultation may be needed are also covered.

11.1 Principles of responding to stakeholder comments

This section describes how to respond to comments received from stakeholders about the draft guideline. The same principles apply when responding to comments on the draft scope (see [section 2.6](#)).

11.1.1 Responding to comments

Most comments will be received from registered stakeholders. These comments, and the responses to them, are sent to stakeholders with the advance copy of the full guideline, and are posted on the NICE website when the guideline is published (see [section 12.2](#)). Comments received from non-registered stakeholders, and comments received after the deadline for submission, are not considered and are not responded to; such comments will be returned to the sender.

11.1.2 Format of comments

All comments received by NICE are entered into a 'guideline consultation table' in a Microsoft Word file, which is sent to the NCC. The table contains the following information:

- Organisation – name of the organisation that submitted the comments.

- Document – full guideline or NICE guideline.
- Section – this column can be used by the NCC and Guideline Development Group (GDG) to facilitate the identification of comments by section.
- Page number.
- Comments – comments received from stakeholders, which are entered unchanged.
- Responses – blank column for the NCC and GDG to complete.

The GDG considers the comments received, and the NCC then responds to the comments. The following key points should be taken into account when responding to comments from stakeholders.

- Each comment must be acknowledged and answered as fully and as factually as possible. It is important to acknowledge that each point has been seen and understood. Some comments may be presented as general commentary, but they should still be acknowledged.
- If changes are made to the guideline as a result of the comment, this must be made clear in the response. If no changes have been made, it should be made clear why not.
- For draft guidelines, responses to comments and changes to the guideline must be made with the agreement of the GDG before publication. The NCC must maintain an audit trail of changes.

Examples of responses to types of comments received during consultation on a clinical guideline are given in table 11.1.

Table 11.1 Examples of responses to stakeholder comments received on the clinical guideline Drug misuse: psychosocial interventions (NICE clinical guideline 51 [2007]; NCC for Mental Health)

Type of comment	Example of a response
Compliments about the guideline	Thank you for your comments.

<p>A specific change was recommended and has subsequently been made</p>	<p>Thank you; we have changed 'legal' to 'pharmacy provided medication'.</p> <p>Thank you for your comment; we have addressed this issue in section 7.6 of the full guideline.</p>
<p>A specific change was recommended and has subsequently been partially made</p>	<p>Thank you for your comment; we have added a section on families and carers in the introduction which draws together material on families and carers discussed in other parts of the guideline. We have incorporated some of your suggestions into the text.</p>
<p>A specific change was recommended and has subsequently NOT been made</p>	<p>Although we accept your comments on the use of oral fluid testing as an option for contingency management programmes there are a number of factors supporting the decision to consider urinalysis as the preferred method. Firstly, the longer drug detection time afforded by urinalysis. Secondly, there is a larger evidence base for urinalysis which is still the most established method of testing. Thirdly, urinalysis is less costly.</p>
<p>Asks for something that is outside the scope of the guideline</p>	<p>In response to your comment on alcohol, the scope of the guideline was concerned with drug misuse and did not include alcohol, although the issue of alcohol misuse in addition to primary drug misuse was considered where appropriate.</p>
<p>Concern about impact of the guideline</p>	<p>We appreciate that the impact upon benefits is an important issue and it is under consideration by the implementation team where it is within their remit to do so.</p>

11.2 Consultation on the guideline

This section describes what to expect during the consultation phase. Draft versions of both the full guideline and the NICE guideline are consulted on.

11.2.1 Stakeholders

Draft versions of the full guideline and the NICE guideline are made available on the NICE website for the consultation. Registered stakeholders are informed by NICE that the documents are available.

11.2.2 External expert review

Although NICE does not routinely commission peer review from external experts, NCCs may occasionally consider arranging additional external expert review of part or all of a clinical guideline. These experts may include healthcare professionals, those commissioning care, social care professionals or people with a patient and carer perspective. This review may take place during guideline development or at the consultation stage. If it occurs during development, the process and comments remain confidential, but the adviser(s) should be named in the final full guideline. Comments from external expert advisers during the development of the guideline should be discussed by the whole GDG. If external advisers comment during consultation, their comments are responded to in the same way as comments from registered stakeholders and are published in the guideline consultation table on the NICE website under 'expert advisers'. All expert advisers are required to complete a declaration of interests form (see [section 3.2.1](#)).

11.2.3 NICE staff

NICE staff also comment on the consultation draft of the guideline, before and/or during the consultation. These staff include the Patient and Public Involvement Programme (PPIP) lead, the implementation lead and the lead editor for the guideline, as well as technical advisers (including a health economist), the Guidelines Commissioning Manager and the Centre for Clinical Practice (CCP) lead for the guideline.

Comments from NICE received during consultation are entered into the guideline consultation table and are responded to by the NCC in the same way as comments from registered stakeholders, but are not posted on the NICE website.

11.3 Considering a second consultation

In exceptional circumstances, the CCP Director may consider the need for a further 4-week stakeholder consultation. This additional consultation may be required after the

standard 6-week consultation has ended if either of the following criteria has been met:

- Information or data that would significantly alter the guideline has been omitted from the first draft.
- Evidence was misinterpreted in the first draft of the guideline and the amended interpretation significantly alters the guideline.

The final decision on whether to hold a second consultation will be made by NICE.

^[16] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

12 Finalising and publishing the guideline

Once the consultation period has ended, the Guideline Development Group (GDG) meets to consider any changes to the guideline that are required in response to the stakeholder comments received during consultation. Once the changes have been agreed, modifications are made to the full guideline and the NICE guideline. The revised versions are then sent to NICE. It is essential for the National Collaborating Centre (NCC) or the NICE Internal Clinical Guidelines Programme^[17] to keep an audit trail of what changes have been made, by whom, and for what purpose.

The final draft of the guideline and the responses to stakeholder comments are reviewed by NICE. The Guidelines Commissioning Manager (GCM) and the lead editor at NICE liaise with the NCC about any further changes that are required. After changes have been agreed, the guideline is signed off by NICE's Guidance Executive (see [section 12.2](#)).

This section summarises the main stages involved in finalising the guideline.

12.1 Editorial checks and review by NICE

The guideline recommendations are edited by the NICE lead editor before the guideline is submitted by the NCC for review by NICE.

12.1.1 Editorial checks

The lead editor works with the NCC to edit the guideline recommendations before submission of the revised guideline to NICE. The lead editor also revises the NICE pathway and 'Information for the public' in line with changes to the guideline recommendations.

