National Institute for
Health and Clinical Excellence

The guidelines manual

January 2009

The guidelines manual

About this document

This document describes the methods used in the development of NICE guidelines. It will be updated as described in section 1.5.

The document will replace 'The guidelines manual' (published April 2007) and 'The guideline development process – an overview for stakeholders, the public and the NHS' 3rd edition (published April 2007; N1233).

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Contents

Acknowledgements 6
Main changes from the April 2007 manual 7
1 Introduction 9
1.1 NICE guidance 9
1.2 Who this manual is for 10
1.3 NICE clinical guidelines 10
1.4 The development process for clinical guidelines 12
1.5 Updating the guidelines manual 18
2 The scope 20
2.1 Purpose of the scope 20
2.2 The scoping group 21
2.3 Stage 1: selecting key clinical issues and drafting the scope 22
2.4 Stage 2: checking the selected key clinical issues with stakeholders 25
2.5 Stage 3: consulting on the draft scope 26
2.6 Stage 4: finalising the scope after consultation 27
2.7 Amending the final scope after publication on the NICE website 27
2.8 Further reading 28
3 The Guideline Development Group 29
3.1 Forming the GDG 29
3.2 Code of conduct and conflicts of interest 38
3.3 Identifying and meeting training needs 39
3.4 Running the GDG 40
3.5 Making group decisions and reaching consensus 42
3.6 Further reading 43
4 Developing review questions and planning the systematic review 44
4.1 Number of review questions 44
4.2 Developing review questions from the scope 44
4.3 Formulating and structuring review questions 45
4.4 Planning the systematic review 52
4.5 Further reading 53
5 Identifying the evidence: literature searching and evidence submission 54
5.1 Introduction 54
5.2 Searching for clinical evidence 54
5.3 Searching for economic evidence 60
5.4 Quality assurance of search strategies 62
5.5 Reference management software 62
5.6 Acquiring the full text of references 63
5.7 Documenting the search strategy 63
5.8 Timing of searches 64
5.9 Re-running searches 64
5.10 Calls for evidence from stakeholders 65
5.11 Additional requirements for service guidance 67
5.12 Further reading 68
6 Reviewing the evidence 69
6.1 Selecting relevant studies 69
6.2 Questions about interventions 70
6.3 Questions about diagnosis 75

6.4 Questions about prognosis 76
6.5 Using patient experience to inform review questions 76
6.6 Published guidelines 77
6.7 Further reading 78
7 Assessing cost effectiveness 81
7.1 The role of the health economist in clinical guideline development 81
7.2 Modelling approaches 84
7.3 Economic evidence and guideline recommendations 89
7.4 Further reading 90
8 Linking clinical guidelines to other NICE guidance 92
8.1 Technology appraisals 92
8.2 Interventional procedures 96
8.3 Public health guidance 98
9 Developing and wording guideline recommendations 101
9.1 Interpreting the evidence to make recommendations 101
9.2 'Only in research' recommendations 105
9.3 Wording the guideline recommendations 105
9.4 Prioritising recommendations for implementation 112
9.5 Formulating research recommendations 113
9.6 Further reading 116
10 Writing the clinical guideline 118
10.1 Guideline structure 118
10.2 Style 120
11 The consultation process and dealing with stakeholder comments 123
11.1 Principles of responding to stakeholder comments 123
11.2 Consultation on the full and NICE versions 125
11.3 Working with the editors 127
11.4 Considering a second consultation 129
12 Finalising and publishing the guideline 130
12.1 Editorial checks and review by the Guideline Review Panel (GRP) 130
12.2 The pre-publication check 132
12.3 Signing off the guideline versions 133
12.4 Typesetting and final checks before publication 134
12.5 Launching and promoting the guideline 134
13 Implementation support for clinical guidelines 136
13.1 The range of implementation support tools 136
13.2 Developing the implementation support tools 137
13.3 Publishing the implementation support tools 140
13.4 Post-publication support 140
13.5 Working with national organisations 140
13.6 Other NICE implementation services and products 141
14 Updating clinical guidelines and correcting errors 142
14.1 Collecting information after guideline publication 142
14.2 The normal updating process 142
14.3 Exceptional updates 145
14.4 Format of draft updates for consultation 146
14.5 Maintaining records 146
14.6 Correcting errors in published clinical guidelines 147
14.7 Further reading 147

Appendices

Appendix A: Agreements and advice for Guideline Development Group members 150
Appendix B: Study design checklist 158
Appendix C: Methodology checklist: systematic reviews and meta-analyses 160
Appendix D: Methodology checklist: randomised controlled trials 164
Appendix E: Methodology checklist: cohort studies 172
Appendix F: Methodology checklist: case–control studies 180
Appendix G: Methodology checklist: the QUADAS tool for studies of diagnostic test accuracy 186
Appendix H: Methodology checklist: economic evaluations 194
Appendix I: Methodology checklist: qualitative studies 208
Appendix J: Methodology checklist: prognostic studies 218
Appendix K: Evidence tables 223
Appendix L: Modified GRADE profile 228
Appendix M: Abbreviations and glossary 231
Appendix N: Guide to the short clinical guideline process 255
Appendix O: How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS 266

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- The Centre for Public Health Excellence
- The Clinical and Public Health Directorate
- The editorial team

Others

- The National Collaborating Centres (NCCs)
- Philippa Davies, who provided input to several chapters and the checklists

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Main changes from the April 2007 manual

Chapter	Change
1 Introduction	Chapter restructured and information updated.
2 The scope	Chapter completely rewritten to describe the new scoping process. Only minor changes to sections 2.6.1 and 2.6.2 (formerly 2.4.1 and 2.4.2).
Old chapter 3 (workplan)	This chapter has been removed.
3 The Guideline Development Group	Boxes 3.2, 3.3 and 3.4 have been revised. New section (3.5) added on making group decisions and reaching consensus.
4 Developing review questions and planning the systematic review	Major revisions, including introduction of the term 'review question'. Introduction of examples for different types of review questions. Extension of sections on review questions about diagnosis (4.3.2) and prognosis (4.3.3). New section 4.3.4 on using patient experience to inform review questions.
5 Identifying the evidence	Chapter completely rewritten.
6 Reviewing the evidence	Chapter rewritten. Addition of sections on economic evaluations (6.1.2) and the GRADE approach (6.2.1.1). Information provided on assessment of study quality and presenting results for questions about interventions, diagnosis and prognosis, including cost effectiveness and quality of patient experience.
7 Assessing cost effectiveness	Chapter shortened (some information moved to chapter 6). Chapter focuses on modelling.
8 Linking clinical guidelines to other NICE guidance	Some changes to section 8.1 (technology appraisals); section 8.1.2.2 on economic modelling updated. Sections 8.2 (interventional procedures) and 8.3 (public health guidance) completely rewritten.
9 Developing and wording guideline recommendations	Chapter completely rewritten. New sections on 'only in research' recommendations (9.2) and wording the guideline recommendations (9.3) added. Section on research recommendations (9.5) rewritten.
Old chapter 9 (making group decisions and reaching consensus)	Chapter removed. Part of content moved to chapter 4 and to new chapter 9.
10 Writing the clinical guideline	Some changes (not major).
11 The consultation process and dealing with stakeholder comments	Table 11.1 changed. Substantial changes to section 11.2 (consultation on the full and NICE versions). New section 11.3 added.
12 Finalising and publishing the guideline	New chapter. Includes some information from old chapter 14. Section 12.2 describes a new stage in the process: the pre-publication check.
13 Implementation support for clinical guidelines	Completely rewritten.

14 Updating clinical guidelines and correcting errors	Updating process revised.
Appendix A: Agreements and advice for Guideline Development Group members	Declaration of interests policy and forms removed from Appendix (available from the NICE website).
Appendix B: Study design checklist	New appendix.
Appendix C: Systematic review checklist	New checklist and notes.
Appendix D: Randomised controlled trials checklist	New checklist.
Appendix E: Cohort studies checklist	New checklist.
Appendix F: Case–control studies checklist	Editing changes only.
Appendix G: QUADAS tool for diagnostic test accuracy checklist	New checklist.
Appendix H: Economic evaluations checklist	New checklist.
Appendix I: Qualitative studies checklist	New checklist.
Appendix J: Prognostic studies checklist	New checklist.
Appendix K: Evidence tables	Tables revised. New evidence table for prognostic studies.
Appendix L: Modified GRADE profile	New appendix.
Appendix M: Abbreviations and glossary	Some terms deleted and some new ones added.
Appendix N: Guide to the short clinical guideline process	New appendix.
Appendix O: How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS	Rewritten.

1 Introduction

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 professionals, patients and carers[1], the academic world and the healthcare industry.

1.1 NICE guidance

NICE produces the following types of guidance:

- Clinical guidelines – guidance on the treatment and care of people with specific diseases and conditions.
- Technology appraisal guidance – guidance on the use of new and existing health technologies (including drugs, medical devices, diagnostic techniques and surgical procedures).
- Interventional procedures guidance – guidance on the efficacy and safety of surgical, endoscopic and endovascular procedures and related techniques.
- Public health guidance – guidance on the promotion and protection of good health and the prevention of disease.

All types of NICE guidance are developed using the best available evidence and involving stakeholders in a transparent and collaborative manner. Stakeholders include national organisations that represent patients and carers, healthcare professionals, the NHS, organisations that fund or carry out research, and 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 all legal obligations to:

- promote race and disability equality, and equality of opportunity between men and women, and
- eliminate unlawful discrimination on grounds of race, disability, age, sex and gender, sexual orientation, and religion or belief in the way it carries out its functions and in its employment policies and practices.

NICE's equality scheme sets out how it is meeting these obligations on equality and discrimination and what it still needs to do[2].

[1] The term 'patients and carers' is used to cover all lay people involved in developing NICE clinical guidelines, including organisations representing patient and carers. 'Patients' can include service users, parents and healthy pregnant women.
[2] The equality scheme and action plan are available at www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp

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)'[3].

1.2 Who this manual is for

This guidelines manual explains how NICE develops 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) 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, the expertise of the clinical guidelines team in the Centre for Clinical Practice (CCP) at NICE and the experience of the NCCs. It is based on internationally acceptable criteria of quality, as detailed in the Appraisal of Guidelines Research and Evaluation (AGREE) instrument[4].

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 O.

1.3 NICE clinical guidelines

NICE's clinical guidelines are recommendations, based on the best available evidence, for the care of people by healthcare 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 clinical care that is suitable for most patients with a specific condition in the NHS in England and Wales[5]
- aim to improve the quality of clinical care
- assess the clinical and cost effectiveness of treatments and ways of managing a particular condition

[3] www.nice.org.uk/aboutnice/howwework/socialvaluejudgements/socialvaluejudgements.jsp
[4] www.agreetrust.org
[5] NICE clinical guidelines are reviewed locally for their applicability to Northern Ireland (see www.dhsspsni.gov.uk).

- are developed using a process that takes account of the views of those who might be affected by the guideline (including healthcare 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 sound and transparent.

Healthcare 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 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, the first of which was published in 2007, 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 standard clinical guidelines, most short clinical guidelines are overseen by the Short Clinical Guidelines Team within the Centre for Clinical Practice (CPP) at NICE. Occasionally, NICE commissions an NCC to develop a short guideline. In all cases, a GDG is responsible for formulating the recommendations.

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 the document 'Guide to the short clinical guideline process' (appendix N).

1.3.2 Service guidance

Sometimes the Department of Health asks NICE to develop service guidance as part of the 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[6]).

The development process for NICE service guidance is largely the same as that for clinical guidelines, apart from a few differences in the composition of the GDG and the evidence base (see sections 3.1.1 and 5.11 respectively).

Some NICE clinical guidelines include recommendations about service guidance as well as about clinical management.

[6] www.nice.org.uk/Guidance/CSG/Published

1.4 The development process for clinical guidelines

The development time for a NICE clinical guideline 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 standard clinical guidelines, and their key tasks during guideline development, are listed in table 1.1.

Table 1.1 Groups involved in clinical guideline development

	Key tasks
NICE	The Centre for Clinical Practice (CCP) at NICE commissions one of the NCCs to coordinate development of the clinical guideline For short guidelines, the Short Clinical Guidelines Team within the CCP develops the guideline with the GDG The CCP lead for the guideline (Associate Director) signs off the scope The Guidelines Commissioning Manager, technical team and CCP lead support and advise the NCC during guideline development The CCP provides training for the GDG Chairs NICE's Guidance Executive approves ('signs off') the final guideline and confirms that the correct process has been followed for its development NICE publishes the NICE version of the guideline, the quick reference guide and 'Understanding NICE guidance' (see section 1.4.3) The Implementation Directorate at NICE develops the implementation support tools (see section 1.4.3 and chapter 13)
National Collaborating Centre (NCC)	Prepares the draft scope and revises the scope after consultation (see chapter 2) Prepares the workplan[7] Helps run the stakeholder scoping workshop with the CCP at NICE (see chapter 2) Appoints and works with the GDG to develop the guideline (see chapter 3) Provides full technical and managerial support for the GDG (see chapter 3) Develops the review questions with the GDG (see chapter 4) Searches, assesses and synthesises the evidence (the NCC technical team only; see chapters 3–7) Prepares the first draft of the guideline for consultation. Compiles the responses to consultation comments on the draft guideline on behalf of the GDG

[7] 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.

	Revises the guideline in response to comments received during the consultation and in accordance with NICE's review processes (see chapter 11) Responds to issues raised during the Guideline Review Panel (GRP) review of the guideline (see section 12.1.2) Corrects factual errors reported by stakeholders during the pre-publication check (see section 12.2) Publishes the final full guideline Advises NICE on issues concerning publication, dissemination, implementation and updating of the guideline
Guideline Development Group (GDG)	Contributes to preparing the scope (GDG Chair and Clinical Adviser only) Defines the review questions that will guide the search for evidence Discusses the evidence Translates the evidence into broad conclusions Develops the guideline recommendations Responds to comments received during consultation and agrees on necessary changes to the guideline Works with NICE to develop the quick reference guide, 'Understanding NICE guidance' and implementation tools (see section 1.4.3 and chapters 11–13)
Patient and Public Involvement Programme (PPIP) at NICE	Advises on patient and carer issues Identifies and approaches potential patient and carer stakeholders for each clinical guideline Provides one member of the scoping group – the PPIP lead for the guideline (see section 2.2) Encourages and facilitates applications from patients and carers who are interested in becoming GDG members Advises, supports and provides training for patient and carer members of GDGs Comments on the draft guideline recommendations from a patient and carer perspective
Guideline Review Panel (GRP)	Comments on the draft scope and draft guideline, and on the likelihood that the recommendations can be implemented Ensures that stakeholder comments on the draft scope and draft guideline have been responded to appropriately
Peer reviewers[8]	Carry out an independent review of statistical and health economic aspects of the consultation draft of the guideline

[8] NCC Health Technology Assessment (NCCHTA) peer review (see chapter 11), commissioned by NICE.