After the revised guideline has been submitted to NICE, the editor sends the NICE guideline and the latest drafts of the NICE pathway and 'Information for the public' to the NCC and GDG to be checked and for queries to be answered. The NCC and GDG editorial nominees (see [section 10.3.4](#)) are notified in advance of the timetable for this. This check should be done initially by the NCC Director or project manager, as well as the Chair, Clinical Adviser (if there is one) and editorial nominees from the GDG. The PPIP (Patient and Public Involvement Programme) lead for the guideline at NICE also comments on 'Information for the public' from a patient and carer perspective.

It is important to check all versions carefully at this stage, because only essential changes can be made to the recommendations after sign-off. When checking the documents, the NCC and GDG members should give special attention to:

- queries and comments from the editors
- dosages, units, normal ranges or abnormal cut-offs (for example, for electrolytes or blood constituents)
- consistency of the recommendations between the guideline, the NICE pathway and 'Information for the public'

'Information for the public' is written in language that can be understood by a lay reader. The NCC and GDG editorial nominees should check that no inaccuracies or inappropriate generalisations have been introduced, and that the use, definitions and explanations of medical terms are correct.

After this stage, the NCC and lead editor work together to resolve outstanding queries on the recommendations, including any raised by the NICE team that reviews the guideline (see section 12.1.2).

The lead editor keeps an audit trail of any changes made to the recommendation wording in the NICE guideline. The NCC is responsible for ensuring that the wording of the recommendations in the full guideline matches that in the NICE guideline.

12.1.2 Review by NICE

When the revised full guideline is submitted by the NCC, a team from the Centre for Clinical Practice (CCP) at NICE (including the CCP lead for the guideline, the GCM and technical advisers) reviews both the guideline and the 'guideline consultation table' that lists stakeholder comments received during consultation and the responses by the NCC. If any outstanding issues are raised by NICE, the GCM will inform the NCC, indicating whether further changes to the full guideline should be considered.

The NCC should respond to any issues raised by NICE, indicating how it will amend the guideline. If it is not willing to make changes, the NCC should provide a detailed explanation of why not. This may lead to further dialogue between the NCC and the CCP Director and GCM at NICE.

The NCC should continue to maintain an audit trail of changes made to the full guideline. Any changes to the recommendations will be transferred to the other versions of the guideline by the lead editor.

12.2 Final steps

12.2.1 Signing off the guideline versions

After review of the revised guideline by NICE and liaison with the NCC to address any outstanding issues, all guideline versions will be signed off:

- The full guideline is signed off by NICE's Guidance Executive.
- The NICE guideline is also signed off by NICE's Guidance Executive,
- 'Information for the public' is signed off by the PPIP lead and the CCP lead for the guideline at NICE.
- The NICE pathway is signed off by the CCP lead for the guideline and the NICE pathways group.

12.2.2 Final checks before publication

Once the guideline has been signed off, the lead editor sends the NICE pathway and 'Information for the public' for a final accuracy check by the NCC and GDG editorial nominees (the NICE guideline is also sent, for information). This needs to be done quickly (usually within 48 hours), so the editor will give as much notice as possible of when the check is taking place.

Once the lead editor receives final comments on 'Information for the public' and the NICE pathway from the NCC, the GDG Chair and the GDG editorial nominees, the documents are finalised.

12.2.3 Releasing an advance copy to stakeholders

An advance copy of the final full guideline (and a copy of the responses to stakeholder comments made during the public consultation) is made available for information purposes to registered stakeholders 2 weeks before the official publication date. This information is

confidential until the guideline is published. This allows stakeholders to prepare for publication, but it is not an opportunity to comment further on the guideline.

12.2.4 Publication

All versions of the guideline (the full guideline, the NICE guideline, the NICE pathway and 'Information for the public') are published together. Costing tools, audit support and some other implementation tools are published at the same time (see [chapter 13](#)).

12.3 Launching and promoting the guideline

Members of the NCC and GDG work with NICE to promote awareness of the guideline, both at the point of launch and afterwards.

12.3.1 The press launch

The communications lead at NICE will talk to the NCC and GDG about what kind of launch is appropriate for each guideline – this may be a press conference or a more targeted approach to the specialist or trade press.

If there is likely to be substantial media interest in the guideline, a press conference will be held 1 or 2 days before publication, usually at NICE's offices. This allows journalists to interview those involved in the development of the guideline and other commentators, and to prepare articles or broadcast pieces in advance. Information provided to the media is confidential until the launch date for the guideline.

Ideally, a press conference panel includes a representative from NICE (preferably the Executive Lead who is responsible for signing off the guideline), the Chair of the GDG, a healthcare professional, a patient and carer representative, and a nurse, midwife or allied healthcare professional. NICE provides training for panel members.

The NICE communications lead also ensures that relevant stakeholder organisations, such as the Royal Medical Colleges and patient organisations, are involved in the launch if appropriate.

All GDG members are encouraged to provide details of case studies that can be used to illustrate some of the guideline's key recommendations, as these are a good way of

creating media interest.

The aim of the press briefing is to clearly communicate key messages about the guideline to the press and media; it is not a conference for healthcare professionals. If the NCC or GDG would like to arrange separate events at which healthcare professionals can learn more about the guideline or to showcase the guideline directly to peers, the communications team at NICE can provide support.

12.3.2 Reaching the target audience

NICE welcomes input from GDG members on how to identify groups of healthcare professionals and specialists who should be sent details of the guideline. GDG members may also be able to identify other ways of raising awareness of the guideline – for example via newsletters, websites or training programmes of organisations they are affiliated to (particularly for patient and carer organisations), or by suggesting relevant conferences at which the guideline can be promoted.

NICE implementation services are described in [section 13.6](#).

^[17] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

13 Implementation support for clinical guidelines

The aim of NICE implementation support is to encourage and promote the uptake of NICE guidance. Priorities identified by the Guideline Development Group (GDG), recommendations identified as having significant resource implications or resulting in a change in practice, and information from stakeholder consultation will inform the focus of the implementation support work for a clinical guideline. Support work may include a range of activities to promote uptake and the provision of practical support tools.

Implementation tools are produced by staff in the implementation programme at NICE. Three leads are involved in developing the tools: the audit lead, the costing and commissioning lead and the implementation adviser. Tools are developed in consultation with:

- the GDG
- the National Collaborating Centre (NCC) or the NICE Internal Clinical Guidelines Programme^[18]
- the Centre for Clinical Practice (CCP) Guidelines Commissioning Manager (GCM)
- the lead from the Patient and Public Involvement Programme.

This chapter outlines the methods and process for developing the implementation tools, and the contributions of the GDG, NCC and CCP to this process.

13.1 Needs assessment, support plan and tools

Each clinical guideline is routinely accompanied by three implementation tools:

- a baseline assessment tool
- clinical audit tools
- a costing report and costing template, or a costing statement.

For each guideline, the implementation adviser analyses the information gathered from the

GDG, stakeholders and other sources to carry out a needs assessment, and produces an implementation support plan which details the activities that will be undertaken by NICE to address the key implementation issues. During the needs assessment, the implementation adviser will consult with members of the GDG, the NCC and the GCM. Tailored solutions are then developed according to need.

The tools are described below; for more information see the NICE website.

13.1.1 Baseline assessment tool

The baseline assessment tool is prepared by the audit coordinator. It is an Excel spreadsheet that organisations can use to identify whether they are in line with practice recommended in the guideline, and to help them plan activity to implement the recommendations.

13.1.2 Clinical audit tools

Clinical audit tools are prepared by a clinical audit specialist. They help organisations to carry out clinical audits based on some of the guideline's measurable recommendations. They consist of audit standards, data collection tools and action plans. Some will also be produced as Excel electronic audit tools that provide a basic data analysis and clinical audit report.

13.1.3 Costing tools

Costing tools are prepared by a costing analyst. They are intended to help organisations assess the costs and potential savings associated with implementing the guideline. The costing analyst assesses the recommendations to identify those with the greatest resource impact^[19]. NICE usually provides two types of costing tools to accompany a clinical guideline:

- a costing report, which summarises the estimated national costs and savings associated with implementing the guideline and discusses the assumptions made in reaching this figure
- a costing template, which allows users to estimate the local impact of implementing the guideline based on their population and to change the assumptions and variables to reflect local circumstances.

Occasionally, implementing the recommendations in a guideline may not be estimated to result in significant additional costs or savings. No costing report or costing template is produced in these cases. Instead, a costing statement is produced that explains why the cost impact is not considered to be significant.

13.1.4 Tailored implementation tools based on the needs assessment

In addition to the implementation tools described above, the needs assessment may identify additional tools that would be useful for addressing specific learning or education needs of staff and organisations. These targeted tools for clinical guidelines are prepared by the implementation adviser. There is some evidence that barriers to uptake of a guideline that are identified in advance can be overcome by designing specific interventions to address them, although it is not always very clear how best to identify the barriers and which particular types of interventions are best for each barrier (Baker et al. 2010).

Where there is an agreed need for specific implementation tools to support recommendations about drugs and prescribing, the implementation adviser will work with the [NICE Medicines and Prescribing Centre](#) to produce these materials.

See [Into Practice on the NICE website](#) for examples of the types of tailored tools that are produced. These could include:

- learning and development slide sets
- clinical case scenarios
- podcasts
- training plans
- online educational tools
- examples of how NICE guidance has been put into practice
- shared decision aids.

There might also be signposting to, or 'joint badging' of, resources developed and promoted with other organisations, such as professional or patient groups.

13.2 Developing the implementation tools

The needs assessment and development of the implementation tools usually start during consultation and continue through to publication of the guideline.

13.2.1 Initial involvement during guideline development

At the start of the guideline development process, an implementation team is assigned to work with the NCC and GDG. The team consists of a costing lead, an audit lead and an implementation adviser.

During scoping of the guideline (see [chapter 2](#)), the implementation adviser carries out an initial assessment to ensure that all critical stakeholders have registered and starts to record a log of any implementation issues that arise. This log is kept up to date throughout guideline development to inform the development of the implementation support plan.

At GDG meeting 2 or 3, GDG members will be given a general briefing paper from the implementation team explaining its work and future involvement.

At the end of guideline consultation, the costing analyst and the implementation adviser will usually attend a GDG meeting to hear the outcome of the consultation and to consider how this will affect key implementation issues. The costing lead may be given a slot at a GDG meeting to discuss their work.

The GDG may also invite other members of the implementation team to meetings at any time if discussion about other implementation issues is needed.

Volunteers from the GDG are needed to work with the implementation teams. Two members are required to contribute to the development of the costing tools (the 'GDG costing nominees') and two to the development of the implementation support tools (the 'GDG implementation support nominees'). After consultation, the implementation adviser will liaise with the GDG implementation support nominees to discuss the implementation support plan and to agree their level of input into tool development.

13.2.2 Commenting on the draft implementation tools

13.2.2.1 Costing tools

The costing analyst uses the recommendations in the consultation draft of the guideline to identify the potential significant changes in resource use that are likely to arise from implementation of the guideline. This will be based on baseline practice, how practice might change and the effect on resources for the areas identified. This is assisted by input from the GDG, the NCC health economist and costing research.

The costing analyst updates the draft costing tools when the final draft of the guideline is submitted. The tools are sent to the NCC and the GDG costing nominees 4–5 weeks before publication of the guideline for a 2-week consultation period. Comments are invited on:

- whether the assumptions made are reasonable
- the usability of the costing template at a local level.

The NCC and the GDG nominees send their comments back to the costing analyst, with a copy to the GCM.

13.2.2.2 Clinical audit tools

The audit coordinator sends drafts of the audit support tools to the NCC and the GDG for a 2-week consultation period, approximately 9 weeks before publication of the guideline.

The NCC and the GDG send their comments back to the audit coordinator, with a copy to the GCM.

13.2.2.3 Other tailored tools

Other draft implementation tools will usually be sent to the NCC and the GDG for comment around 4–5 weeks before publication of the guideline for a 1-week or 2-week consultation period, depending on the nature of the tool. Advance notice will be given of all timelines. Any delays to the development of the final guideline may reduce these periods.

Comments are invited on accuracy, clarity and whether the tool provides an accurate interpretation of the key messages of the guideline.

13.3 Publishing the implementation tools

When implementation tools are published at the same time as a clinical guideline by NICE, they are downloaded more frequently than if they are published later. Therefore the aim is to publish the implementation tools at the same time as the guideline wherever possible.

Achieving this is dependent on the final signed-off version of the guideline being available with sufficient lead time for development of and consultation on the tools. For some support tools, a later timeline after publication of the guideline may be necessary.

Publication of the tools is announced on the NICE website and in the e-newsletter; the latter is available to everyone who wants to be kept up to date with important developments at NICE.

13.4 Post-publication support

NICE and the NCC may also carry out activities to help users implement a clinical guideline after it has been published. These activities are identified in the implementation support plan (see [section 13.1](#)) and may include:

- speaking at, and encouraging and supporting GDG members to speak at, relevant conferences and events
- encouraging and supporting GDG members to contribute to or write journal articles about the guideline
- contributing to or writing journal articles about the guideline
- speaking about the implementation tools at events
- supporting workshops and regional events
- working with the implementation consultants (see [section 13.6](#))
- providing feedback and encouraging submission of shared learning (see [section 13.6](#))
- supporting the development of an online educational tool and other educational initiatives, such as incorporating NICE into curricula
- supporting work to review uptake of the guidance

- adding a notification on the [National Clinical Audit Forum](#) that new NICE clinical audit tools are available, with details of the topics they relate to
- adding some of the electronic tools to the [Clinical Audit Knowledge Exchange](#) database.