Stakeholders	Attend the stakeholder scoping workshop to discuss the scope of the guideline and the recruitment of GDG members Comment on the draft scope Respond to calls for evidence from the NCC Comment on the draft guideline Highlight any factual errors in the guideline during the pre-publication check (see section 12.2) Contribute to developing the implementation tools

More information about key groups and individuals involved in clinical guideline development is given in appendix O and on the NICE website[9].

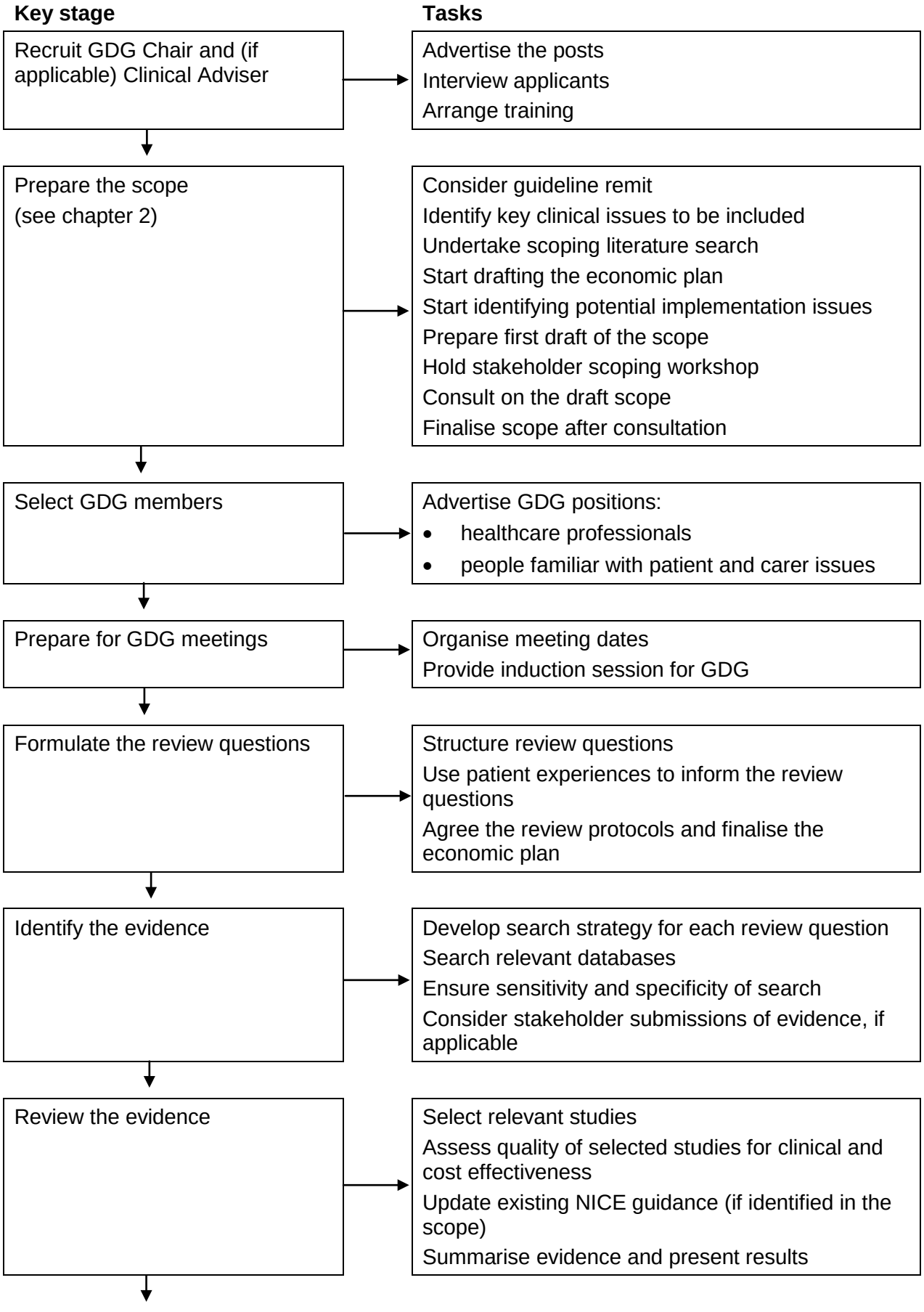
1.4.2 Summary of the clinical guideline development process

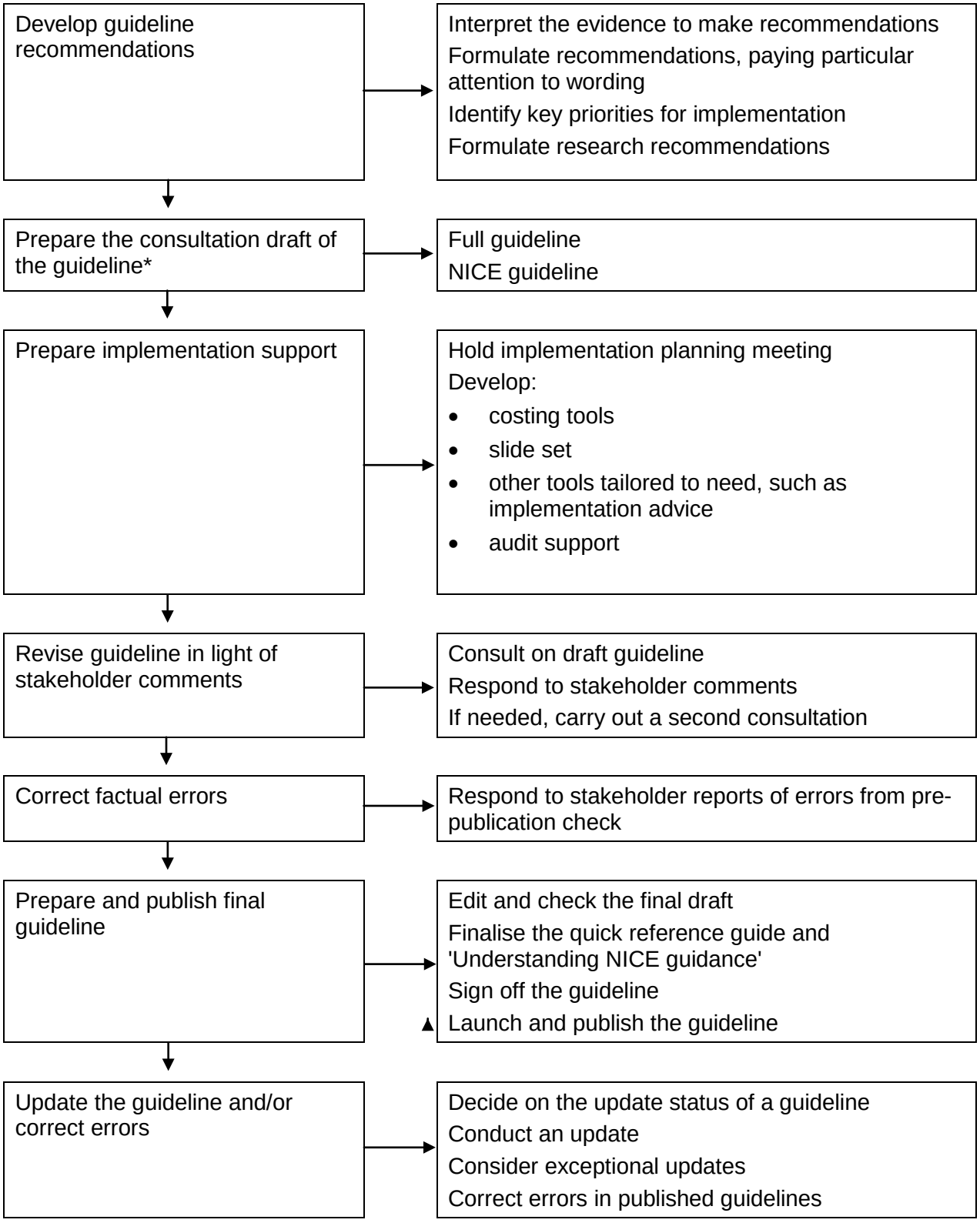
Clinical guideline topics are referred from the Department of Health. For more details on the topic selection process, see appendix O and the NICE website[10].

The key stages in the development of NICE clinical guidelines are summarised in figure 1.1.

[9] www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines
[10] www.nice.org.uk/aboutnice/howwework/howguidancetopicsarechosen

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 standard 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.
- The NICE guideline contains only the recommendations from the full guideline, without the information on methods and evidence.
- The quick reference guide summarises the recommendations in an easy-to-use format for healthcare professionals.
- 'Understanding NICE guidance' summarises the recommendations in the NICE guideline in everyday language for patients and carers.

For short clinical guidelines, three versions are usually published: the full guideline, the quick reference guide and 'Understanding NICE guidance'. A NICE version is also produced when an NCC develops a short clinical guideline.

In addition to the different versions of the guideline, NICE also produces tools to support implementation, which may include a costing report and costing template, a slide set, audit support and other tools tailored to need, such as implementation advice. (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 (www.nice.org.uk). The quick reference guide and 'Understanding NICE guidance' are also available in printed form, and anyone can obtain a copy from NICE (via NICE publications on 0845 003 7783 or publications@nice.org.uk).

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 Centre for Clinical Practice 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, NICE guideline and short clinical guideline)
- 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 from the Department of Health
- 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
- a table of stakeholder comments on the consultation draft of the scope and responses
- project history, and information on progress of the guideline
- the consultation draft of the guideline
- a table of stakeholder comments on the consultation draft of the guideline and responses
- the 'pre-publication' version of the guideline
- a list of factual errors in the pre-publication version of the guideline reported by stakeholders (if applicable) and responses
- all versions of the published guideline
- details of related NICE guidance
- 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. These should be addressed to: guidelinesmanual@nice.org.uk.

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.

2 The scope

Topics for clinical guidelines are referred to NICE by the Department of Health, based on recommendations from topic selection consideration panels. (More details on the topic selection process can be found on the NICE website[11].) The referral gives a remit that identifies the broad areas to be covered by the guideline. This remit is then translated into the scope for the guideline. Preparing the scope is the first step in developing a clinical guideline; it 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) and the remit from the Department of Health
- inform the development of the detailed review questions from the key clinical issues (see chapter 4) and the search strategy (see chapter 5)
- provide information to healthcare 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. It 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.
- Healthcare setting – for example, primary, secondary or tertiary care.

[11] www.nice.org.uk/aboutnice/howwework/howguidancetopicsarechosen

- 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 (see chapter 8).

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 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 (see section 2.4.1)
- 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)
- Project manager
- Information specialist
- Systematic reviewer
- Health economist

GDG

- Chair
- Clinical Adviser (if there is one)

NICE

- Guidelines Commissioning Manager (Centre for Clinical Practice), 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 section 2.4.1) and again after the workshop to refine the draft scope for consultation. It also discusses the 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, identifying the key clinical issues for inclusion in the scope, searching the literature and consulting with experts.

2.3.1 Considering the remit

The remit received by NICE from the Department of Health forms the basis of the scope, and all issues specified by the remit are addressed in the scope. Sometimes NICE may request clarification from the Department of Health on the remit and the topic. This may involve redefining the remit in order to specify the boundaries and the extent of the work.

In general, service configuration and delivery issues are not included in a clinical guideline unless specifically requested in the remit.

2.3.2 Identifying the key clinical issues

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. These issues should be developed out of a care pathway or a similar analytical framework. They are not the same as review questions, which specify in some detail the particular interventions to be compared and the health outcomes of interest (see chapter 4). Nevertheless, 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

- Antispasmodics for the management of IBS (irritable bowel syndrome)
- Antibiotics for preventing wound infection in women who have had an elective caesarean section
- Decision aids in prostate cancer

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. The NCC should also consider the composition of the GDG at this stage (covered in 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 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, race and ethnicity, disability, age, sexual orientation and gender reassignment, 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.

2.3.2.1 Main outcomes

The scope should include 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 or to address potential review questions in any detail. It should be based on the need to reasonably inform the content of the scope as set out above. Further searches to identify systematic reviews and economic evaluations will be necessary once the review questions have been determined (see chapter 5).

Suggested sources for this scoping search are listed in box 2.4; 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)

- Cochrane Database of Systematic Reviews – CDSR (Cochrane Reviews)[a]
- Health Technology Assessment (HTA) Database (Technology Assessments)[b]
- MEDLINE/MEDLINE In-Process
- National Guideline Clearinghouse (United States)
- National Library for Health (NLH)
- NHS Economic Evaluation Database (NHS EED) (Economic Evaluations)[b] and the Health Economic Evaluations Database (HEED), if subscribed to
- Websites of NICE and the National Institute for Health Research (NIHR) HTA Programme for guidelines 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:

- DH-Data and the King's Fund library catalogue (or the Health Management Information Consortium [HMIC] database)

[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 from the topic selection process. This includes briefing papers, extracts from minutes of the meetings, and questionnaires submitted by patient and carer organisations.

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. The up-to-date version of this template should be used by NCCs for

preparing the scope. The template is available from NICE's webboard for NCCs and from the guidelines team 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.

2.4 Stage 2: checking the selected key clinical issues with stakeholders

It is essential to seek the views of experts in the field, stakeholders and patients with the condition 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 (see section 2.5.1) are invited to a scoping workshop to discuss the key clinical issues selected by the scoping group. One person from each registered stakeholder organisation may attend. This person attends from their own perspective and does 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 scoping group also invites to the workshop key people active in the topic area in the UK, and people based in the UK who have led on national published guidelines and/or recent key reviews in the topic area.

This 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 Associate Director of the Centre for Clinical Practice at NICE who is the lead for the guideline.

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

NICE, 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 one of NICE's editors before consultation and may be modified by NICE following 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 and from the Guideline Review Panel (GRP) for that guideline (see section 2.5.2).

2.5.1 Stakeholder organisations

Organisations representing healthcare 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 O and the NICE website[12] contain details about how to register as a stakeholder and how to contribute to the guideline development process.

2.5.2 The Guideline Review Panel (GRP)

Each guideline is allocated to one of four GRPs. Information about GRP membership and allocation of guidelines to each GRP can be found on the NICE website[13]. The GRPs play an important role in providing NICE with external validation of its guideline development process. For each clinical guideline, the focus of the GRP's work is to review the scope and drafts of the guideline to ensure, in particular, that stakeholder comments have been addressed appropriately.