13.5 Working with national organisations

The implementation adviser works in partnership with other NICE teams to engage with national organisations and networks. This work might include embedding recommendations from NICE clinical guidelines into other guidelines or initiatives, or encouraging the development of patient information (for example, joint tools with the NHS Blood and Transplant Service to support the organ donation guideline [NICE clinical guideline 135] and a referral tool for suspected autism in adults with the NHS National Institute for Health Research to support the autism in adults guideline [NICE clinical guideline 142]).

The implementation advisers welcome suggestions from GDG members on how to work with national organisations to support the implementation of a clinical guideline.

13.6 Other NICE implementation services and products

NICE also provides a range of services and products to assist NHS and non-NHS clinicians and other practitioners and organisations in the implementation of its clinical guideline recommendations. The following support is available:

- A [field-based team](#) of seven implementation consultants work with organisations to help to put NICE guidance into practice. Each consultant visits NHS, local authority and other organisations in their area, ensuring regular interaction with NICE stakeholders.
- Web-based examples of how organisations have implemented NICE clinical guidelines are provided on the [shared learning database](#).
- NICE reports and published articles relating to the uptake of NICE guidance are provided on the 'uptake database' – [ERNIE \(Evaluation and review of NICE implementation evidence\)](#).

- Commissioning guides are also provided to support commissioners of services. These aid in the local implementation of NICE clinical guidelines through commissioning, and are underpinned by the guidelines. Each commissioning guide:
 - signposts and provides topic-specific information on key clinical and service-related issues to be considered during the commissioning process
 - offers an indicative benchmark of activity to help commissioners determine the level of service needed locally
 - includes an interactive tool that provides data for local comparison against the benchmark, and resources to estimate and inform the cost of commissioning intentions.

Because the guides are focused on services commissioned, they may bring together elements from one or more pieces of NICE guidance rather than focusing on one particular guideline. For example, the commissioning guide 'Biologic drugs for inflammatory disease in rheumatology, dermatology and gastroenterology' brings together the clinical guideline on rheumatoid arthritis (CG79) and several technology appraisals.

13.7 Further reading

Auerback AD, Landefeld CS, Shojania KG (2007) The tension between needing to improve care and knowing how to do it. *New England Journal of Medicine* 357: 608–13

Baker R, Camosso-Stefinovic J, Gillies C et al. (2010) Tailored interventions to overcome identified barriers to change: effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews* 2010, issue 3

Cabana MD, Rand CS, Powe NR et al. (1999) Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 282: 1458–65

Eccles M, Grimshaw J, Walker A et al. (2005) Changing the behavior of healthcare professionals: the use of theory in promoting the uptake of research findings. *Journal of Clinical Epidemiology* 58: 107–12

Michie S, Johnston M, Hardeman W et al. (2008) From theory to intervention: mapping theoretically derived behavioural determinants to behaviour change. *Techniques in Applied Psychology: An International Review* 57: 660–80.

^[18] Information throughout this manual relating to the role of the National Collaborating Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

^[19] See [Assessing cost impact – methods guide](#).

14 Updating published clinical guidelines and correcting errors

Changes to review process from August 2013

An [interim clinical guideline surveillance process and methods guide](#) was published by NICE in August 2013, which replaces sections 14.1 and 14.2 in this guidelines manual. This interim process applies to guidelines being considered for updating from August 2013 onwards. After evaluation over a 12-month period, the process will be used to inform the NICE guidance development project and will be subject to formal consultation.

Clinical guidelines developed by NICE are published with the expectation that they will be reviewed and updated as necessary. Any decision to update a guideline must balance the need to reflect changes in the evidence against the need for stability, because frequent changes to guideline recommendations would make implementation difficult. This chapter describes the process and methods for reviewing the need to update NICE clinical guidelines and for producing an updated guideline.

The responsibility for updating a clinical guideline usually rests with the National Collaborating Centre (NCC) that originally developed it (or the NICE Internal Clinical Guidelines Programme if applicable). In some circumstances, an NCC or the NICE Internal Clinical Guidelines Programme^[20] may be asked to update a guideline developed by another NCC. This will occur only after consultation with the relevant NCCs, and clarification of copyright issues.

When scheduling updates of guidelines into its work programme, NICE prioritises topics for updated guidelines and topics for new guidelines according to the need for new guidance. The relative priorities will be communicated to NCCs through the NICE business planning process.

This chapter also describes the process for correcting errors that are identified after publication of a guideline.

14.1 Process and methods for reviewing the need to

update a published guideline

After publication of a clinical guideline, NICE collects information relevant to the guideline that might affect the timing or content of a subsequent update. This may include any queries or comments received by NICE or the NCC after publication, and evidence submitted by researchers or other stakeholders. However, NICE and the NCC will not actively seek new evidence, unless it has been identified in the guideline that important new information is likely to emerge before the 3-year scheduled review that may result in the need for an exceptional update or amendment (see [section 14.4](#)).

A formal review of the need to update a guideline is usually undertaken by NICE 3 years after its publication. The review includes the following key stages and methods (see figure 14.1 for a summary of the process and methods):

14.1.1 Stage 1

- Collect information from members of the Guideline Development Group (GDG) that developed the original guideline (including patient, service user and carer members) using a questionnaire, and from the NCC, about new developments in the field.
- Collate other types of information, including the results of a re-run of the original search used for the scope of the published guideline (see [section 2.3.3](#)), post-publication comments and feedback about guideline implementation (for example, feedback gathered by the NICE field team of implementation consultants and local and national audit data).
- Conduct a broad search for relevant ongoing clinical trials.
- Conduct a high-level search for evidence for relevant systematic reviews and randomised controlled trials (RCTs) using MEDLINE, MEDLINE In-Process, Embase and Cochrane (CDSR and Central only), with PsycINFO as an optional database for specific mental health topics.
- Use the review protocol and inclusion and exclusion criteria from the published guideline to assess the relevance of, and summarise the evidence from, the systematic reviews and RCTs identified in the high-level search, based on abstracts only.

- Collate all information and evidence identified so far to assess the need to conduct further focused searches on specific clinical areas in the guideline and/or new areas that may be important for an update of the guideline.
- Discuss with the original guideline GDG Chair and/or Clinical Adviser, as well as other GDG members if necessary, to confirm the decisions on further focused searches and to develop PICO (population, intervention, comparator and outcome) frameworks for the focused searches.