All GRP members and the GRP Chair are sent the draft scope at the start of the consultation period. GRP members submit their individual comments to the Chair, who collates and summarises these comments into a formal report, which is submitted to NICE. The GRP comments are then circulated to the scoping group along with the comments from the stakeholders.

The GRP Chair comments on the following:

- The overall size of the scope, and whether the amount of work required is reasonable within the timescale for development of the guideline.
- Specific methodological issues that may arise.
- Whether the scope falls within the remit from the Department of Health.

[12] www.nice.org.uk/ourguidance/niceguidancebytype/clinicalguidelines/shregistration/shregistration.jsp

[13] www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/guidelinereviewpanels

- The clarity of areas detailed in the scope.
- Any other concerns or queries about the proposed limits of the scope.

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 suggested additions 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 Signing off the final scope

GRP members and the GRP Chair review the revised scope and consider whether stakeholder comments have been addressed appropriately and adequately by the scoping group. The GRP Chair then prepares a report. Subject to any amendments agreed by NICE as a result of the Chair's report, the revised scope is signed off by the Director of the Centre for Clinical Practice at NICE.

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 is 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. 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.

2.8 Further reading

Department of Health (2006) Selection criteria for referral of topics to NICE. London: Department of Health. Available from: www.nice.org.uk/niceMedia/pdf/DH_selection_criteria_July_06.pdf

National Institute for Health and Clinical Excellence (2006) Guide to the topic selection process: interim process manual. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk/niceMedia/pdf/boardmeeting/brdnov06item4.pdf

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 professionals (both specialists in the topic and generalists)
- patients and/or carers
- the technical team (systematic reviewer, information specialist, health economist).

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 through the Guideline Review Panels and 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 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 National Collaborating Centre (NCC) 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 guideline lead (Associate Director) at the Centre for Clinical Practice (CCP) at NICE. A workable size for a GDG is 13–15 people, including the technical team from

the NCC. This balances the opportunity for individuals to contribute effectively with the need for a broad range of experience and knowledge.

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 the social care professions where relevant
- patient and carer members
- technical members
- a project manager.

Box 3.1 presents an example of GDG membership.

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).

Box 3.1 GDG membership for the clinical guideline 'Heavy menstrual bleeding' (NCC for Women's and Children's Health [NCC-WCH], published January 2007)

- Two gynaecologists
- One obstetrician
- Two GPs
- One gynaecology specialist nurse practitioner
- One radiologist
- One epidemiologist
- One clinical director
- Two members representing women's interests ('patient and carer members')
- NCC-WCH technical team (information specialist, systematic reviewer, health economist, Director)

As far as possible, the GDG will have an appropriate balance with regard to the principles of NICE's equality scheme[14].

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 (see section 3.2.3). They are expected to attend all

[14] See www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp

GDG meetings (usually between 12 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. In exceptional circumstances, if additional expertise is needed or if a GDG member needs to be replaced, the NCC should 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 (primary care trusts in England and local health boards in Wales, including specialist commissioning bodies)
- relevant clinical networks
- a chief executive or director of public health 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[15]. Templates for job descriptions and person specifications are available from NICE's webboard for NCCs, and from the guidelines team 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 3.2).

[15] www.nice.org.uk/getinvolved/joinnwc/join_a_nice_committee_or_working_group.jsp

Box 3.2 Key roles and functions of the GDG Chair

The Chair needs background knowledge about the guideline, including:

- in-depth knowledge of the scope of the guideline (as a member of the scoping group) and the topics to be covered during GDG meetings
- good knowledge of the skills mix within the GDG.

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 conflicts of interests and handles any conflicts as they arise, in line with NICE's policy[16]
- 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 (see sections 1.1.1 and 3.2.3).

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)[17], 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. 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

[16] www.nice.org.uk/getinvolved/joinnwc/patientsandlaypeople/invitationtoapplyforlaymembershipofnicescommissioningprogrammesteeringgroup/declaration_of_interests.jsp

[17] Available from: www.nice.org.uk/384476

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, the Director of the CCP (or delegate) and a non-executive director of NICE.

3.1.3 The Clinical Adviser

The Clinical Adviser is a member of the GDG with additional responsibilities. He or she works closely with the NCC technical 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, 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 2.4.1). They should represent the perspective(s) of the healthcare professionals (and social care 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 3.3.

Box 3.3 Key roles of healthcare professional members of the GDG

GDG members from the healthcare professions are expected to:

- help develop the review questions from 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 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 and feed back to the implementation team at NICE to inform the development of the implementation support tools (see section 13.2)
- with other members of the GDG, approve the review protocols (see section 4.4.2)
- 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), a completed equality monitoring form and a statement explaining how they meet the criteria laid out in the person specification. Members are selected by the Director of the NCC and the GDG Chair, and may be asked to attend an interview. Appointments will be subject to confirmation by the Director of the CCP 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 3.4.

Box 3.4 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[18] 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).

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[19]. 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[20].

- People who respond 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 and submit a personal statement 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.

[18] 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.
[19] www.nice.org.uk/getinvolved/joinnwc/join_a_nice_committee_or_working_group.jsp
[20] For details of GDGs seeking patient and carer members, see www.nice.org.uk/getinvolved/patientandpublicinvolvement

- 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 technical team

A core technical team from the NCC supports the GDG with technical experience and expertise. This team usually includes the NCC Director, an information specialist, a lead systematic reviewer (who can also be the project manager) and a health economist.

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 technical team (see chapters 4–6). The role of the information specialist involves:

- contributing to the setting of review questions
- designing and testing population and study design search filters (see section 5.2.2.7)
- contributing to discussions among the technical 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:

- setting review questions
- 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 technical 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. This is described in more detail in chapter 7.

3.1.6.4 Project manager

The project manager oversees and facilitates the whole process, organising GDG meetings and providing administrative support to the GDG Chair and members.

3.1.7 Non-GDG members attending GDG meetings

Occasionally, people who are not members of the GDG may attend a meeting, as either expert advisers or observers. They may be healthcare 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 3.2.2).

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

Observers need the prior permission of the group to attend a GDG meeting. An observer at a GDG meeting may be asked to sit apart from the group, and should not enter into the discussions unless invited to do so by the GDG. Observers 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.

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[21].

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 10.1.1).

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.

[21] See www.nice.org.uk/getinvolved/joinnwc/patientsandlaypeople/invitationtoapplyforlaymembershipofnicescommissioningprogrammesteeringgroup/declaration_of_interests.jsp

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)[22]. They should also make sure that GDG members are aware of NICE's equality scheme and action plan[23].

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 1-day training session for GDG Chairs, in collaboration with the NCCs. Everyone who is appointed as a GDG Chair is required to attend one of these training sessions. The training covers the key tasks that the Chair is expected to perform. Box 3.5 outlines the content of the training session.

Box 3.5 Content of the GDG Chair training session

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

In addition to the training 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.

[22] www.nice.org.uk/aboutnice/howwework/socialvaluejudgements/socialvaluejudgements.jsp
[23] www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp

3.3.2 Healthcare professional members

To work effectively, GDG healthcare 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 professional members should be provided by the NCC at an early GDG meeting, and should include components similar to those outlined in box 3.5.

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 technical 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 (see section 3.2.3).

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 developing the review questions. The GDG should examine the scope (including key clinical issues) and build review questions based on it. 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 a subsequent GDG meeting, the lead editor, implementation lead, costing lead and communications lead for the guideline from NICE give presentations to explain their roles. At the same time, the NICE leads will ask for nominations for GDG members to work with them on the following aspects:

- the quick reference guide and 'Understanding NICE guidance' – the GDG editorial nominees (see sections 11.3, 12.1 and 12.4)
- the implementation support tools – the GDG implementation nominees and costing nominees (see section 13.2)
- promoting the guideline (see section 12.5).

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

Most of the work with the NICE leads is done between submission of the consultation drafts of the guideline and its publication. The lead editor may also attend one or two GDG meetings towards the end of the guideline development process, and can advise on the wording of recommendations as needed.

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 developing 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 NCC for Chronic Conditions to agree key recommendations (now 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'[24].

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 outside the GDG (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 (2008) Social value judgements: principles for the development of NICE guidance, 2nd edition. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk/aboutnice/howwework/socialvaluejudgements/socialvaluejudgements.jsp

National Institute for Health and Clinical Excellence (2006) Appointments to guidance producing bodies advisory to NICE. Available from: www.nice.org.uk/384476

[24] Available from www.nice.org.uk/CG5

4 Developing review questions and planning the systematic review

Once the final scope of the clinical guideline has been agreed (see chapter 2), the key clinical issues listed in the scope need to be broken down into review questions. These 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 review questions should be developed as soon as 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) technical team 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.

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. However, they will contain more detail than the scope, and should be seen as building on the key clinical issues in the scope.

Review questions are usually drafted by the NCC technical 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. Often the main questions need refining again once the evidence has been searched, and this may generate sub-questions.

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 studies 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 health service use.

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, the majority of 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 (patient, intervention, comparison and outcome) framework (see box 4.1). This divides each question into four components:

- the patients (the population under study)
- the interventions (what is being done)
- the comparators (other main treatment options)
- the outcomes (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

Patients/population: Which patients or 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?

Comparison: 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. 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] Available from www.nice.org.uk/CG61)

By how much do antibiotics reduce wound infection in women who have had an elective Caesarean section compared with no treatment?

(Adapted from: Caesarean section. NICE clinical guideline 13 [2004]. Available from www.nice.org.uk/CG13)

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 an appendix of the 'Cochrane handbook for systematic reviews of interventions'[25].

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 physiopathological basis for treatment.

[25] See www.cochrane-handbook.org [accessed 17 August 2008].

4.3.2 Review questions about diagnosis

Review questions about diagnosis are concerned with the performance of a diagnostic test. 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 two types:

- questions about the diagnostic accuracy of the test
- 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) are compared with those of the best available test (the reference standard) in a sample of patients.

The PICO framework described in section 4.3.1 is useful when formulating review questions about diagnostic test accuracy (see box 4.3). The intervention is the test under investigation (the index test), 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

Patients/population: To which patients or population of patients would the test be applicable? How can they be best described? Are there subgroups that need to be considered?

Intervention: The test being evaluated (the index test).

Comparison: The test with which the index test is 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 outcome – this may not be the one that is routinely used in practice).

Target condition: The disease, disease stage or subtype of disease that the index test and the reference standard are being used to establish.

Outcome: The diagnostic accuracy of the test 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 diagnostic test accuracy 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 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' (see section 4.5).

Box 4.4 Examples of review questions on diagnostic test accuracy

What is the diagnostic accuracy of:

CT compared with MRI in assessing invasion of mediastinal structures and chest wall invasion in patients with potentially curable lung cancer?

CT compared with MRI in assessing the presence of cerebral metastases in patients with stage III disease?

(Adapted from: Lung cancer: the diagnosis and treatment of lung cancer. NICE clinical guideline 24 [2005]. Available from www.nice.org.uk/CG24)

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 after a diagnostic test (in combination with a management strategy) with those of patients who receive the usual diagnostic or 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]. Available from www.nice.org.uk/CG16)

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]. Available from www.nice.org.uk/CG45)

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]. Available from www.nice.org.uk/CG52)

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) are 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 have 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 (see section 4.3.1) should take into account the patient experience. Patient experience, which may vary for different patient groups ('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 representatives 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]. Available from www.nice.org.uk/CG57)

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]. Available from www.nice.org.uk/CG50)

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]. Available from www.nice.org.uk/CG37)

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

Although clinical guidelines do not in general cover issues of service delivery, sometimes NICE receives a remit from the Department of Health specifically asking for service guidance (see section 1.3.2). Examples of review questions relating to service delivery are given in box 4.7.

Box 4.7 Examples of review questions on service delivery

Does delay in the referral of patients with lesions suspicious of skin cancer by GPs affect stage of disease at presentation?

In patients with successfully treated primary small cell cancer (SCC), how effective is follow-up in secondary care in improving survival?

In patients with successfully treated primary melanoma, how effective is follow-up in secondary care in improving survival?

What are the needs of transplant patients in terms of skin cancer services?

(From: NICE cancer service guidance: Improving outcomes for people with skin tumours including melanoma. The evidence review [Feb 2006]. Available from www.nice.org.uk/CSGSTIM)

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 effects 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.

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 chapters 10 and 11). Any changes made to a protocol in the course of the work should be described.

4.5 Further reading

Cochrane Diagnostic Test Accuracy Working Group. Cochrane handbook for diagnostic test accuracy reviews (under development). Available from: http://srdta.cochrane.org/en/authors.html [accessed 18 August 2008].

Higgins JPT, Green S, editors (2008) Cochrane handbook for systematic reviews of interventions, version 5.0.0 (updated February 2008). The Cochrane Collaboration. Available from www.cochrane-handbook.org [accessed 26 August 2008].

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.

NHS Centre for Reviews and Dissemination (2001) Undertaking systematic reviews of research on effectiveness: CRD's guidance for those carrying out or commissioning reviews. CRD Report 4, 2nd edition. York: NHS Centre for Reviews and Dissemination, University of York. Available from: www.york.ac.uk/inst/crd/report4.htm [accessed 21 November 2007].

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.

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 National Collaborating Centre (NCC) technical teams and in the Short Clinical Guidelines Team based at NICE. 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.

Table 5.1 Databases that should be searched (listed in suggested order of searching)

Question type	Databases
Review questions about interventions, diagnosis, prognosis[a], patient experience and service delivery	*Core databases:* Cochrane Database of Systematic Reviews – CDSR (Cochrane reviews)[b] Database of Abstracts of Reviews of Effects – DARE (other reviews)[c] Cochrane Central Register of Controlled Trials – CENTRAL (clinical trials)[b] Health Technology Assessment (HTA) database (technology assessments)[c] MEDLINE/MEDLINE In-Process EMBASE CINAHL (Cumulative Index to Nursing and Allied Health Literature) *Subject-specific databases (this list is not exhaustive):* AMED (Allied and Complementary Medicine Database) C2 Register of Interventions and Policy Evaluations – C2-RIPE (Campbell Collaboration) SPECTR (Campbell Collaboration) ERIC (Education Resources Information Center) PEDro (Physiotherapy Evidence Database) PsycINFO

[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.

[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.

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. 2008a). 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, 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. 2008b).