14.1.2 Stage 2

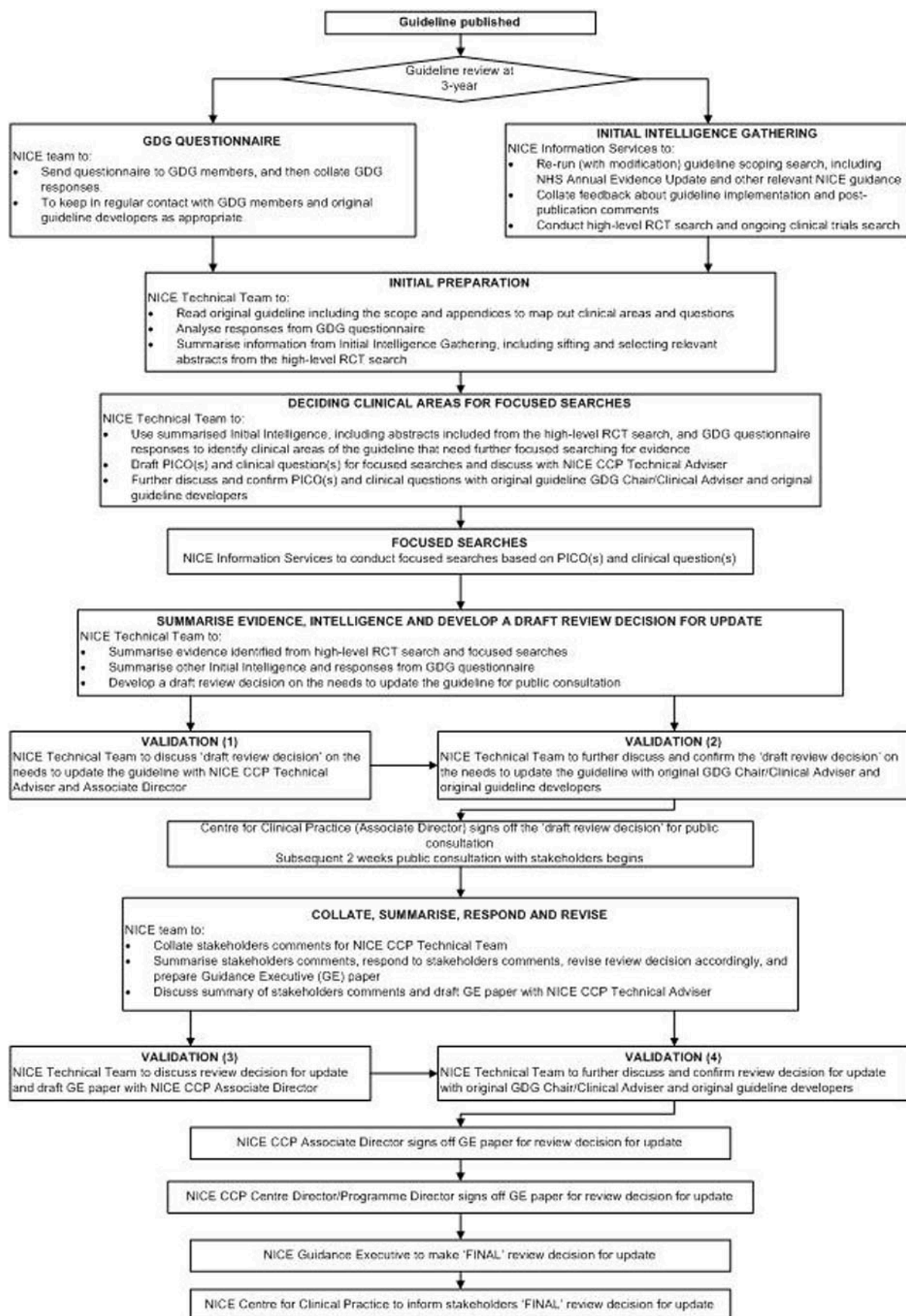
- Conduct further focused searches based on the relevant PICO frameworks using MEDLINE, MEDLINE In-Process, Embase and Cochrane (CDSR and Central only), plus two optional extra databases: PsycINFO (for mental health and psychological interventions questions only) and NHS EED (for health economics and cost effectiveness questions only).
- Use the review protocol and inclusion and exclusion criteria from the published guideline to assess the relevance of, and summarise the evidence identified from, the focused searches, based on abstracts only.
- Assess and summarise all information and evidence collected in stages 1 and 2, and develop a draft review decision on the need to update the guideline.
- Discuss with the original guideline GDG Chair and/or Clinical Adviser, as well as other GDG members if necessary, to confirm that they agree with the draft review decision before consultation with stakeholders.

14.1.3 Stage 3

- Check the stakeholder list for the original guideline with both the NICE Patient and Public Involvement Programme (PPIP) and other NICE teams to ensure that stakeholder details are up to date.
- Consult stakeholders on the draft review decision for 2 weeks.
- Consider (and if necessary revise) the draft review decision, taking into account the stakeholders' comments, and decide on the advice for NICE's Guidance Executive (see [section 14.2](#)).

- NICE Guidance Executive makes the final review decision.

Figure 14.1 Process and methods for the 3-year formal review of the need to update a published clinical guideline



14.2 Deciding whether to update a clinical guideline

The Centre for Clinical Practice (CCP) at NICE considers the draft review decision in the light of evidence and information identified during the review process and stakeholders' comments.

CCP advises NICE's Guidance Executive on whether an update is needed and, if so, whether it should be a full update of the guideline or whether only particular areas of the guideline need updating. CCP may also advise that no update is needed. Two other options that can be suggested by CCP are transferring the guideline to the 'static list' or withdrawing the guideline.

Guidance Executive will decide which of these options is most appropriate. The decision is based on predefined criteria, as listed in table 14.1. The decision will take into account the competing priorities of other guideline topics and the capacity to schedule the work within the guidelines programme.

Table 14.1 Criteria for deciding whether to update a guideline

Updated decision	Criteria	Actions
Update of whole guideline	<ul style="list-style-type: none"> • Major sections of the guideline need updating • Many of the recommendations are no longer necessary • New clinical areas have been identified 	<ul style="list-style-type: none"> • Prepare a new scope • Consult on the scope

<p>Update of part of guideline</p>	<ul style="list-style-type: none"> • Some recommendations need updating in the light of new evidence, or because they are unclear <p>and/or</p> <ul style="list-style-type: none"> • New clinical areas have been identified that need to be covered in the guideline 	<ul style="list-style-type: none"> • Prepare a new scope • Consult on the scope
<p>Exceptional update</p>	<ul style="list-style-type: none"> • A small number of recommendations may need updating in the light of new evidence • Exceptional updates may also be triggered by the identification of errors in a guideline after publication 	<ul style="list-style-type: none"> • Use the original scope • Do not consult on the scope • Inform stakeholders
<p>No update</p>	<ul style="list-style-type: none"> • No new evidence has been identified that would overturn any of the recommendations • There is no evidence from clinical practice to indicate that any of the recommendations need changing • There is no evidence from clinical practice that the original scope need changing 	<ul style="list-style-type: none"> • The guideline is not updated • The guideline is reviewed after a further 3 years to determine its update status
<p>Transfer to the 'static list'</p>	<ul style="list-style-type: none"> • The recommendations are unlikely to change in the foreseeable future 	<ul style="list-style-type: none"> • No further update planned • May be reviewed if new evidence emerges

Withdraw the guideline	<ul style="list-style-type: none"> • The guideline no longer applies 	<ul style="list-style-type: none"> • Consult with stakeholders
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14.3 Next steps

14.3.1 Conducting an update

If the entire guideline needs to be updated, the NCC prepares a new scope, following the process described in [chapter 2](#).