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)	www.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
National Institute for Health Research National Research Register (NRR) Archive	https://portal.nihr.ac.uk/Pages/NRRArchiveSearch.aspx
Web of Science	www.scientific.thomson.com/products/wos
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/sites3/page.cfm?orgId=527&pid=24601
National or regional registers, for example cancer registers	
National or regional audits	
Database of Individual Patient Experiences (DIPEx)	www.dipex.org
Surveys of patients' experiences	

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 (patient, intervention, comparison and outcome) framework (see section 4.3.1 and

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 comparisons (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.

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[26] and precision[27]. 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.

[26] Defined as 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).

[27] Defined as the number of relevant records retrieved by a search strategy as a proportion of the total number of records retrieved (Jenkins 2004).

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:
  - Final search set
  - Exp Animals/ not Humans/
  - 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 below) 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. 2008b) 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[28], 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 (see sections 5.3.1 and 5.3.2).
- 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 7.2.2 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.

[28] www.york.ac.uk/inst/crd/intertasc

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

- NHS EED (NHS Economic Evaluation Database)[29], 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 [Centre for Reviews and Dissemination] search filter developed to identify economic evaluations for NHS EED). Information specialists should use their judgement as to 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.

[29] 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.

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.
- Investigate why relevant papers have not been retrieved by the search strategy, 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.

Adept Scientific supplies EndNote, Reference Manager and ProCite in the UK and also provides technical support for the software. Import filters and output styles can be downloaded free of charge from the Adept Scientific website[30]; Adept Scientific will also create or modify import filters and output styles on request.

[30] www.adeptscience.co.uk

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). For most journals the online content dates back to around 1996, although some go back further and are gradually adding content from earlier years. 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 (www.freemedicaljournals.com)
  - Genamics JournalSeek (www.journalseek.net).
- NHS Core Content and its Welsh equivalent, HOWIS, provide free access to some journals for all NHS staff and staff in organisations such as the NCCs that work exclusively for the NHS. An Athens log-in is needed to access NHS Core Content, which can be obtained by applying to the Information Services team at NICE (library@nice.org.uk).
- 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 2008.

- 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 of results and/or a Reference Manager/Endnote/ProCite database of results.

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

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.

The MEDLINE search strategies for each review question and for the economic searches should be made available to stakeholders during consultation on the draft guideline. They should also be published at the same time as the final full guideline in either print (as an appendix) or electronic format. 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 consultation on the draft guideline begins. 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

The health economist should discuss the need for any re-runs with the information specialist. As for clinical searches, economic evaluation literature searches should be re-run 6–8 weeks before consultation on the draft guideline begins. 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 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 7.2.2).

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, data on adverse effects, economic models, and studies of the experiences of patients, carers or healthcare 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 participants, intervention, comparisons, outcome 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.

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 in order 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[31].

[31] For example, see www.nice.org.uk/229411

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 5.7), 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 identify 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 guidance 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: fourth national survey 1991–1992', Office for National Statistics[32].

[32] www.statistics.gov.uk/CCI/SearchRes.asp?term=morbidity+statistics+from+general+practice

5.12 Further reading

Centre for Reviews and Dissemination (2001) Undertaking systematic reviews of research on effectiveness: CRD's guidance for carrying out or commissioning reviews. 2nd edition [online]. Available from: www.york.ac.uk/inst/crd/report4.htm [accessed 21 July 2008].

Glanville J (2001) Phase 3: identification of research. In: Undertaking systematic reviews of research on effectiveness: CRD's guidance for carrying out or commissioning reviews. 2nd edition. Centre for Reviews and Dissemination. Available from: www.york.ac.uk/inst/crd/report4.htm [accessed 21 July 2008].

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

Lefebvre C, Eisinga A, McDonald S, Paul N (2008a) 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 (2008b) Searching for studies. In: Higgins JPT, Green S, editors. Cochrane handbook of systematic reviews of interventions. Version 5.0.1 (updated September 2008). The Cochrane Collaboration. Available from www.cochrane-handbook.org [accessed 24 November 2008].

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

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 four major steps:

- 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 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 criteria agreed by the GDG. Abstracts that do not meet the 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 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 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. Because it is sometimes difficult to identify the exact design used in a study, a checklist is provided to help the systematic reviewer to classify study design for answering questions of effectiveness (see appendix B).

Once a study has been classified, it should be assessed using the methodology checklist for that type of study (see appendices C–F). To minimise errors and any potential bias in the assessment, two reviewers should independently assess 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 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

GRADE is a system developed by an international working group for appraising and summarising the quality and strength of recommendations (see box 6.1)[33].

Box 6.1 The GRADE approach to assessing the quality of evidence

In the GRADE system, the following features are assessed for the evidence found for each relevant outcome from a systematic review:

- study design (as a proxy for bias)
- limitations in the methodological quality of the study (mainly allocation concealment, blinding and loss to follow-up)
- consistency of an effect across studies
- directness (the degree to which the results directly address the question posed or, for example, are for a somewhat different population).

Other considerations:

- imprecision
- likelihood of reporting bias
- strength of association
- evidence of a dose–response relationship
- expected effect of plausible confounders.

NICE has begun to use elements of the GRADE approach for questions about interventions in its clinical guidelines, although it will take some time for this to affect all guidelines, as it is being phased in. The main differences between NICE's approach and that of the GRADE system are that NICE:

- also integrates a review of the quality of cost-effectiveness studies
- has no overall summary labels for the quality of the evidence or the strength of a recommendation
- uses the wording of recommendations to reflect the strength of the recommendation (see chapter 9).

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 K1). 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.

[33] See British Medical Journal series, appendix L and www.gradeworkinggroup.org for more details about GRADE.

The body of evidence addressing a question should then be presented within the text of the full guideline as an evidence profile or 'Summary of findings' table, as described in the GRADE system (see appendix L). GRADEpro software can be used to prepare these. Evidence profiles summarise the quality of the evidence and the outcome data for each important clinical outcome. A 'Summary of findings' table includes a limited description of the quality of the evidence. If these tables are used, full evidence profiles should be presented in an appendix. 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 the NHS Centre for Reviews and Dissemination, and the Cochrane Collaboration handbook (see section 6.7).

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

6.2.3 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 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 H). 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 H) 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). There is also a section on the methodological quality of the study; that is, the extent to which it succeeds in fulfilling its stated objectives (analogous to the GRADE ‘limitations’ criterion). .

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 the study 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 an individual 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.

6.2.4 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 evidence profile (see appendix L). Whenever a GRADE evidence 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.

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

A short evidence statement should be presented alongside the evidence profile, 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; these are described in 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 and management strategy) should be addressed in the same way as intervention studies (section 6.2.1).

6.3.1 Assessing study quality

Studies of diagnostic test accuracy should be assessed using the methodology checklist for QUADAS (Quality Assessment of Studies of Diagnostic Accuracy included in Systematic Reviews) (appendix G). Characteristics of data should be extracted to a standard template for inclusion in an evidence table (see appendix K2). 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 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, 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. The GRADE working group is developing an approach for summarising the evidence for diagnostic tests and strategies. 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 (appendix G) 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 J). 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 J) 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, whether to exclude certain studies, and when summarising and presenting the body of evidence for the question about prognosis as a whole (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 J 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 K3).

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 I). 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, 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 I 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 tabulating the studies included to aid presentation. Methods to synthesise qualitative studies (for example, meta-ethnography) are evolving rapidly, 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 K4).

6.6 Published guidelines

Relevant published guidelines may be identified in the search for evidence. These can be NICE clinical guidelines or other guidelines.

6.6.1 NICE clinical guidelines

NICE clinical guidelines should be fully referenced and the evidence underpinning the recommendations should be left unchanged, provided it is not out of date. If there is new published evidence that would significantly alter the existing recommendations, the NCC should follow the process for the early update of clinical guidelines (described in chapter 14).

6.6.2 Other guidelines

Other relevant published guidelines identified in the search should be assessed for quality using the AGREE (Appraisal of Guidelines Research and Evaluation) instrument (The AGREE Collaboration 2003) 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 the early update of NICE clinical guidelines (described in chapter 14).

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 (for example, national service frameworks).

6.7 Further reading

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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.

Higgins JPT, Green S, editors (2008) Cochrane handbook for systematic reviews of interventions. Version 5.0.0 [updated February 2008]. The Cochrane Collaboration. Available from: www.cochrane-handbook.org

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.

Edwards P, Clarke M, DiGuiseppi 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, Vist GE et al. for the GRADE Working Group (2008) GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. British Medical Journal 336: 924–6.

Guyatt GH, Oxman AD, Kunz R et al. for the GRADE working group (2008) What is "quality of evidence" and why is it important to clinicians? British Medical Journal 336: 995–8.

Guyatt GH, Oxman AD, Kunz R et al. for the GRADE working group (2008) Going from evidence to recommendations. British Medical Journal 336: 1049–51.

Guyatt GH, Oxman AD, Kunz R et al. for the GRADE working group (2008) Incorporating considerations of resources use into grading recommendations. British Medical Journal 336: 1170–3.

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

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

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.

NHS Centre for Reviews and Dissemination (2001) Undertaking systematic reviews of research on effectiveness: CRD's guidance for those carrying out or commissioning reviews. CRD Report Number 4, 2nd edition. York: NHS Centre for Reviews and Dissemination, University of York. Available from: www.york.ac.uk/inst/crd/report4.htm

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.

Schunemann 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.

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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.

The AGREE Collaboration (2003) Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. Quality and Safety in Health Care 12: 18–23. Available from: www.agreetrust.org [accessed 6 February 2008]

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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.

Guideline recommendations should be based on the estimated costs of the treatment options 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 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 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) technical team, and should be involved at the earliest opportunity – from the beginning of scoping if possible (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 useful input into the interpretation of clinical data.

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

- advise on economic issues
- review economic evaluations
- prioritise questions for further economic analysis
- 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 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). This document is prepared by the health economist in consultation with the rest of the NCC technical team and the GDG, and is discussed and signed off by NICE, usually within 3 months of 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. The rationale for the final choice of priorities for economic modelling should be explained in the full guideline.

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'[34] (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) perspective, and measurement of quality of life (QoL) 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

Examining relevant published economic information is an important component of clinical guideline development. Processes for searching for, selecting, appraising and summarising economic evaluations are discussed in sections 5.3, 6.1.2, 6.2.3 and 6.2.4.

The general approach to reviewing economic evaluations should be systematic but focused. 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 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 criteria for economic evaluations should be designed to filter out such papers (see section 5.3).

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 models should be developed selectively, unless an existing model can easily be adapted to answer the question.

[34] www.nice.org.uk/aboutnice/howwework/socialvaluejudgements/socialvaluejudgements.jsp

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 modelling 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 model assumptions are plausible
- the results of the analysis are interpreted appropriately and the limitations acknowledged.

Economic analysis is potentially useful for any question in which one intervention or programme 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, economic modelling 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 when 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 QALYs (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 health-related QoL (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. In 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.

Table 7.1 Summary of the reference case[35]

Element of health technology assessment	Reference case
Defining the decision problem	The scope developed by the Institute
Comparator	Therapies routinely used in the NHS, including technologies regarded as current best practice
Perspective on costs	NHS and PSS
Perspective on outcomes	All health effects on individuals
Type of economic evaluation	Cost-effectiveness analysis
Synthesis of evidence on outcomes	Based on a systematic review
Measure of health effects	QALYs
Source of data for measurement of HRQoL	Reported directly by patients and/or carers
Source of preference data for valuation of changes in HRQL	Representative sample of the public
Discount rate	An annual rate of 3.5% on both costs and health effects
Equity weighting	An additional QALY has the same weight regardless of the other characteristics of the individuals receiving the health benefit
HRQoL, health-related quality of life; PSS, personal social services; QALYs, quality-adjusted life years.	

The 'Guide to the methods of technology appraisals' also states:

> 'For the reference case, the perspective on outcomes should be all direct health effects, whether for patients or, when relevant, other people (principally carers). The perspective on costs should be that of the NHS and PSS. Some interventions 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). If costs to other government bodies are believed to be significant, they may be included in a sensitivity analysis and presented alongside the reference case results. Productivity costs and costs borne by

[35] This is table 5.1 in 'Guide to the methods of technology appraisal' (updated June 2008); available at: www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/guidetothemethodsoftechnologyappraisal.jsp. Further detail about these methods is provided in a series of briefing papers that are available on the NICE website.

patients and carers that are not reimbursed by the NHS or PSS should not be included in any analyses.

'Sensitivity analysis should be used to explore the impact of potential sources of bias and uncertainty on model results. Potential bias resulting from key structural assumptions should be explored through deterministic sensitivity analyses, testing whether and how the model results change under alternative plausible scenarios. Deterministic sensitivity analysis should also be used to test the impact of potential bias resulting from the selection of data sources for key model parameters. Probabilistic sensitivity analysis is preferred for exploring uncertainty arising from imprecision in model parameters. This enables the uncertainty associated with all parameters to be reflected simultaneously in the results. In non-linear decision models, probabilistic methods also provide the best estimates of mean costs and outcomes. However, models incorporating probabilistic methods are more time-consuming to construct and may not always be a priority for health economists working on clinical guidelines. In such cases, the decision not to use probabilistic methods should be clearly stated and justified in the full guideline, and the impact of parameter uncertainty should be thoroughly explored through deterministic sensitivity analysis.'

The 'Guide to the methods of technology appraisal' includes other useful advice for health economists developing economic models for use in clinical guidelines.

7.2.1 General principles

Regardless of the modelling approach taken, the following principles should be observed.

- The question for the economic analysis should be clearly specified and appropriate, with comparison of all relevant alternatives for specified groups of patients.
- Analysis should be carried out by the health economist in collaboration with the rest of the GDG.
- An economic analysis should be underpinned by the best-quality clinical evidence.
- There should be the highest level of transparency in the reporting of methods and results. Conventions on reporting economic evaluations should be followed (see Drummond and Jefferson 1996).
- Potential sources of bias and uncertainty should be explored using appropriate sensitivity analysis and discussed with the GDG.
- Limitations of the approach taken and methods used should be discussed with the GDG.

7.2.2 Identification and selection of model inputs

The NICE reference case (table 7.1) states that evidence on health outcomes should be obtained from a systematic review. It is not necessary to conduct formal systematic literature searches for all types of information required for economic modelling. However, health economists should use transparent processes for identifying other model inputs, assure their quality and justify their inclusion.

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' report or the Department of Health tariff. Information on costing can also be found in the NICE document 'Developing costing tools: methods guide'[36] and through discussion with the NICE costing analyst for the guideline. Some information about epidemiology or health service use might also be better obtained from national statistics or databases than from studies in the literature.

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 look at pragmatic options for identifying inputs. Examples include using the clinical evidence for that key clinical issue (and perhaps other relevant issues) and liaising with the systematic reviewer, other GDG members and other experts. 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.

QoL data are often needed for economic models. Many of the QoL 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 QoL 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 QoL search filter when executing additional searches for key clinical issues of high economic priority. The provision of QoL 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. Another resource for identifying useful sources of utility data for economic modelling is the database of preference weights on the CEA (Cost-Effectiveness Analysis) Registry website[37].

[36] www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines
[37] http://160.109.101.132/cearegistry/default.asp

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 incremental cost-effectiveness ratio (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'[38]. 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

[38] www.nice.org.uk/aboutnice/howwework/socialvaluejudgements/socialvaluejudgements.jsp

> 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.'

Decisions about whether to recommend an intervention should not be based on cost effectiveness alone. The GDG should also take into account other factors, including the requirements to prevent discrimination and to promote equality[39]. As described in chapter 9, these factors should be explained in the 'evidence to recommendations' sections of the full guideline.

If a key clinical issue has not been prioritised for new economic analysis, the GDG should still consider the likely cost effectiveness of associated recommendations. This assessment may be based on published estimates of cost effectiveness if available, or a qualitative judgement if necessary.

7.4 Further reading

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

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.

NHS Centre for Reviews and Dissemination (2001) Improving access to cost-effectiveness information for health care decision making: the NHS Economic Evaluation Database. CRD report number 6, 2nd edition. York: NHS Centre for Reviews and Dissemination, University of York. (Superseded by the 2007 NHS EED handbook: www.york.ac.uk/inst/crd/pdf/nhseed-handb07.pdf)

[39] See NICE's equality scheme: www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp

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. Available from: www.bmj.com

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 cover broad aspects of 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.

The Centre for Health Technology Evaluation at NICE develops technology appraisal and interventional procedures guidance. Public health guidance is the responsibility of the Centre for Public Health Excellence. Details of the development processes and methods for other programmes can be found on the NICE website (www.nice.org.uk).

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 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 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.
- 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.

Process guides for technology appraisals are available on the NICE website[40]. Updated process guides for MTAs and STAs will be published by NICE in 2009.

8.1.1 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 two possible approaches:

- The technology appraisal guidance is incorporated verbatim into the clinical guideline.
- The technology appraisal guidance is updated through the clinical guideline development process (see section 8.1.2).

Relevant recommendations from a published technology appraisal that do not need updating should be reproduced unchanged in the most appropriate section of the clinical guideline.

If technology appraisal recommendations are being incorporated into a clinical guideline, any 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. An example might be where the appraisal recommendation covers both primary and secondary care, but the guideline recommendation is concerned with secondary care only.

8.1.2 Updating technology appraisal guidance in a clinical guideline

Planning the update of a technology appraisal is described in the technology appraisal process guides[40]. The National Collaborating Centre (NCC) becomes a commentator for the appraisal, which allows it to have formal input into the process of updating the appraisal. The final decision on whether an 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 updating a technology appraisal, the objective for a GDG is to determine whether any new evidence that has become available since the publication of the appraisal means that the original recommendations need to be changed. The original recommendations should be changed only if warranted by new evidence and supported by cost-effectiveness analysis. The reasons for any changes should be clearly documented in the full version of the clinical guideline. When a technology appraisal is updated in a clinical guideline, the original appraisal will be withdrawn when the guideline is published. The funding directive (which states that the NHS provides funding and resources for medicines and treatments that have been recommended by NICE technology appraisals, normally within 3 months from the date that NICE publishes the guidance) will no longer apply.

[40] www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp

Early planning is essential to identify how the NCC will undertake any updates of technology appraisals that fall within the scope of a clinical guideline. The mechanisms described below will facilitate an update.

8.1.2.1 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.

8.1.2.2 Economic modelling

If there is significant new clinical evidence or a change in costs since the original technology appraisal, the NCC will need to conduct an economic evaluation to determine whether a change in the guidance is appropriate. 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). 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 at NICE during development of the economic plan.

8.1.3 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, to ensure that the final recommendations in the guideline and the appraisal are complementary and consistent:

- timing
- exchange of information
- publication of recommendations.

8.1.3.1 Timing

Where possible, the development of related clinical guidelines and technology appraisals should be coordinated so that the published appraisal recommendations can be incorporated into the consultation draft of the guideline (see chapter 11). Details of the timelines should be negotiated between the NCC and the guidelines and appraisals teams at NICE.

8.1.3.2 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 may 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 (usually the technical lead for the appraisal) will advise the GDG on the integration of the appraisal into the guideline, and will attend GDG meetings as appropriate.
- The GDG will act as a commentator for the relevant appraisal. Commentators have an opportunity to comment on all documents (scope, assessment report and appraisal consultation document). However, they are not required to make a submission and they do not have the right to appeal against the final appraisal determination.
- 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. 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.

8.1.3.3 Publication of recommendations

The GDG should not publish its own recommendations in a clinical guideline in areas already covered in the scope of any relevant ongoing technology appraisal.

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

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

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'[41] [an updated version is due for publication in early 2009].)

Published IP guidance that is relevant to the guideline may 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[42]. As clinical guidelines focus on placing established treatments in the care pathway, they will generally only include IP guidance published under '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 GDG decides that IP guidance for which 'normal' arrangements are recommended is relevant to its clinical guideline but does 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 evidence on that procedure, they will inform the IP Programme at NICE.

Review question justified

If the GDG considers that a procedure published under 'normal' arrangements for IP guidance justifies a review question, the NCC will consider the clinical and cost effectiveness of the procedure using the usual methods for clinical guidelines (see chapters 6 and 7). NICE will include the IP Programme Associate Director as a stakeholder so that the IP team can comment on the scope and review the relevant sections of the guideline.

[41] www.nice.org.uk/aboutnice/howwework/developingniceinterventionalprocedures/interventionalproceduresprogrammemanual
[42] www.nice.org.uk/usingguidance/implementationtools/interventionalproceduresarrangements

If a procedure is found to be clinically and cost effective, the GDG will recommend its use in practice. In such cases, use of the procedure will become a recommendation in the guideline and the existing IP guidance will remain active. This is because the IP guidance may 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 footnote referring to the IP guidance, and a note referring to the clinical guideline will be inserted on the NICE webpage for the IP guidance.

When a procedure is found to be not clinically and/or cost effective, the GDG will recommend that it should not be used. In such cases, the IP guidance for that procedure will be withdrawn. In some cases, the clinical guideline and the IP guidance may address different but overlapping indications. This will mean that sometimes the IP guidance will need to remain current even if it is superseded by a clinical guideline for one or some indications.

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 (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.

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 the procedure should only be carried out in research or that it should not be used. These recommendations are made if the IP Advisory Committee deems the evidence base insufficient to make recommendations for even conditional use, or – in the case of a recommendation not to use the procedure – if there is no evidence of efficacy and/or safety, or evidence of lack of efficacy and/or safety. The evidence base for such procedures 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 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 should be 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 Guidelines Commissioning Manager that the notified procedure is relevant to the 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 'The public health guidance development process: an overview for stakeholders, including public health practitioners, policy makers and the public' (to be published during 2009).

The Department of Health 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 Programme Development Group (PDG) or the Public Health Interventions Advisory Committee (PHIAC) for the prevention and/or early identification of a condition – the CPHE manages the PDG and PHIAC.
- The GDG for clinical management – the NCC manages the GDG and reports to the Guidelines Commissioning Manager 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 Guidelines Commissioning Manager
- PDG or PHIAC 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, 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 PDG and the GDG (PHIAC is a standing advisory committee) 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 PDG (or PHIAC) 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.

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 professionals.

In the full guideline, the aim should be to show clearly how the GDG moved from the evidence to the recommendation. This is best done in a section called ‘evidence to recommendations’ or similar 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 (Schunemann 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 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 only choosing outcomes for which there were statistically significant results.

It may be important to note outcomes that were not considered useful, and why (such as surrogate outcomes if longer-term, more relevant outcomes are available).

9.1.2 Trade-off between clinical benefits and harms

A key stage in moving from evidence to recommendations is balancing 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.

9.1.4 Quality of the evidence

There should be discussion of how the presence of potential biases and uncertainty in the clinical and economic evidence has influenced the recommendation, and why. For example, evidence on the frequency of adverse effects is often of low quality, which may make the balance of benefits and harms less clear.

This 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 this 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[43] have been discharged in reaching the recommendation(s). This covers inequalities related to sex and gender, race and ethnicity, disability, age, sexual orientation and gender reassignment, religion and belief, 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.

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. Some of the common challenges and possible solutions are listed in table 9.1.

[43] www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp

Table 9.1 Evidence into recommendations: challenges and possible solutions

Challenge	Possible solution
The literature search has found no evidence that addresses the review question	The GDG should consider using consensus to identify current best practice. This process should be robust; it may follow the methods of formal consensus, or the issues may be resolved through discussions in the GDG (see section 3.5).
The quality of the clinical evidence is poor	Generating evidence specifically for the purposes of the guideline is unlikely to be feasible. If this approach is considered, the GDG should decide what sort of research could best address the question, and whether this might be possible. There is unlikely to be value in the GDG commissioning research that results in poor-quality evidence. Proposals to commission research to generate evidence should be discussed with NICE.
The available clinical evidence is conflicting	All efforts should be made to identify the reasons for conflicting evidence. If, for example, this is because different groups of people respond differently to an intervention, then the GDG should consider making very specific recommendations.
The clinical evidence is not directly applicable to the population covered by the guideline, for example because of a different age group	The GDG may wish to extrapolate to the recommendations from the evidence – for example, from high-quality evidence in a largely similar patient group. 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.
There is no published estimate of cost effectiveness that is applicable to the relevant population	The GDG should consider whether to develop its own estimate of cost effectiveness through further economic analysis (see section 7.1.3). If this is not considered a priority for the health economist's time, or if it is not possible because of lack of data, the GDG should still consider whether the proposed recommendation is likely to represent a cost-effective use of NHS resources.
The GDG is unsure whether healthcare professionals would endorse a recommendation	It can be difficult to make recommendations if there is little reliable evidence. Use of formal consensus methods to test the level of stakeholder agreement has been advocated as a way to provide more representative views than can be obtained from the GDG. However, it should be noted that stakeholders will be giving 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. Such techniques also effectively allow some stakeholders an 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 these techniques, and should discuss any proposed use with NICE. The final decision on whether these methods are warranted is 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 (see chapter 3), and should:

- focus on the actions readers need to take
- 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
- 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 also 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.

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.'

- 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'.

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 being considered, offer to refer the patient to a specialist surgeon to discuss the risks and benefits.'

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.

Examples

- Instead of 'an intervention may be offered', say 'consider offering 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).

9.3.2 Include what readers need to know

Recommendations should be clear and concise, but should contain enough information to be understood without reference to supporting material. This is important, because in the NICE guideline and the quick reference guide the recommendations are published without details of the evidence they are based on.

- Define any specialised terminology that is used in the recommendations, and make sure it is unambiguous (for example, the abbreviation ‘CV’ could stand for cardiovascular or cerebrovascular).
- Define the target population unless it is obvious from the context.
- Include cross-references to other recommendations if necessary to avoid the need to repeat information such as treatment regimens or definitions of terms.
- 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 (see section 9.3.3).
- 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.

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.

Example

- 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.

9.3.3.2 Recommendations for interventions that should or should not be used

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

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

Example

- Offer bariatric surgery as a first-line option (instead of lifestyle interventions or drug treatment) for adults with a BMI of more than 50 kg/m^2.

Use similar forms of words for recommendations on interventions that should not be used because the GDG is confident that they are not worthwhile for most patients.

Example

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

A ‘should’ recommendation can be combined with (or followed by) a ‘could’ recommendation – for example, where treatment is strongly recommended but there are two or more options with similar cost effectiveness, and the choice will depend on the patient’s preference.

Examples

- Offer drug therapy, adding different drugs if necessary, to achieve a target blood pressure of 140/90 mmHg.

- For patients aged 55 or older or black patients of any age, consider a calcium-channel blocker or a thiazide-type diuretic as initial therapy.

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 are similarly cost effective, or some patients may opt for a less effective but cheaper intervention. The choice of intervention (or the decision on whether to have an intervention at all) is therefore likely to vary depending on a person's values and preferences. NICE's report on social value judgements[44] 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.'

Where possible, word recommendations of this type as direct instructions (see section 9.3.1), rather than using the word 'could'. Add 'consider' before the verb to indicate that the recommendation is less strong than a 'should' recommendation – for example, 'consider offering a referral'.

Example

- Consider offering bariatric surgery to adults with obesity if all of the following criteria are fulfilled: …

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, use 'offer' and 'discuss' in recommendations, rather than 'prescribe' or 'give'.

Use words such as '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.

9.3.5 Recommendations on drugs, waiting times and ineffective interventions

Guideline developers should follow NICE's standard procedure when referring to drugs or waiting times (see below). It is also acceptable to make recommendations that advise stopping the use of an ineffective intervention.

9.3.5.1 Drugs

Use generic names

Give the recommended international non-proprietary name (rINN), as listed in the 'British national formulary' (www.bnf.org). 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.

[44] 'Social value judgements: principles for the development of NICE guidance' (2nd edition; 2008); available at: www.nice.org.uk/aboutnice/howwework/socialvaluejudgements/socialvaluejudgements.jsp

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 clear evidence about the effectiveness of different dose levels. SPCs can be found in the Electronic Medicines Compendium (www.emc.medicines.org.uk).

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 for which the drug regulatory authority has allowed the manufacturer to market the drug (called a marketing authorisation; often referred to as the licensed indications) in the UK. The application for a marketing authorisation is accompanied by an SPC, which describes the indications, cautions and contraindications for a drug based on the best available information at the time.

Use for an indication for which the product does not have a marketing authorisation (off-label or off-licence use) may be recommended if there is clear evidence to support this. The National Collaborating Centre and GDG should check recommended uses against 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 and that informed consent should be obtained and documented. 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.

Box 9.1 Examples of footnotes to guideline recommendations about the off-label use of drugs

Where use is outside the licensed indication:

Vaginal PGE_2 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 PGE_2 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 PGE_2 for women with ruptured membranes, and informed consent should be obtained and documented.

[From: Induction of labour. NICE clinical guideline 70 (2008). Available from www.nice.org.uk/CG70]

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. There is strong evidence for its effectiveness and safety. This evidence 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. Informed consent on the use of metformin in these situations should be obtained and documented.