Recruitment of GDG members follows the usual process (see [section 3.1](#)). The NCC should inform members of the original GDG that they are recruiting a new GDG, but the composition of the GDG should be tailored to the requirements defined by the new scope. The time required for development of the guideline is agreed between NICE and the NCC, and depends on the number of review questions. The guideline is developed using the same process as for a new guideline and is subject to the normal 6-week consultation period (see [chapter 11](#)). The usual process for finalising and publishing the guideline is also followed (see [chapter 12](#)).

If only part of the guideline is being updated, there are two possible scenarios:

- some recommendations need to be updated **and/or**
- new clinical areas have been identified that require new recommendations.

For both of these scenarios, a new scope is prepared and consultation with stakeholders takes place through the usual process (see [chapter 2](#)). The scope will make clear exactly which sections of the guideline are and are not being updated. The scope will also make clear that all recommendations in the original guideline, including those that have not been otherwise reviewed, will be checked to ensure that they comply with NICE's equality duties.

The NCC recruits a new GDG to undertake the work, using the usual recruitment process (see [section 3.1](#)). The time needed to undertake the update is agreed between NICE and the NCC.

14.3.2 No update

If it is decided that a guideline does not need to be updated, the guideline will be reviewed after a further 3 years. The same process for deciding whether an update is needed will be followed.

14.3.3 The 'static list'

There may be circumstances in which the clinical areas covered in a guideline do not need to be considered for updating. This may be the case, for example, if the evidence base is so poor that it is unlikely that any of the recommendations will change in the foreseeable future. In this case the guideline will be transferred to the 'static list' and no further update will be required. When a guideline has been placed on the static list, this will be made clear on the home page for the guideline on the NICE website. Guidelines on the static list may be transferred back to the 'active list' for further review if new evidence or information from clinical practice becomes available that is likely to mean that changes to the recommendations are required.

14.3.4 Withdrawing the guideline

It may be decided that the recommendations in a guideline no longer apply, but that the guideline is not of sufficiently high priority for updating. In this case the guideline will be withdrawn. This decision will be consulted on with stakeholders.

14.4 Exceptional updates

Exceptionally, significant new evidence may emerge that necessitates an update of a guideline before the formal 3-year review. This might be a single piece of evidence, an accumulation of evidence or other published NICE guidance (such as other clinical guidelines or technical appraisal guidance). This evidence must be sufficiently robust to make it likely that:

- one or more recommendations in the guideline will need updating in a way that will change practice significantly **or**
- patient safety issues need to be addressed

Examples of such evidence include significant data from RCTs, changes in licensing and

patents or warnings issued by licensing agencies, or major changes in costs. Exceptional updates may also be triggered by the identification of errors in the guideline after publication (see [section 14.7](#)).

14.4.1 Determining the need for an exceptional update

CCP advises NICE's Guidance Executive on the following questions:

- Is the update necessary?
- Is there any other evidence (published, unpublished or from ongoing studies) that is relevant to the newly identified evidence?
- Which recommendations need to be reviewed in the light of the new evidence?

Guidance Executive then decides on the need for an update based on the answers to these questions. If an exceptional update is necessary, CCP commissions an NCC to carry out the work. Stakeholders are informed at this point by NICE.

The aim of an exceptional update is to be responsive to new evidence, so it is imperative that changes to recommendations are published quickly. The process for developing exceptional updates should be the same as that for conducting an update, except that the original scope is used (see [section 14.3](#)).

14.5 Presenting updates

When presenting guidelines that have been partly updated, the aim is to ensure that there is a single set of publications that bring together relevant information from all previous versions of the guideline and the updated information. In this way, readers of the updated guideline will be able to easily identify which recommendations were made when. The rest of this section covers general principles to be used when part of a guideline has been updated.

As noted earlier in this chapter, a decision may be made to update the whole guideline. In this case, the process is as for a new guideline, except that the previous version of the guideline should be available for comparison.

The NCC and the CCP at NICE should agree as early as possible how the full guideline will be presented for consultation. Usually, the updated sections will be integrated into a single

document with the existing full guideline.

14.5.1 Submitting the consultation draft

Before the NCC submits the draft guideline to NICE, the following should be checked:

- Sections of the full and NICE guidelines have been updated as agreed at the scoping stage, or in line with any changes to the plan agreed with the Guidelines Commissioning Manager since scoping.
- The full and NICE guidelines include standard text at the beginning, setting out which sections have been updated, how these are marked in the consultation draft and which sections are open for comment during consultation.
- In the full guideline, updated sections (including the evidence, evidence to recommendations and recommendations) are clearly marked with paragraph borders, preferably a strip down the right hand side of the relevant pages bearing the word 'updated' and the year of the update. This will allow stakeholders to easily identify what they can comment on. The text that is superseded is placed in an appendix.
- The recommendations have been marked up as described in box 14.1.
- Recommendations from sections not being updated have been checked to determine whether any changes are essential (for example, if a drug is no longer available).
- Changes in recommendations from sections that have not been updated are kept to a minimum (for example, changing from the passive to the active voice) and have been checked with the Guidelines Commissioning Manager and the CCP lead for the guideline.
- There is an appendix in the full and NICE guidelines containing a table summarising the proposed changes to the original recommendations (see below for more information).
- The status of any guidance incorporated into the previous version of the guideline has been confirmed with NICE. For example, has the other guidance been updated by the guideline update?
- All current recommendations (new, updated and unchanged) have been assessed for the purposes of identifying key priorities for implementation.

- All current recommendations (new, updated and unchanged) have been assessed with respect to NICE's equality duties.

Box 14.1 Labelling and rewording recommendations

In both the consultation and final published versions of the full and NICE guidelines, label all recommendations so that it is clear when the evidence was reviewed and whether the recommendation is new. The example below is of a guideline first published in 2008 with an update published in 2012.