[From: Diabetes in pregnancy: management of diabetes and its complications from pre-conception to the postnatal period. NICE clinical guideline 63 (2008). Available from www.nice.org.uk/CG63]

9.3.5.2 Waiting times

Avoid giving targets for waiting and referral times: refer to relevant targets set by the Department of Health or the Welsh Assembly Government. If no target exists, recommendations may include a maximum time if the GDG considers this to be essential.

9.3.5.3 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

Non-trauma-focused interventions such as relaxation or non-directive therapy, that do not address traumatic memories, should not routinely be offered to people who present with PTSD symptoms within 3 months of a traumatic event.

From: Post-traumatic stress disorder (PTSD): the management of PTSD in adults and children in primary and secondary care. NICE clinical guideline 26 (2005). Available from www.nice.org.uk/CG26

9.3.6 Using tables in recommendations

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

Healthcare professionals should use a stepped approach for managing atopic eczema in children. This means tailoring the treatment step to the severity of the atopic eczema. Emollients should form the basis of atopic eczema management and should always be used, even when the atopic eczema is clear. Management can then be stepped up or down, according to the severity of symptoms, with the addition of the other treatments listed in table 2.

Table 2 Treatment options

Mild atopic eczema	Moderate atopic eczema	Severe atopic eczema
Emollients	Emollients	Emollients
Mild potency topical corticosteroids	Moderate potency topical corticosteroids	Potent topical corticosteroids
	Topical calcineurin inhibitors	Topical calcineurin inhibitors
	Bandages	Bandages
		Phototherapy
		Systemic therapy

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). Available from www.nice.org.uk/CG57

9.4 Prioritising recommendations for implementation

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. Users of the guideline will need to decide which recommendations they should implement first. To help with these decisions, GDGs are required to identify 'key priorities for implementation'. These are the recommendations likely to have the biggest impact on patient care and patient outcomes in the NHS as a whole. The number of recommendations prioritised in this way will vary depending on the guideline, and should normally be between five and ten. These recommendations are the ones for which NICE provides clinical audit support, promotional slide sets and other tools to aid implementation (see chapter 13).

Many different criteria can be used to select the key priorities for implementation, but key priorities should always be recommendations 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
- 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 Support Team. Criteria 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 key priority. 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. This section provides a framework for highlighting these uncertainties and translating them into research recommendations. Advice is also given about identifying ‘high-priority’ research recommendations for inclusion in the NICE version of the guideline.

Research recommendations can cover questions about any aspect of the guidance and are designed to address uncertainties that have been identified. Examples include clinical or cost effectiveness, implementation, outcomes, equality issues, the accuracy of a test, diagnosis, prognosis, rates of harm or other events, patients’ experience, measurements of outcome, and service delivery and organisation. Primary research or secondary research (for example, systematic reviews) can be recommended.

In undertaking economic modelling for a clinical guideline, part of the analysis is to identify the parameter and structural uncertainties to which the decision is most sensitive. This information can help with decisions about future research priorities. As part of cost-effectiveness analysis, formal value-of-information methods may also sometimes be used to estimate the ‘value for money’ of additional research.

9.5.1 Principles for formulating research recommendations

Research recommendations should be formulated as questions. A section that includes the questions requiring further research should be included as an appendix to the full guideline. These research questions may also be highlighted in individual chapters.

Each research question should relate to an uncertainty or evidence gap that has been identified during the guideline development process. Each research recommendation should be formulated as an answerable question or a set of closely related questions (see box 9.4). This should use the PICO (patient, intervention, comparison and outcome) framework as presented in chapter 4 (box 4.1).

Box 9.4 An example of a research question

Is benzoyl peroxide or adapalene more clinically and cost effective at reducing the number of non-inflammatory lesions in the treatment of acne vulgaris in adolescents?

9.5.2 Selecting high-priority research recommendations for the NICE guideline

To help ensure that research addresses key areas, for a standard clinical guideline the GDG should select up to five high-priority research recommendations to include in the NICE version of the clinical guideline. These should be identified using the criteria in table 9.2.

Table 9.2 Criteria for selecting high-priority research recommendations

Criterion	Explanation
Importance to patients or the population	What would be the impact on the population of any new or altered guidance (for example, acceptability to patients, quality of life, morbidity or disease prevalence, severity of disease or mortality)?
Relevance to NICE guidance	How would the answer to this question change future NICE guidance (that is, generate new knowledge and/or evidence)? How important is the question to the overall guideline? The research recommendation should be categorised into one of the following categories of importance: • High: the research is essential to inform future updates of key recommendations in the guideline • Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates • Low: the research is of interest and will fill existing evidence gaps.
Relevance to the NHS	What would be the impact on the NHS and (where relevant) the public sector of any new or altered guidance (for example, financial advantage, effect on staff, impact on strategic planning or service delivery)?
National priorities	Is the question relevant to a national priority area (such as a national service framework or white paper)? The relevant document should be specified.
Current evidence base	What are the problems with the current evidence base? (that is, why is further research required?) Reference should be made to the section of the full guideline that describes the current evidence base, including details of trials and systematic reviews.
Equality	Does the research recommendation address equality issues? For example, does it focus on groups that need special consideration, or focus on an intervention that is not available for use by people with certain disabilities?
Feasibility	Can the proposed research be carried out within a realistic timescale and at an acceptable cost? Are there any ethical or technical issues?
Other comments	Any other important issues should be mentioned, such as potential funders or outcomes of previous attempts to address this issue, or methodological problems. However, this is not a research protocol.

Each high-priority research recommendation should be summarised in a single paragraph (ideally no longer than 150 words) that describes why the proposed research is important (for an example, see box 9.5). The reasons for selecting each high-priority research recommendation should be presented in a table in an appendix to the full guideline, using table 9.2 as a template, and indicating if any information is unavailable.

The high-priority research recommendations for each clinical guideline will be posted on the NICE website[45]. They will then go through a second prioritisation process within NICE that considers all research recommendations relating to all types of guidance produced by NICE.

Box 9.5 An example of a high-priority research recommendation

Research recommendation

Further research should be undertaken to determine whether benzoyl peroxide or adapalene is more clinically and cost effective at reducing the number of non-inflammatory lesions in the treatment of acne vulgaris in adolescents.

Why this is important

Acne affects up to 80–90% of adolescents, and research has shown that it can have serious effects on self-esteem. Retinoids are currently recommended as first-line treatment for acne, despite the lack of robust evidence comparing them with treatments that have been demonstrated to be clinically and cost effective. A community-based double-blind randomised controlled trial is required to compare the clinical and cost effectiveness of 0.1% adapalene and 5% benzoyl peroxide gels. The trial should enrol adolescents aged 12–18 years with mild or mild/moderate inflammatory or polymorphic facial acne vulgaris (grade 0.5–1.5 on the Burke and Cunliffe scale) with at least 15 inflamed and 15 non-inflamed lesions. Adolescents with acne primarily on their back and chest, nodular acne, comedonal acne or acne owing to secondary causes should be excluded. The primary outcome measure should be a self-assessment of improvement at each visit (6-point Likert scale). Secondary outcome measures should include quality of life, overall satisfaction with product and the combined acne severity score.

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.

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.

[45] www.nice.org.uk/research/index.jsp?action=rr

Sackett DL, Straus SE, Richardson WS (2000) Evidence-based medicine: how to practice and teach EBM, 2nd edition. Edinburgh: Churchill Livingstone.

Schunemann 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.

10 Writing the clinical guideline

At the end of the process of guideline development, four separate documents are published for standard clinical guidelines (see section 1.4.3). These are:

- the full guideline
- the NICE guideline
- a quick reference guide (a summary of all the recommendations for healthcare professionals)
- 'Understanding NICE guidance' (information for patients and carers).

The National Collaborating Centre (NCC) (with the Guideline Development Group [GDG]) writes the full guideline and the NICE guideline. The lead editor from NICE writes the quick reference guide and 'Understanding NICE guidance', working with the NCC and GDG (see sections 11.3, 12.1.1 and 12.4 for more details).

This chapter is aimed at those responsible for writing the full and NICE guidelines. It describes the key principles for writing guidelines and what each version should include.

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 which version of the guidelines manual was used for developing the guideline.

The structure and format of the full guideline are at the discretion of the NCC, but core elements should be as follows:

- a summary section containing:
  - all the recommendations, highlighting the recommendations that are key priorities for implementation and the reasons for selecting them
  - the algorithm(s) (see section 10.2.4)
- an introduction, containing information on:
  - funding
  - GDG membership
  - epidemiological data
  - aim and scope of the guideline
  - scheduled review of the guideline
- a methods section, containing information on:
  - the literature search strategy (see chapter 5)
  - how the evidence was reviewed and synthesised, including economic analysis (see chapters 6 and 7)
  - any consensus techniques used that involved people outside the GDG (see section 3.5.2)

  - interpretation of the evidence and development of the recommendations
  - other work relevant to the guideline (for example, related NICE guidance that has been published or is in preparation; related NHS documents)
- chapters dealing with the review questions and the evidence that led to the recommendations, each with the following content:
  - review question(s) (PICO [patient, intervention, comparison and outcome] format) (see chapter 4)
  - evidence profile (modified GRADE profile [see section 6.2.1.1 and appendix L], including summary of economic studies)
  - evidence statement (short text summary of the evidence on clinical and cost effectiveness)
  - 'evidence to recommendations' (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 [see section 9.1])
  - recommendation(s)
  - recommendations for research (if applicable)
- references
- appendices, which should include:
  - declarations of interest
  - review protocols (see chapter 4)
  - details of search strategies (see chapter 5)
  - evidence tables (preferably on a CD-ROM) (see appendix K)
  - prioritisation of research recommendations (see section 9.5).

10.1.2 The NICE guideline

The NICE guideline presents the recommendations from the full guideline in a format that focuses on implementation by healthcare professionals and NHS organisations. 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 that needs to be added to the NICE guideline template is:

- a brief introduction (not more than a page) explaining why the guideline is needed, and the key issues that the guideline will address
- the 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)
- related NICE guidance
- GDG membership.

Background information should not usually be 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. The NICE lead editor can advise on this if required.

The NICE Word template includes a standard section on patient-centred care which covers general issues such as informed consent, providing information tailored to the patient's needs, and involving and supporting carers and families. Specific recommendations should not be made on these issues unless there are particular reasons to do so that relate to the guideline topic. Examples include:

- where there are issues relating to provision of information to patients, or to patients' support needs, that are specific to the condition discussed by the guideline
- where certain drugs are prescribed off-label or off-licence (see section 9.3.5.1) and more detailed forms of consent than usual are required from patients.

The NICE guideline should contain the algorithm(s) (see section 10.2.4) as an appendix.

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' (available from the NICE webboard for NCCs).

The full guideline and the NICE guideline should be written in a style that can be understood by the non-specialist healthcare practitioner and by anyone who has a good knowledge of the area 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 as much as possible. The NICE editorial team can advise on this.

Use of numbered chapters and corresponding numbered headings helps readers to navigate the document. A maximum of four levels of numbered heading (for example, 2, 2.1, 2.1.4, 2.1.4.2) should be used in the full guideline. For unnumbered headings, use the same style (such as bold or italic) to denote the same level or type of heading in each section or chapter.

Recommendations in the NICE version of the guideline may be numbered 1, 2, 3 etc. (or R1, R2, R3 etc.) if this is the style used by the NCC in the full guideline. Alternatively, the numbering in the NICE version may follow the headings (for example, 1.1.1, 1.1.2, 1.1.3).

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 only 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 if a lot are used.

10.2.4 Algorithm

An algorithm is a flow chart of the clinical decision pathway described in the guideline in which decision points are represented by boxes linked by arrows.

The full and NICE versions of the guideline should contain an algorithm unless this is inappropriate for the topic (for example, most mental health topics). The algorithm may form the basis of the quick reference guide (see section 11.3.2), and should be discussed by the lead editor and the NCC (and GDG members if appropriate) during the development of the guideline.

The algorithm should be uncluttered: boxes should be limited to those defining the clinical problem and those representing a clear decision point. Arrows should mostly flow from top to bottom. A logical sequence should be maintained so that each decision flows from the question that precedes it. It may be necessary to produce more than one algorithm if the recommendations cannot be summarised into one chart.

If an algorithm is not appropriate, the recommendations may be summarised in other ways, including tables, boxes or flow charts showing the care pathway.

Algorithms and other summary charts should summarise recommendations; they should not include any further information or advice.

11 The consultation process and dealing with stakeholder comments

Consultation with stakeholders, which lasts 8 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 National Collaborating Centres (NCCs) on responding to stakeholder comments following consultation.

This chapter also includes information on what to expect during the consultation process, including how members of the Guideline Development Group (GDG) and the NCC work with editors at NICE on the different versions of the guideline. 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 2.6.1).

11.1.1 Responding to comments

It is expected that most comments will be received from registered stakeholders. These comments, and the responses to them, are posted on the NICE website when the pre-publication check of the full guideline takes place (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 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 or NICE version.
- Section – this column can be used by the NCC and GDG to facilitate the identification of comments by section.
- 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 has been 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 comments made on draft guidelines:
  - responses and changes must be made with the agreement of the whole GDG before publication, preferably through a GDG meeting (the date for which should be agreed in advance to ensure that all GDG members can attend)
  - any changes must be reflected in both the NICE and full guidelines; 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]; available from: www.nice.org.uk/CG51) (NCC for Mental Health)

Type of comment	Example of a response
Compliments about the guideline	Thank you for your comments.
A specific change was recommended and has subsequently been made	Thank you; we have changed 'legal' to 'pharmacy provided medication'. Thank you for your comment; we have addressed this issue in the full guideline (section 7.6).
A specific change was recommended and has subsequently been partially made	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.
A specific change was recommended and has subsequently NOT been made	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.
Asks for something that is outside the scope of the guideline	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.
Concern about impact of the guideline	We appreciate that the impact upon benefits is an important issue and it is under consideration by the implementation team.

11.2 Consultation on the full and NICE versions

This section describes what to expect during the consultation phase. Draft versions of both the NICE guideline and the full guideline are consulted on.

11.2.1 Stakeholders

Draft versions of the full and NICE guidelines 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

11.2.2.1 The NCC Health Technology Assessment (NCCHTA) review

NICE commissions in-depth expert statistical and health economic reviews of all clinical guidelines through a third party, the National Coordinating Centre for Health Technology Assessment (NCCHTA, www.ncchta.org), which is part of the NHS National Institute for Health Research. This review takes place during consultation on the guideline. Comments from the NCCHTA reviewers 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 'external expert review'.

11.2.2.2 Additional external expert advice

Occasionally, NCCs may consider arranging additional external expert review of part or all of a clinical guideline. These experts may include healthcare professionals, 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 The Guideline Review Panel (GRP)

Comments are also received from members of the GRP, who send their comments to NICE via the GRP Chair. GRP members aim to ensure that:

- the guideline is clinically relevant
- any major areas of concern are identified
- the guideline contains realistic expectations of NHS service providers and those who commission NHS care.

The GRP also ensures that stakeholder comments on the draft guideline have been responded to appropriately (see section 12.1.2).

The GRP Chair is expected to ensure that:

- all elements of the agreed scope have been addressed
- the guideline produces recommendations for the NHS, and for other bodies only in specific circumstances.

Comments from the GRP are entered into the guideline consultation table and are responded to in the same way as comments from registered stakeholders, but they are not posted on the NICE website.

If there are any queries or concerns about significant issues raised, the NCC should contact the Guidelines Commissioning Manager at NICE as soon as possible to discuss an appropriate response.

11.2.4 NICE staff

NICE staff also comment on the consultation draft of the guideline, both before and during the consultation (see section 11.3.1). These staff include the Patient and Public Involvement Programme (PPIP) lead, the implementation lead and the lead editor for the guideline, as well as the health economist and the Guidelines Commissioning Manager from the Centre for Clinical Practice.

Comments from NICE staff received during consultation are entered into the guideline consultation table and are responded to in the same way as comments from registered stakeholders, but these are not posted on the NICE website.

11.3 Working with the 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 quick reference guide (QRG) and 'Understanding NICE guidance'. The lead editor and other members of the editorial team work on these documents 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. The timelines and fine details are agreed between the NCC and NICE around the time that the draft guideline is sent to NICE.

11.3.1 NICE guideline

The lead editor carries out a detailed edit of the NICE guideline before consultation starts, and agrees changes with the NCC. Comments from the other NICE teams are also discussed at this stage. Agreed changes to recommendation wording are transferred to the full guideline.

The lead editor also comments on the NICE version of the guideline during consultation (like other stakeholders).

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, as well as during updating of the guideline.

11.3.2 Quick reference guide (QRG)

The QRG is a practical resource for healthcare professionals to use on a day-to-day basis. It presents the guideline recommendations in a concise, easy-to-use format, and is printed and distributed to healthcare professionals and managers in the NHS. It contains the key priorities for implementation verbatim, as well as a summary of the guideline recommendations. It usually includes all the recommendations, but occasionally highly specialised recommendations may be omitted, with signposting to the NICE version of the guideline for more details if needed.

The QRG is written by the lead editor, working closely with nominated members of the NCC and GDG (see section 11.3.4). It may be based on the algorithm(s) (see section 10.2.4), so early discussion between the editor and the NCC is helpful.

General discussions on content and possible formats of the QRG should begin before the draft guideline is submitted to NICE. A detailed plan is prepared by the lead editor during the consultation period.

11.3.3 'Understanding NICE guidance'

'Understanding NICE guidance' summarises the recommendations in the NICE guideline 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 leaflets.

'Understanding NICE guidance' is drafted during the consultation period by the lead editor, working closely with the NCC and nominated members of the GDG (see section 11.3.4). The PPIP lead for the guideline comments on the wording of 'Understanding NICE guidance' from a patient perspective.

11.3.4 Role of GDG members

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 QRG and 'Understanding NICE guidance'. Ideally these GDG editorial nominees should include at least one clinician for the QRG, and at least one patient and carer member for 'Understanding NICE guidance'. Their role is to:

- attend a meeting with the lead editor during the consultation period (see below)
- gather the views of GDG members on key issues concerning the QRG and 'Understanding NICE guidance'
- check for clinical accuracy, answer queries and check revisions on behalf of the GDG.

During the consultation period, a meeting is arranged between the lead editor, the GDG editorial nominees and at least one staff member from the NCC (such as the project manager); the GDG Chair may also attend. The main aim

of this meeting is to discuss the plan for the QRG and the first draft of 'Understanding NICE guidance', which are circulated in advance. The wording of the recommendations in the NICE version of the guideline may also be discussed.

The NCC is responsible for circulating drafts of the QRG and 'Understanding NICE guidance'; the GDG editorial nominees may be involved in collating comments from other GDG members.

11.4 Considering a second consultation

In exceptional circumstances, the Director of the Centre for Clinical Practice at NICE may consider the need for a further 4-week stakeholder consultation. This additional consultation may be required after the standard 8-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.

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 updated versions are then sent to NICE. It is essential for the National Collaborating Centre (NCC) to keep an audit trail of what changes have been made, in which version(s) of the guideline, by whom, and for what purpose.

The final draft of the guideline is reviewed by the Guideline Review Panel (GRP) and by NICE. The Guidelines Commissioning Manager and the lead editor at NICE will liaise with the NCC about any further changes that are required.

After changes have been agreed, the guideline undergoes the pre-publication check (see section 12.2) and is signed off by NICE's Guidance Executive (see section 12.3).

This section summarises the main stages involved in finalising the guideline. The timelines and fine details are agreed between the NCC and NICE around the time that the updated guideline is sent to NICE.

12.1 Editorial checks and review by the Guideline Review Panel (GRP)

The NICE guideline is edited by the NICE editors (see section 12.1.1) at the same time as the full guideline is reviewed by the GRP (see section 12.1.2).

12.1.1 Editorial checks

When the updated versions of the full and NICE guidelines are returned to NICE, the lead editor will:

- edit the NICE guideline
- draft the quick reference guide (QRG), working with the GDG editorial nominees (see section 11.3.4) and the NCC to ensure clinical accuracy
- update the draft 'Understanding NICE guidance' in line with changes to the guideline recommendations and advice from the GDG and NCC.

Before the pre-publication check (see section 12.2), the lead editor sends the edited NICE guideline and latest drafts of the QRG and 'Understanding NICE guidance' to the NCC and GDG to be checked and for queries to be answered. The NCC and GDG editorial nominees 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/or editorial nominees from the GDG. The PPIP (Patient and Public Involvement Programme) lead for the guideline at NICE also comments on the draft of 'Understanding NICE guidance' from a patient and carer perspective.

The NCC is responsible for circulating drafts of the QRG and 'Understanding NICE guidance' to the rest of the GDG if appropriate, and for collating comments. The NCC is also responsible for ensuring that all final queries are answered before publication, and should be prepared to respond rapidly if required.

It is important to check all of the documents carefully at this stage, because only essential changes can be made to recommendations after the pre-publication check. When checking the edited documents, the developers should give special attention to:

- queries and comments from the editors (these will be highlighted as Word comments in the text)
- dosages, units, normal ranges or abnormal cut-offs (for example, for electrolytes or blood constituents)
- consistency of the recommendations between the full guideline, the NICE guideline, the algorithm(s), the QRG and 'Understanding NICE guidance'
- the accuracy of the care pathways in the algorithm(s)
- reference details.

'Understanding NICE guidance' 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.

All comments from the NCC and GDG should be collated and returned to the lead editor as a single response. The GDG editorial nominees should ensure that any conflicting views within the GDG have been resolved before comments are returned to the editor.

After this stage, the NCC and lead editor work together to resolve outstanding queries on the NICE guideline, including any raised by the GRP and other teams at NICE (see section 12.1.2). This should be completed before the pre-publication check. Final changes to the 'Understanding NICE guidance' and quick reference guide can be agreed during the pre-publication check.

The lead editor keeps an audit trail of any changes made to the recommendation wording in the NICE guideline. Changes may be made during or after GRP review of the full guideline (see below). When all changes have been agreed, the NCC is responsible for ensuring that the wording of the recommendations in the full guideline matches that in the final NICE guideline.

12.1.2 Review by the GRP

In parallel with the editorial checks, the GRP reviews the revised full guideline and the 'guideline consultation table' that lists stakeholder comments received during consultation and the responses by the developers. If any outstanding issues are raised by the GRP Chair at this point, NICE will inform the NCC, indicating whether further changes to the full guideline should be considered. Any issues raised by teams at NICE will be discussed with the NCC at the same time.

The GDG may meet for a final time after receiving the comments from the GRP and NICE, if this is needed to resolve any issues identified.

The NCC should respond to any issues raised by the GRP Chair, indicating how it will amend the guideline. If it is not willing to make changes, the NCC should provide a detailed explanation as to why not. This may lead to further dialogue between the NCC, the Director of the Centre for Clinical Practice (CCP) and the Guidelines Commissioning Manager at NICE, and the GRP Chair.

The NCC should 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 The pre-publication check

The pre-publication check provides registered stakeholders with the opportunity to raise any concerns about factual errors and inaccuracies that may exist in the revised full guideline after consultation. This is intended to assist NICE in ensuring that it produces accurate guidance that contains no factual errors.

A pre-publication check is not a second consultation (see section 11.4), or an opportunity to reopen arguments and issues on which the GDG has made recommendations. Nor is it an opportunity for stakeholders to ask why the guidance has not been amended in response to their comments. New evidence will not be accepted.

Factual errors are instances where there is an objective error of material fact in the proposed full final guideline that should be corrected before publication. Box 12.1 gives examples of what may be considered as a factual error by NICE. Factual errors do not include disagreements surrounding scientific or clinical interpretation or judgement. Where there is a body of respected scientific or medical opinion that would support a conclusion, even if that conclusion is not the majority view, this cannot be defined as an objective error of fact.

Box 12.1 Examples of what may be considered as a factual error

- Incorrect referencing of studies – for example, wrong year or wrong journal
- Errors in the transcription of data – for example, '4.9 months' instead of '4.9 years', '£100' instead of '£1000'
- Incorrect reference to the licensed indications of a drug
- Errors of fact in the appraisal of a study – for example, describing it as randomised when it was not

12.2.1 The pre-publication check process

The pre-publication check occurs after the NCC and the GDG have responded to stakeholder comments from consultation on the draft guideline and the GRP has reviewed the comments and responses (see section

12.1.2), but before NICE's Guidance Executive signs off the final version of the guideline (see section 12.3). Because the pre-publication check takes place before final proofreading, the wording of some of the recommendations may subsequently change in the final published version, for reasons other than factual accuracy.

During the pre-publication check, the full guideline is posted on the NICE website for a period of 15 working days, together with the guideline consultation table that lists comments received during consultation from stakeholders and responses from the developers. All registered stakeholders are informed of the posting. Stakeholders are invited to report factual errors (see above). Reporting of errors must be done using a standard proforma. Reports of errors are not considered if they are received after the 15-working-day period, are from non-registered stakeholders, or are in a format other than using the proforma.

12.2.2 Dealing with reports of errors received during the pre-publication check

NICE, the NCC and the GDG Chair consider the reports of errors received from registered stakeholders, and respond only to those related to factual errors as defined above. A decision is made as to whether corrections are needed. If corrections are not needed, the guideline is considered by NICE's Guidance Executive for final sign-off (see section 12.3).

If corrections are needed, errors are corrected and the full guideline is revised by the developers and resubmitted to NICE, together with a list of the reported factual errors and the responses. The revised full guideline is then considered by Guidance Executive for final sign-off.

The list of reported errors from the pre-publication check and the responses are published on the NICE website together with the final guideline.

12.3 Signing off the guideline versions

Once the pre-publication check has been completed, the other versions of the guideline will be revised if required. All guideline versions will then be signed off:

- The full guideline is signed off by NICE's Guidance Executive on advice from the GRP.
- The NICE guideline is also signed off by NICE's Guidance Executive, but only when the full guideline has been finally signed off by NICE.
- 'Understanding NICE guidance' is signed off by the PPIP lead and the CCP lead for the guideline (Associate Director) at NICE.
- The QRG is signed off by the CCP lead for the guideline (Associate Director) at NICE.

12.4 Typesetting and final checks before publication

Once the guideline has been signed off, the lead editor sends the NICE guideline and the typeset proofs of 'Understanding NICE guidance' and the QRG for a final check by the NCC and GDG. As before, the GDG editorial nominees coordinate the response from the GDG members. This check needs to be done quickly (usually within 48 hours), so the editor will give as much notice as possible of when to expect the proofs.

Once the editor receives final comments on the proofs for 'Understanding NICE guidance' and the QRG from the NCC, the GDG Chair and the GDG editorial nominees, the documents are updated and sent to be printed. Printing happens at least 2 weeks before the launch date of the guideline.

The guideline is published on the fourth Wednesday of the month (except in December, when it is earlier).

12.5 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.

12.5.1 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 London office. 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.

12.5.2 Reaching the target audience

NICE welcomes input from GDG members on how to identify groups of healthcare professionals and specialists who should receive 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, including the 'Shared learning database', which gives examples of how organisations have successfully met the challenges of putting NICE guidance into practice, are described in section 13.6.

13 Implementation support for clinical guidelines

The aim of the NICE implementation support strategy is to encourage and promote the uptake of NICE recommendations. The key priorities for implementation (see section 9.4) form the focus of the implementation support work for a clinical guideline.

The implementation support tools are developed by staff from the Implementation Directorate at NICE, in consultation with the Guideline Development Group (GDG), the National Collaborating Centre (NCC), the Centre for Clinical Practice (CCP) Guidelines Commissioning Manager and the Patient and Public Involvement Programme lead for the guideline.

This chapter outlines the methods and process for developing the implementation support tools, and the contributions of the GDG, NCC and CCP to this process.

13.1 The range of implementation support tools

Each clinical guideline is supported by the following implementation support tools:

- a slide set (in the form of a PowerPoint presentation)
- audit support
- a costing report and costing template.

Further 'bespoke' implementation support tools are developed according to need (see section 13.1.4).

The slide set and bespoke implementation tools are written by an implementation adviser, the audit support is prepared by an audit specialist, and a costing analyst is responsible for the costing tools. The GDG and the NCC technical team are consulted during the development of all of the implementation support tools. A description of each of the tools is available on the NICE website[46].

13.1.1 Slide set

The slide set is designed to raise awareness of the guideline by providing a framework for discussion at a local level. The slides cover the key priorities for implementation from the guideline, and can be modified for local use.

13.1.2 Audit support

Audit support consists of audit criteria and a data collection tool for each guideline, to assist organisations in monitoring and reviewing their practice against the key priorities for implementation.

13.1.3 Costing tools

Costing tools are provided to help organisations in assessing the cost of implementing NICE clinical guidelines. The cost-impact work carried out by

[46] www.nice.org.uk/usingguidance/implementationtools

the costing analyst involves assessing all guideline recommendations to identify those with greatest resource impact[47] – these will not necessarily be the key priorities for implementation. NICE provides two types of costing tools to accompany a clinical guideline:

- The costing report, which summarises the estimated national costs of implementing the guideline and discusses the assumptions made in reaching this figure.
- The costing template, which allows users to estimate the local cost impact of implementing the guideline based on their population and by changing the assumptions and variables to reflect local circumstances.