Sections where the evidence has been updated

- New recommendations, either an additional clinical area for the guideline or changed because of new evidence – add **[new2012]** to the end of the recommendation.
- Unchanged recommendations where the evidence has been reviewed for the 2012 update but the recommended action is the same as in the 2008 guideline – add **[2012]**. Reword these recommendations into the direct style (see [section 9.3.1](#)), but check with the GDG that rewording has not changed the meaning.

Sections where the evidence has not been reviewed

- For the consultation, add a grey background tint to recommendations that are not being updated, to indicate that they are not being consulted on.
- **Unchanged recommendations** from 2008, where the evidence has not been reviewed for the 2012 update – add **[2008]** to the end of the recommendation.
- **Change to recommendation wording that changes the meaning** (for example, because of equalities duties or a change in the availability of drugs, or incorporated guidance has been updated) – add **[2008, amended 2012]** to the end of the recommendation, mark the change with yellow highlighting for the consultation and add a footnote explaining the reason for the change. This also applies if part of a recommendation (for example, a bullet point) has been deleted because it has been updated by other NICE guidance.
- **Evidence has not been reviewed, but there have been minor changes** in 2012 to the wording of a 2008 recommendation that do not affect the meaning, for specific reasons such as changes in terminology – add **[2008]**. For the consultation, mark small changes in these recommendations with yellow highlighting. Include a general note about these changes in the appendix table.
- **Recommendation is incorporated from another published guideline** – use the label to show when that other guideline was published, for example **[2006]**

Explaining the proposed changes in the consultation version

Standard text at the beginning of the guideline

Refer to the latest full guideline and NICE guideline templates for the standard text.

Appendix explaining the changes

Create a table (which will form an appendix to the full and NICE guidelines) summarising the proposed changes to the original recommendations, including:

- The text and recommendation number(s) of the recommendations that have been deleted in the update (either because they are being changed significantly in light of new evidence, or because they have become redundant), and the number(s) and text of any replacement recommendations. If there is no replacement for a recommendation, explain the reasons for the deletion.
- A general note about any small changes made to recommendations that have not been updated, such as terminology changes. (These changes are marked with yellow highlighting for the consultation.)
- A note about every change to a recommendation that has changed the meaning without an evidence review (labelled 'amended' and marked with yellow highlighting for the consultation). Include the new text of the recommendation.

Keep explanations as short as possible – only brief details are needed.

14.5.2 Submitting the final draft

Before the NCC submits the final draft of the full guideline, the following should be checked:

- The recommendations are labelled as described in box 14.1.
- Grey shading and yellow highlighting have been removed from the recommendations.
- Footnotes explaining changes to recommendations labelled **[2008,amended2012]** are retained.

- The appendix table summarising the changes to recommendations has been revised in line with the final recommendations.
- The appendix with the superseded text is retained.
- The paragraph borders indicating which sections have been updated are retained.
- The standard text box at the beginning of the guideline explaining which sections have been updated has been revised.

The following should also be checked in the NICE guideline:

- The recommendations are labelled as described in box 14.1.
- Grey shading and yellow highlighting have been removed from the recommendations.
- Footnotes explaining changes to recommendations labelled **[2008,amended2012]** are retained.
- The appendix table summarising the changes has been removed.
- The standard text box at the beginning of the guideline explaining which sections have been updated has been revised.

14.5.3 The NICE pathway and 'Information for the public'

NICE pathway

The NICE pathway for the existing guideline (if there is one) will be updated in line with the updated guideline. If there is no existing NICE pathway for the topic, one will be produced. If the existing guideline has a quick reference guide, this will be withdrawn.

A general description of what has been updated will be included at the start of the NICE pathway and will point to more detailed information in the NICE guideline about changes to individual recommendations.

'Information for the public'

When the updated guideline is published, the existing 'Information for the public' (or 'Understanding NICE guidance') will be withdrawn and replaced by a new 'Information for

the public' in web format. Usually, the new 'Information for the public' will not differentiate between old and new recommendations. Sometimes it may be useful to explain which sections have been updated, particularly if it has been a rapid update, and patients are likely to notice changes in their care (for example, in drug treatment).

14.6 Maintaining records

In accordance with its contract with NICE, the NCC should maintain records throughout the development of an updated clinical guideline to ensure that the following information is readily available:

- Details of the GDG membership, including declarations of interest.
- Search strategy details, including when the most recent search was conducted.
- Copies of the papers used.
- Data-extraction forms.
- Evidence tables.
- Minutes of GDG meetings.
- Any additional information presented to the GDG.

14.7 Correcting errors in published clinical guidelines

Measures are in place throughout the development of a clinical guideline to ensure that errors in the collection, synthesis, interpretation or presentation of the evidence are avoided as far as possible. However, on rare occasions errors may be found after publication of the guideline. These errors may not always warrant changes to the guideline, in which case they will be logged for consideration when the guideline is reviewed for updating. If an error is found, the following criteria and process will be used by NICE and the NCCs to determine whether changes are necessary.

14.7.1 Criteria and process for a correction

Corrections or changes to a published clinical guideline will be made if an error:

- puts patients at risk, or impacts on their care **or**
- damages NICE's reputation **or**
- significantly affects the meaning of the recommendation.

If it is necessary to correct an error in a published guideline, we will follow our internal policy for dealing with errors. The individual or organisation who reported the error will be contacted in writing, and we will explain our rationale for the decisions and actions taken.

If a correction is to be made, a notification is put on the guideline's 'home' page on the NICE website. Depending on the nature and significance of the error and the time since publication of the guideline, stakeholders may also be notified in writing (usually by email). The relevant web-based documentation is corrected, and this is also highlighted on the guideline's home page on the NICE website.

14.8 Further reading

Clark E, Donovan EF, Schoettker P (2006) From outdated to updated, keeping clinical guidelines valid. *International Journal for Quality in Health Care* 18: 165–6

Eccles M, Rousseau N, Freemantle N (2002) Updating evidence-based clinical guidelines. *Journal of Health Services Research and Policy* 7: 98–103

Shekelle P, Eccles MP, Grimshaw JM et al. (2001) When should clinical guidelines be updated? *British Medical Journal* 323: 155–7

Shekelle PG, Ortiz E, Rhodes S et al. (2001) Validity of the Agency for Healthcare Research and Quality clinical practice guidelines: how quickly do guidelines become outdated? *Journal of the American Medical Association* 286: 1461–7

Shojania et al. (2007) Updating systematic reviews. Technical Review, Number 16, AHRQ Publication No. 07-0087

Turner T, Misso M, Harris C et al. (2008) Development of evidence-based clinical practice guidelines (CPGs): comparing approaches. *Implementation Science* 3: 45–52

^[20] Information throughout this manual relating to the role of the National Collaborating

Centres in guideline development also applies to the Internal Clinical Guidelines Programme at NICE.