Occasionally, implementing the recommendations in a clinical guideline may not 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 'Bespoke' implementation support tools

In addition to the implementation support tools that are produced routinely, the implementation team will develop bespoke tools. These are tailored to needs that are identified in the implementation planning meeting (see section 13.2.2) or in other discussions with stakeholders. Examples of bespoke implementation support tools include:

- implementation advice to aid with action planning at an organisational level
- templates for referral letters
- flow charts
- fact sheets
- checklists.

These might include 'jointly badged' initiatives; that is, tools developed jointly with other organisations such as professional or patient groups.

13.2 Developing the implementation support tools

Some implementation support tools are developed during development of the clinical guideline, whereas others are developed nearer to guideline publication.

13.2.1 Initial stages during guideline development

During scoping of the guideline (see chapter 2), the NICE implementation adviser starts a log to identify potential implementation issues that may arise. This log is kept up to date throughout the guideline development process to inform the development of the implementation support tools.

The costing analyst and the implementation adviser attend a GDG meeting to give a short presentation about their work and how the GDG can support this.

[47] See 'Developing costing tools – methods guide'; available at www.nice.org.uk/usingguidance/implementationtools/costingtools/costing_tools.jsp?domedia=1&mid=F3E04B99-19B9-E0B5-D46097AFA4B0DCE6

The GDG nominates three members to contribute to the development of the slide set, bespoke tools and audit support (the 'GDG implementation nominees') and two members to contribute to the development of the costing tools (the 'GDG costing nominees').

During the development of the clinical guideline, the costing analyst identifies 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 general research, including discussions at the implementation planning meeting (see below).

13.2.2 The implementation planning meeting

The NICE implementation adviser (together with the NICE implementation support coordinator) organises an implementation planning meeting during public consultation on the draft guideline. This meeting is attended by the GDG Chair, one of the GDG implementation nominees, the NCC director, and the implementation adviser, costing analyst and other staff from NICE. Registered stakeholder organisations may also be invited to attend the meeting. The purposes of this meeting are:

- to seek the views of national organisations and professional bodies on the key implementation issues, including barriers to and levers for the implementation of the guideline recommendations
- to identify possible opportunities for joint working or linked initiatives.

At the meeting, the GDG Chair usually presents the draft key priorities for implementation and any other implementation issues that have been identified by the GDG. Presentations are also given on the implementation support tools.

Attendees at the implementation planning meeting may present their views, but it is important that registered stakeholders also submit their written comments on the draft guideline using the formal consultation process (see chapter 11).

Following the implementation planning meeting, the implementation adviser writes a support plan that highlights key activities to be undertaken. The support plan is shared with the CCP Guidelines Commissioning Manager, the NCC and the GDG to ensure that they are aware of the range of activities being undertaken and which tools will be produced.

13.2.3 Commenting on the draft implementation support tools

The NCC and the GDG implementation nominees receive a copy of the first drafts of the implementation support tools for comment. They are invited to comment on the following general aspects:

- accuracy
- whether the tools relate directly to the recommendations in the guideline
- whether the tools are based on the key priorities for implementation
- clinical relevance.

The different implementation support tools are published at different times, and so drafts are sent for comments at different times.

13.2.3.1 Slide set and costing tools

The draft slide set is sent to the NCC and the GDG implementation nominees 4–5 weeks before publication of the guideline for a 1-week consultation period. Comments are invited on:

- content (accuracy, validity and value)
- format and presentation
- usefulness and applicability
- possible questions to promote discussion.

The costing 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 directly back to the NICE implementation adviser or costing analyst, with a copy to the CCP Guidelines Commissioning Manager.

13.2.3.2 Audit support and bespoke tools

Drafts of the other implementation support tools (audit support and bespoke tools) are sent to the NCC and the GDG implementation nominees for their comments approximately 2 weeks before publication of the guideline. There is a 2-week consultation period.

The NCC and the GDG nominees send their comments directly back to the NICE implementation adviser and/or audit specialist, with a copy to the CCP Guidelines Commissioning Manager.

13.3 Publishing the implementation support tools

The publication times of the different implementation support tools are as follows:

- costing tools are published at the same time as the guideline
- the slide set is published 2 weeks after publication of the guideline
- audit support and bespoke tools are published 10 weeks after publication of the guideline.

These publication dates have been scheduled in response to feedback received by NICE about which tools are needed when.

Publication dates are announced in the NICE 'Into practice' bulletin[48].

13.4 Post-publication support

In addition to producing the implementation support tools, NICE and the NCC may also take part in other activities to help NHS staff implement a clinical guideline after it has been published. These activities are identified in the implementation support plan (see section 13.2.2) and may include:

- speaking at, and encouraging/supporting GDG members to speak at, relevant conferences or events, and contributing to and/or writing journal articles about the guideline
- speaking about the implementation support 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.

13.5 Working with national organisations

As well as developing the implementation support tools, the implementation adviser also works in partnership with national organisations and networks. This might include getting recommendations from NICE clinical guidelines incorporated into other guidelines or initiatives (for example, changes in a national screening programme to take account of a NICE guideline) or developing joint implementation tools or events (for example, working with the National Treatment Agency for Substance Misuse on the NICE clinical guidelines about drug misuse[49]). The implementation advisers welcome suggestions from GDG members on how to work with national organisations to support the implementation of a clinical guideline.

[48] For details, see www.nice.org.uk/newsevents/infocus/Intopractice.jsp
[49] See www.nice.org.uk/CG51 and www.nice.org.uk/CG52

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 six implementation consultants[50] work with organisations to help to put NICE guidance into practice. Each consultant works with 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[51]; reports of uptake of guidance are provided on ERNIE [Evaluation and review of NICE implementation evidence][52].
- Commissioning guides are provided to support commissioners of services[53]. These aid in the local implementation of NICE clinical guidelines through commissioning, and are underpinned by the guidelines. Each commissioning guide comprises a series of text-based web pages that signpost and provide topic-specific information on key clinical and service-related issues to be considered during the commissioning process. They also offer an indicative benchmark of activity to help commissioners determine the level of service needed locally. Within each commissioning guide, an interactive tool provides data for local comparison against the benchmark, and resources to estimate and inform the cost of commissioning intentions.
- Guideline-specific education support resources are also provided online.

50 www.nice.org.uk/usingguidance/niceimplementationprogramme/introducing_local_nice_representatives.jsp

51 www.nice.org.uk/usingguidance/sharedlearningimplementingniceguidance

52 www.nice.org.uk/usingguidance/evaluationandreviewofniceimplementationevidenceernie

53 www.nice.org.uk/commissioningguides

14 Updating clinical guidelines and correcting errors

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, frequency and methods for updating NICE clinical guidelines. It also describes the process for correcting errors in guidelines that are identified after publication.

The responsibility for updating a clinical guideline usually rests with the National Collaborating Centre (NCC) that originally developed it. In exceptional circumstances, an NCC may be asked to update a guideline developed by another NCC. This will only occur after consultation with the relevant NCCs, including clarification of copyright issues.

When scheduling updates of clinical guidelines into its work programme, NICE will seek advice from the topic selection team (see chapter 2) on the relative priority of topics for updating and topics for the development of new guidelines. This will be communicated to NCCs through the business planning process.

14.1 Collecting information after guideline publication

After publication of a clinical guideline, the NCC should collect information relevant to the guideline that might affect the timing or content of subsequent updates. This may include any queries or comments received by NICE or the NCC after publication, and evidence submitted by researchers or other stakeholders. This information should be collected and reviewed in order to identify any new information that may warrant a change in guideline recommendations

NICE and the NCC will not actively seek new evidence on an ongoing basis, beyond collating post-publication comments, unless it has been identified in the guideline that important new information is likely to emerge before the 3-year scheduled review. In such instances, the NCC is responsible for alerting NICE to the new evidence and advising on the need for an exceptional update or amendment (see section 14.3).

14.2 The normal updating process

The NCC advises the Centre for Clinical Practice (CCP) at NICE about the need for, and extent of, an update 3 years after publication of a clinical guideline. In determining whether an update is warranted, the NCC should use information from two key sources.

First, the NCC should undertake searches for new evidence, using versions of the original search strategies modified to be precise rather than sensitive (see chapter 5). Examples of evidence that could potentially trigger an update include data from randomised control trials, new diagnostic tests, changes in

licensing or warnings issued by licensing agencies, and major changes in costs. The NCC should consider the quality of the new evidence, but it need not undertake a new systematic review.

Secondly, the NCC should seek the views of healthcare professionals and patients to identify any change in practice or additional relevant published evidence. One approach is to convene an expert advisory group of healthcare professionals and patient and carer organisations. The NCC should ask the group members to identify which of the recommendations in the clinical guideline require updating and to provide a brief explanation of the reasons for this. Members of the group should be asked to submit a list of any new key areas that should be considered. These could be, for example, new technologies, key areas not included in the original guideline because of a lack of evidence, or those suggested by changes in drug licensing. The expert advisory group should discuss the information submitted by members, together with the relevant new evidence identified in the NCC's literature search.

In addition, NICE reviews any information that is available on the implementation and uptake of the guideline recommendations.

14.2.1 Deciding on the update status of a clinical guideline

The CCP at NICE reviews the advice from the NCC about the need for an update of a guideline and the clinical relevance of the new evidence, and advises NICE's Guidance Executive on whether, in order to be brought up to date, the guideline requires:

- a full update (in exceptional circumstances)
- a partial update
- no update.

Two other options that can be suggested by CCP are:

- transferring the guideline to a 'static list'
- withdrawing the guideline.

Guidance Executive will decide which of these options is most appropriate. The decision should be based on predefined criteria, as listed in table 14.1.

The recommendations on updates then need to be set against the competing priorities of new guideline topics, and prioritised taking account of the capacity of the guidelines programme to schedule the work. This will be done with NCCs through the business planning process.

Table 14.1 Criteria for deciding the update status of a clinical guideline

Update decision	Criteria	Actions
Full update	• Major sections of the guideline need updating • Many of the recommendations are no longer necessary • New key areas have been identified	• Prepare a new scope • Consult on the scope
Partial update	• Some recommendations need updating in the light of new evidence, or because they are unclear • No new key areas have been identified that need to be covered in the guideline	• Use the original scope • Do not consult on the scope • Inform stakeholders
	• New key areas have been identified that need to be covered in the guideline	• Prepare a new scope • Consult on the scope
No update	• 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	• The guideline is not updated • The guideline is reviewed after a further 3 years to determine its update status
Transfer to the 'static list'	• The recommendations are unlikely to change in the foreseeable future	• No further update planned • May be reviewed if new evidence emerges
Withdraw the guideline	• The guideline no longer applies	• Consult with stakeholders

14.2.2 Conducting a full update

If a decision is made to conduct a full update of a clinical guideline, the NCC prepares a new scope, following the usual process described in chapter 2.

Recruitment of guideline development group (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; however, the composition of the GDG should be tailored to the requirements of 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 8-week consultation period (see chapter 11). The usual process for finalising and publishing the guideline is also followed (see chapter 12).

14.2.3 Conducting a partial update

If a clinical guideline is being partially updated, there are two possible scenarios:

- In the first scenario, some recommendations need updating but no new key areas have been identified. The original scope is used and NICE informs the stakeholders that it is conducting a partial update of the guideline.
- In the second scenario, new key areas have been identified that need to be included in the guideline. A new scope is prepared and consultation with stakeholders takes place through the usual process.

The NCC recruits a new GDG to undertake the work, using the usual recruitment process (see section 3.1). The NCC should inform members of the original GDG that this is happening; however, the composition of the new GDG should be tailored to the requirements of the section(s) to be updated. The time needed to undertake the update is agreed between NICE and the NCC, but will be no longer than 18 months.

14.2.4 No update

If a decision is made that a clinical guideline does not need updating, the guideline will be reviewed after a further 3 years, and the same process for deciding its update status will be followed.

14.2.5 The ‘static list’

There may be circumstances in which the topic covered in a published clinical guideline does 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 these cases, the guideline will be transferred to a ‘static list’ and no further update will be required. 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 published recommendations are required.

14.2.6 Withdrawing the guideline

It may be decided on reviewing the guideline that its recommendations no longer apply, but that it is not of sufficient priority for updating. In this case the guideline will be withdrawn. This decision will be consulted on with stakeholders.

14.3 Exceptional updates

Exceptionally, significant new evidence may emerge that necessitates a partial update of a clinical guideline before the usual 3-year period. This might be a single piece of evidence, an accumulation of relevant pieces of evidence or other published NICE guidance. This evidence must be sufficient to make it likely that one or more recommendations in the guideline will need updating in a way that will change practice significantly. Examples of such evidence include data from randomised controlled trials, new diagnostic tests, changes

in licensing 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 14.6)

14.3.1 Determining the need for an exceptional update

The 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 might affect the response to the new evidence?
- Which recommendations need to be reviewed in the light of the new evidence?

The Guidance Executive then decides on the need for an update based on the findings. If an exceptional update is necessary, the CCP commissions the relevant 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 a partial update (see section 14.2.3)

14.4 Format of draft updates for consultation

For partial updates and exceptional updates, the NCC should submit the draft revisions to the full guideline in a suitable format for consultation. This should present the evidence considered by the GDG and any new or revised health economic analyses, and should show which recommendations have been amended or deleted from the original guideline and which recommendations are new to the consultation draft; it should be clear from the draft which sections of the full guideline have been updated. This format is intended to aid clarity during consultation and is not carried through to the final published version of the updated guideline.

Agreement should be reached between NICE and the NCC as early as possible on the most appropriate format for an update.

14.5 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.

14.6 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.

14.6.1 Criteria for a correction

Corrections or changes to a published clinical guideline will be made if an error:

- may result in harm to patients
- undermines the conclusions on which the recommendations have been based
- indicates that NICE's quality-assurance procedures have been seriously compromised.

14.6.2 Process for issuing a correction

The CCP Director and the NCC consider the suspected error using the criteria above. Simple typographical errors that don't meet the above criteria may be rectified without seeking the view of Guidance Executive. If one of the criteria is satisfied, the suspected error is reported to NICE's Guidance Executive, which decides what action to take.

If the Guidance Executive considers that there is no error, this is communicated in writing by the CCP Director to the individual or organisation who first reported it, explaining the rationale for the decision.

If a correction is to be made, an error notification is put on front page of the guideline's entry 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. The web versions of the relevant documents are corrected, and this is also highlighted on the front page of the guideline's entry on the NICE website (www.nice.org.uk).

14.7 Further reading

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.