Summary of main changes from the 2009 guidelines manual

Chapter	Title	Revisions
General	N/A	<p>This update of 'The guidelines manual' incorporates changes to the process of guideline development that were discussed at the NICE Board meeting in September 2011.</p> <p>Other changes are small clarifications and minor adjustments to methods to reflect, for example, greater experience in the use of GRADE, and organisational issues such as the expanding remit to include development of social care guidance and the new work programmes within NICE, and changes in names of teams (for example, the Short Clinical Guidelines Team is now called the Internal Clinical Guidelines Programme).</p>
1	Introduction	<p>Minor revisions throughout this chapter, including:</p> <ul style="list-style-type: none"> referring people to the NICE website for details of NICE's other activities rather than detailing them in the manual, to allow for anticipated changes in NICE's functions over the next few years. reflecting the Equality Act 2010.
2	The scope	<p>Revisions throughout the chapter to reflect process changes approved previously by the NICE Board.</p> <p>Editorial changes to emphasise the role of clinical guidelines in informing the subsequent development of quality standards.</p>
3	The Guideline Development Group	<p>Revisions to reflect changes in the wider NHS environment.</p>

4	Developing review questions and planning the systematic review	Minor revisions throughout, including updating the examples of review questions.
5	Identifying the evidence: literature searching and evidence submission	<p>Minor revisions, including:</p> <ul style="list-style-type: none"> • updating links to webpages for databases and other information • removing text from section 5.5 referencing particular suppliers of reference management software.
6	Reviewing the evidence	<p>Minor revisions, including to:</p> <ul style="list-style-type: none"> • reflect further minor changes in GRADE • describe the possible use of indirect and mixed treatment comparisons • reference the update to the AGREE tool.
7	Assessing cost effectiveness	<p>Minor revisions, including to:</p> <ul style="list-style-type: none"> • emphasise the involvement of the health economist within the guideline team at all stages • clarify the use of and methods for reviews of economic studies • clarify the requirements for some aspects of the analysis and reporting of new economic analyses conducted for the guideline, particularly around sensitivity analyses and reporting of all outcomes • refer to the Guide to the methods of technology appraisal for additional considerations (for example, life-extending treatments) that GDGs should take into account when developing recommendations.

8	Linking clinical guidelines to other NICE guidance	Changes to reflect new work programmes within NICE and changes to policy on the appropriate route for appraising significant new medicines within NICE.
9	Developing and wording guideline recommendations	<p>Minor revisions, including to:</p> <ul style="list-style-type: none"> • clarify and revise examples around the interpretation of the strength of evidence, and wording of recommendations • update the text about off-label prescribing (in consultation with the MHRA) • reflect the NICE research recommendations manual • emphasise the potential role of key priorities for implementation for informing subsequent development of quality standards.
10	Writing the clinical guideline and the role of NICE editors	<p>Minor revisions, including to:</p> <ul style="list-style-type: none"> • reflect developments in the templates • remove the requirement to present an algorithm in the NICE guideline • add details about NICE pathways • reflect the name change from 'Understanding NICE guidance' to 'Information for the public'.
11	The consultation process and dealing with stakeholder comments.	<p>Revisions to reflect:</p> <ul style="list-style-type: none"> • changes to validation processes agreed by the NICE Board • removal of commissioned expert peer review.

12	Finalising and publishing the guideline	<p>Revisions to reflect:</p> <ul style="list-style-type: none"> • changes to processes agreed by the NICE Board • changes in the documents produced by NICE.
13	Implementation support for clinical guidelines	Revisions to reflect the evolving role of implementation support.
14	Updating clinical guidelines and correcting errors	<p>Revisions to reflect:</p> <ul style="list-style-type: none"> • the evolution of the methods and process used to assess the need to update guidelines • the way updates to guidelines are presented for consultation and publication • the updated NICE process for handling errors. <p>An interim clinical guideline surveillance process and methods guide was published by NICE in August 2013, which replaces sections 14.1 and 14.2 in this guidelines manual. This interim process applies to guidelines being considered for updating from August 2013 onwards.</p>
Appendix A	Agreements and advice for Guideline Development Group members	Minor revisions.
Appendix B	Study design checklist	Deleted.
Appendix C	Methodology checklist: systematic reviews and meta-analyses	Title change: now appendix B; no change to content.

Appendix D	Methodology checklist: randomised controlled trials	Title change: now appendix C; no change to content.
Appendix E	Methodology checklist: cohort studies	Title change: now appendix D. Minor revisions to the supporting notes.
Appendix F	Methodology checklist: case-control studies	Title change: now appendix E; no change to content.
Appendix G	Methodology checklist: the QUADAS tool for studies of diagnostic test accuracy	Title change: now appendix F. Existing QUADAS checklist replaced by new QUADAS-2 checklist.
Appendix H	Methodology checklist: economic evaluations	Title change: now appendix G. Minor revisions.
Appendix I	Methodology checklist: qualitative studies	Title change: now appendix H. Rewording of some of the current criteria to be more in line with guideline development terminology, and to be more user friendly. Removal of some criteria that are not applicable to guideline development.
Appendix J	Methodology checklist: prognostic studies	Title change: now appendix I; no change to content.
Appendix	Evidence tables	Title change: now appendix J. New examples of tables included.

Appendix L	Modified GRADE profile	Title change: now appendix K. Deletion of the word 'Modified'. Example replaced by a GRADE profile generated by GRADE pro version 3.6.
Appendix M	Abbreviations and glossary	Title change: now appendix L. Removal of terms that are incorporated within the main NICE glossary.
Appendix N	Guide to the short clinical guideline process	Title change: now appendix M. Minor revisions to reflect changes to the process.
Appendix O	How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS	Title change: now appendix N. Changes to reflect changes in manual chapters. Removal of the 'Proposing and selecting topics for clinical guidelines' section (note that NICE's Senior Management Team has decided to remove the clinical guideline topic suggestion facility from the NICE website until future prioritising arrangements can be agreed with the Department of Health and the NHS Commissioning Board). Change in description of 'statutory' stakeholder organisations to 'standing' stakeholder organisations.

Update information

September 2013: Boxed text at the start of [chapter 14](#) about the suspension of routine 3-year reviews has been replaced by text about an [interim clinical guideline surveillance process and methods guide](#) (and this change is reflected in [Summary of main changes from the 2009 guidelines manual](#)). This interim process applies to guidelines being considered for updating from August 2013 onwards.

About this manual

This manual describes the methods used in the development of NICE guidelines. It will be updated as described in [section 1.5](#). It will replace 'The guidelines manual' (published 2009).

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Nothing in this manual shall restrict any disclosure of information by NICE that is required by law (including in particular but without limitation the Freedom of Information Act 2000).

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